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Series Editor: George Y. Wu

Subbaramiah Sridhar
George Y. Wu *Editors*

Diagnostic and Therapeutic Procedures in Gastroenterology

An Illustrated Guide

Second Edition

Humana Press

CLINICAL GASTROENTEROLOGY

Series Editor
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University of Connecticut Health Center
Farmington, CT, USA

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To my parents, Vasanthalakshmi and Subbaramiah, who molded my life; Professor Sir Ferguson Anderson (Glasgow, Scotland) and Professor Richard Hunt (McMaster University, Canada) who molded my career; my brother Nagesh and sister-in-law Jayashree, my sisters and brothers-in law Vani and Satish Murthy, Suma and Srinivas Chakragiri, and my wife Supriya Sridhar for their constant support and encouragement; and finally to all our gastroenterology fellows who are sharp thinkers and not mere scope pushers, for mind is a more powerful tool than endoscope (SS).

I would like to dedicate this book to Roy Lopata and his family whose generous endowment of the Herman Lopata Chair in Hepatitis Research and unflagging encouragement have enabled me to explore many areas of research with freedom and flexibility (GYW).

Foreword

I want to thank the editors for giving me an opportunity to write foreword for the second edition of the Diagnostic and Therapeutic Procedures in Gastroenterology.

The first edition released in 2011 met an unfulfilled need of explaining endoscopy through simple and easy to understand text and illustrations. The second edition builds and expands on the wide range of topics of the first edition, bringing it up-to-date with the current principles and practices in diagnostic and therapeutic endoscopy.

The editors, Drs Sridhar and Wu, are to be congratulated for including a comprehensive and exhaustive list of relevant topics written by well-known and respected international experts. Besides learning the standards of care in endoscopy from these experts, the readers will also benefit from their personal insight based on vast experience and passion for endoscopy.

These are very exciting times for endoscopy and continue to experience unprecedented growth around the world. It was in 2009 when we performed our first case of per oral myotomy (POEM) and now it has become the standard of care for achalasia, practiced around the world. New indications for the submucosal tunneling techniques continue to be added.

While POEM, ESD (endoscopic submucosal dissection), full thickness resection (EFTR) have invigorated the field of luminal endoscopy our ability to better view and carry out therapy in the bile duct using ultra-thin scopes with improved optics and lasers, EUS guided therapy to drain walled off pancreatic fluid collections have been exciting additions to our therapeutic armamentarium outside the lumen of the gastrointestinal tract. Recent advances in imaging such as Confocal endoscopy, and optical coherence tomography (OCT) have opened new vistas for early diagnosis of cancer and therapy.

I believe this book is an important step in enhancing our knowledge of endoscopy and would be of great help to practicing physicians (both gastroenterologists and general surgeons) and those in training, particularly the young endoscopists. Our nursing colleagues with interest in gastroenterology would also find this book useful both for daily practical needs, and as a reference guide.

As we learn from each other and develop and set new standards of care to benefit our patients I am reminded of a Japanese proverb “chisa wa madowazu, yusha wa osorenzu (**智者は惑わず、勇者は恐れず**)” which means, “A wise man does not lose his way, a brave man does not have fear” - be wise and be brave - explore and advance the field of endoscopy.

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Preface

This monograph was originally conceived and designed to address common questions often raised by internists, students, and trainees regarding details of gastrointestinal procedures. Because patients who undergo gastrointestinal procedures are frequently followed by their primary care providers and extenders, those providers need to be familiar with pre- and post-procedural issues in order to select optimal procedures and provide appropriate post-procedure follow-up. This need is not only still present but has intensified due to the remarkable advances in technology and techniques. In particular, GI procedures have become more invasive with greater emphasis on therapeutics than ever before. It is, therefore, fitting that this edition of *Diagnostic and Therapeutic Procedures in Gastroenterology: An Illustrated Guide, Second Edition* continues to focus on providing clear understanding of the concepts that underlie gastrointestinal procedures as it pertains to appropriate decision making for patients with diseases that require gastrointestinal procedures. This volume is a comprehensive textbook describing procedures for the gastrointestinal tract in a simple way, with artistic illustrations of equipment and techniques, and providing clear descriptions of the changes in the anatomy and physiology that result from various operations and procedures, as well as advice on medical management of post-procedure patients. In addition, the book provides information on practical matters such as establishing endoscopy units and maintenance of quality and efficiency of procedures. Finally, as the complexity of the field has grown, so too has the need to develop training and evaluation methods for future generations of endoscopists. The current volume provides information that will be useful for both trainers and trainees.

These are exciting times for endoscopy, and this book reflects the ingenuity and degree of technical skills that have been achieved. However, the real uniqueness of the book is in the interpretation and translation of these advances so that they can be understood and appreciated not only by proceduralists but all levels of health-care providers who care for patients with gastrointestinal disorders.

Augusta, GA, USA — Subbaramiah Sridhar
Farmington, CT, USA — George Y. Wu

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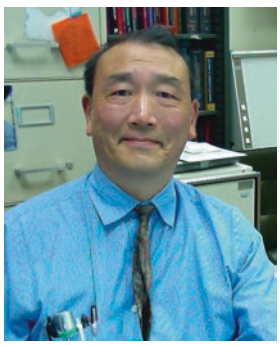

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Part I

Procedures and Devices

History of the Instruments and Techniques of Gastrointestinal Endoscopy

1

Charles Spurr Jr.

The instruments and technique of endoscopy have evolved steadily to the point where the basic instruments seem unchanged and many procedures have become "routine." It is therefore useful, on occasion, to briefly review "how we got here." Detailed historical accounts are available elsewhere. Timelines (Fig. 1.11) have been incorporated as an adjunct to the narrative overview presented here.

Visualization of the intestinal tract was attempted with limited success for many years before the modern era of endoscopy. Earliest endoscopic instruments date to crude specula found in the ashes of Pompeii (Fig. 1.1) [1]. Centuries passed without the development of effective instruments due to the many obstacles to visualization of the intestinal tract including darkness, depth, angulations, and intestinal contents. Modern endoscopy could not have been developed without the three major parallel inventions: (1) Edison's incandescent lamp, (2) fiber optics, and (3) charged couple device (CCD) [2]. The role of these inventions in the development of endoscopy to its current state is described.

Since endoscopy is not possible without adequate illumination, the early years have been described as the "dark age of endoscopy" – referring to the initial struggles encountered in attempting to achieve illumination of the intestinal tract [2]. Philipp Bozzini (1773–1809) is credited with the development of the first endoscope which he referred to as the Lichtleiter or "light conductor" – first described between 1803 and 1808. It combined a vase-shaped housing for his light source, a candle, mirrors, and a series of specula suitable for examination of the urethra, bladder, vagina, and rectum. This device actually never served as a practical instrument and failed due to design or construction flaws and the untimely death of Bozzini. Professional rivalries in Vienna were also said to aid the demise of the "Lichtleiter" [3, 4] (Fig. 1.2).

While the "Lichtleiter" was a practical failure, the basic design served as a template for future endoscopic instrument development. Adaptations of Bozzini's design appeared in cystoscopic instruments developed by Fisher (circa 1824) in the USA and by Segalas (1826) in Paris [3]. However, use of such instruments was very rare until 1855 when Antonin J Desormeaux introduced an improved form of the endoscope, intended for a variety of applications – mainly cystoscopy. His preparation of an associated text, De l'endoscopie, played an important role in popularizing endoscopy. Instead of a candle, the light source consisted of a lamp fueled by "gazogene" – a mixture of alcohol and turpentine. In the USA, few of the instruments were available until the 1870s [3, 5].

The rigid endoscope era is generally agreed to have begun when Adolf Kussmaul made his first successful attempts at gastroscopy in 1868 [3, 6]. His contribution is said to have been scarcely recognized at the time, and no description was actually published. A demonstration of his instrument and technique was made utilizing a cooperative sword swallower [3, 6] (Fig. 1.3). However, despite use of the illumination technique described earlier by Desormeaux, illumination was inadequate due to the weakness of the light and the presence of secretions within the stomach. These obstacles led to Kussmaul's abandonment of the procedure. A hiatus in the development of gastroscopy ensued – lasting about 10 years [3, 7]. The development of an esophagoscope and gastroscope by Johann von Mikulicz, a surgeon working with Vienna instrument maker Josef Leiter, began in 1880. The gastroscope was a failure despite a flexible hinged tip and the use of a complex lighting system consisting of a water cooled and an electrically heated platinum wire loop. However, a simpler rigid esophagoscope utilizing this same lighting system and simple optics allowed the visualization of the esophagus. Despite these advances, the esophagoscope had little utility until the invention of the incandescent

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Fig. 1.1 Crude speculum uncovered from the ashes of Pompeii (Courtesy of Historical Collections & Services, Claude Moore Health Sciences Library, University of Virginia)

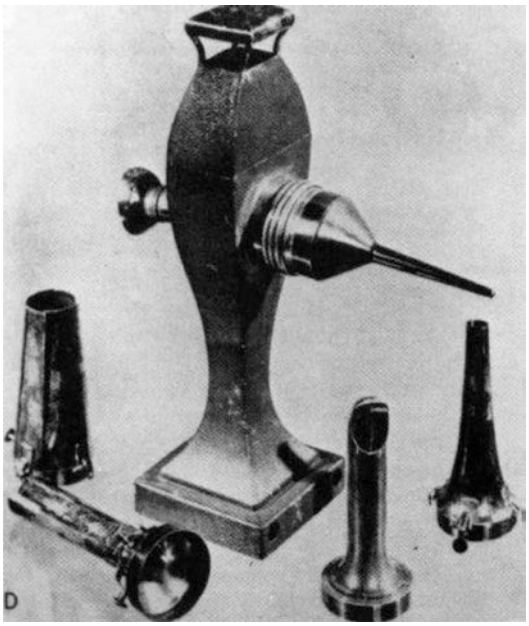

Fig. 1.2 Bozzini's Lichtleiter. First "endoscope" developed circa 1803. Failed due to design flaws and untimely death of the inventor who never lived to perfect his invention (Reprinted with permission Edmonson [3], Elsevier)

bulb by Thomas Edison in 1879. By 1886, the incorporation of a small or "mignon" incandescent bulb at the scope tip proved functional, making von Mikulicz's instrument the first fully functional esophagoscope [3, 8] (Fig. 1.4).

Over the next 50 years, the development of endoscopic instruments progressed along three lines. The principal scope types described during this period included (1) open tubes without lenses or with only proximal telescopes, similar to the rigid proctoscopes of recent past years; (2) flexible tube gastroscopes, to aid insertion only, which could be straightened following placement; and (3) rigid straight tubes with optical system inserts [3, 6]. Of these three groups, the rigid straight tubes with optical systems led in esophagoscope and gastroscope development until the close of the era in 1932. F. Rosenheim modified and experimented with this type of gastroscope in the late 1890s – initially on cadavers but eventually on live patients until he abandoned his efforts. Sadly, the instruments were generally unsafe and results highly operator dependent. Gastroscopy and esophagoscopy failed to proliferate. Procedural complications discouraged many pioneer endoscopists.

In 1911, Elsner reintroduced a modified version of a straight gastroscope, earlier abandoned by Rosenheim. The modification consisted of the addition of a rubber tip at the end of a straight tube – allowing for safer passage with few mishaps. This instrument would become "the first really usable straight gastroscope" and achieved a broader acceptance among endoscopy enthusiasts. Their success prompted the entry of Rudolf Schindler into the field of gastroscopy. Schindler felt strongly that visualization of the stomach would prove valuable in the diagnosis of a variety of upper abdominal complaints that he had encountered caring for German soldiers during World War I. Utilizing an Elsner scope that had "lain unused in the shop for 10 years" [3, 9], he encountered the deficiencies of the scope and by 1923 had introduced a modified scope which included an air outlet to clear the lens. Scope introduction utilized a rubber tip tube (obturator) which was removed following scope introduction and replaced with an inner cannula including optics and a light source. (Fig. 1.5) Using this instrument, Schindler was

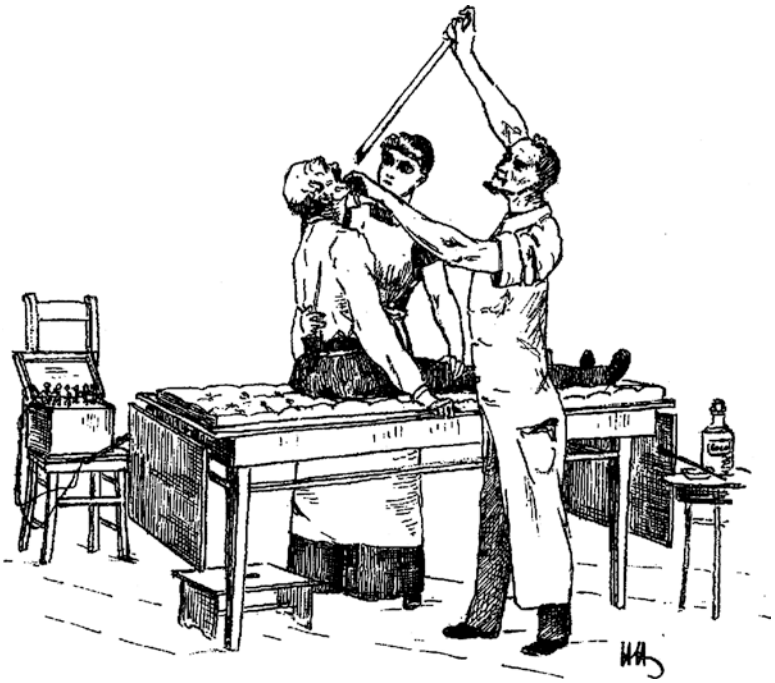

Fig. 1.3 Adolph Kussmaul demonstrates his rigid gastroscope in 1868. "Patient" was a professional sword swallower who was compensated for his services. No description of the technique or procedure was ever published (Reprinted with permission Edmonson [3], Elsevier)

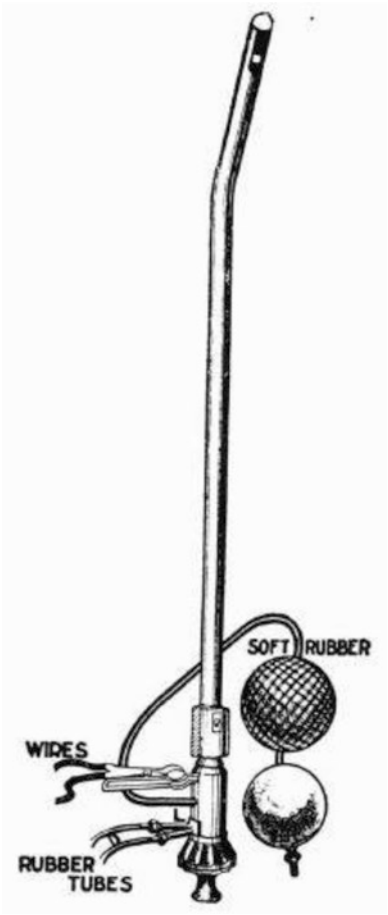

Fig. 1.4 Mikulicz-Leiter gastroscope – 1881. First truly functional gastroscope. Later versions incorporated "mignon" incandescent bulb (Reprinted with permission Edmonson [3], Elsevier)

able to perform more than 400 gastroscopies. Based on his extensive observational experience, Schindler published his *Lehrbuch und Atlas der Gastroskopie* – providing descriptions and pictures of a wide variety of gastric disorders [2, 10]. Acceptance by patients and fellow physicians led to the proliferation of the procedure. However, there were serious limitations to the examination of the stomach using this instrument. Inspection of the stomach was possible in less than 60% of patients. Over the next 10 years, Schindler collaborated with instrument maker Wolf in efforts to overcome these limitations – resulting in the production of a semiflexible gastroscope in 1932. The design depended on a series of short-focus lenses to allow angulation to 34° in several planes while retaining an adequate image. Flexibility was achieved by housing the lenses in a coil of bronze wire, protected by a rubber outer cover [3, 10] (Fig. 1.6). Schindler's semiflexible gastroscope rapidly gained popularity as it provided significantly more information about the stomach at a lower risk than with the rigid scopes. In America, successful trials of the instrument at Massachusetts General Hospital and Johns Hopkins led to acceptance of the technology. Benedict and colleagues at MGH performed over 75 gastroscopic examinations by 1933. They concluded that "the greatest field of usefulness for the gastroscope is probably in gastritis, but it is also useful as an adjunct to the x-ray in gastric ulcer and the various benign and malignant tumors of the stomach" [3, 11].

Schindler's initial success in Germany was short lived. By 1934, he had been seized in a Nazi purge of citizens of Jewish descent and placed in "protective custody." He remained imprisoned for 6 months until he and his wife were able to

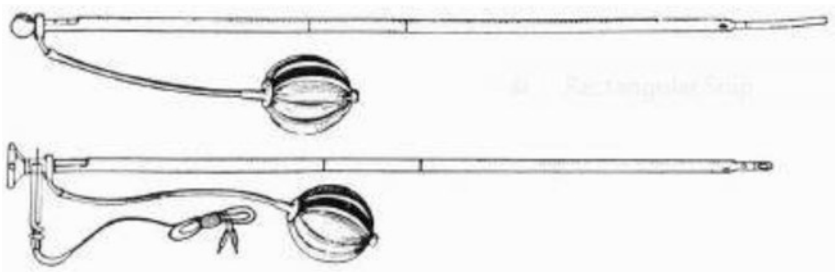

Fig. 1.5 Schindler's modification of earlier rigid scope design 1922. Note the rubber obturator on top panel. Optics inserted following introduction – bottom panel (Reprinted with permission Edmonson [3], Elsevier)

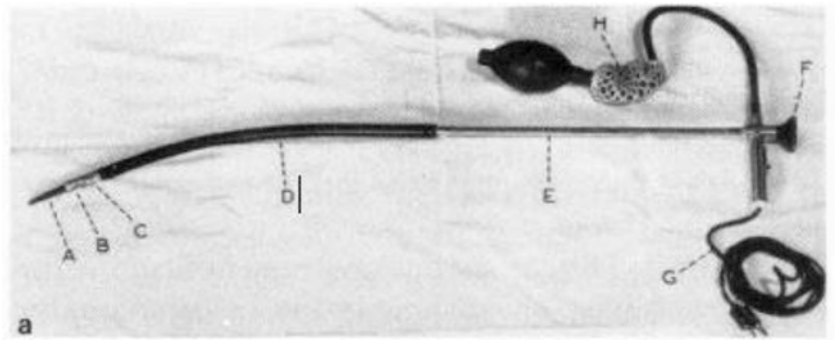

Fig. 1.6 Rudolph Schindler develops semiflexible scope 1932. Multiple lens elements allowed 32° tip deflection (Reprinted with permission Edmonson [3], Elsevier)

broker refuge in the USA. Upon his release, Schindler and his family settled in Chicago under sponsorship of Marie Ortmayer and Walter Palmer of the University of Chicago. In this more welcoming environment, he found support of his efforts to promote gastroscopy – making the city a center for the small circle of physicians practicing gastroscopy over the next decade.

By 1943, Schindler left Chicago for California where his academic career continued at Loma Linda. The "Schindler Era" of endoscopy continued to 1957. During this time, Schindler is credited with the establishment of the "American Gastroscopic Club" (1941) [2, 12], the forerunner of the ASGE. Instrument production shifted abruptly away from Germany and several American manufacturers entered the market – including the Cameron's Surgical Specialty Co., Eder Instrument Company, Metro Tec, and American Cystoscope Manufacturers, Inc. (ACMI). The Cameron-Schindler flexible gastroscope (1940) was the first commercially produced gastroscope in the USA. A successor to this instrument, the Cameron omniangle flexible gastroscope (1943) soon became the standard instrument for gastrointestinal endoscopy [3, 13]. A major contributor to instrument design at Cameron was Louis Streifeneder. Following World War II, he departed Cameron to form the Eder Instrument Co. In collaboration with Schindler and notable American endoscopists, he produced the Eder semiflexible gastroscope model 105 which was "lighter, more flexible, smaller in diameter and overall provided a better image" than the earlier Schindler models [3, 14]. Further refinements led to the production of a controllable gastroscope tip, facilitating a more complete view of the stomach (modified Hermon Taylor gastroscope) in 1949 [3, 15]. Introduction of an operating gastroscope (Benedict 1948) which incorporated a biopsy forceps and suction tube made endoscopic biopsy tenable. American Cystoscope Manufacturers, Inc. (ACMI) entered the American market with a semiflexible gastroscope around the same time period – followed by esophagoscope and operating or biopsy gastroscopes. However, gastroscopy remained a relative infrequent procedure performed by only a handful of gastroenterologists. Note that our discussion has centered around "gastroscopy" since it wasn't until the late 1940s that esophagoscopy was practiced by many gastroenterologists – with the esophagus commonly being considered the territory of the otolaryngologist. However, by the late 1940s the semiflexible or obturator-introduced instruments lessened the risk of posterior pharyngeal laceration leading to a wider practice of esophagoscopy by GI endoscopists. While Schindler also played a major role in shaping the course of esophagoscopy, the Eder-Hufford esophagoscope became the standard esophagoscope following introduction in 1949. The addition of a telescopic eyepiece with 4× magnification proved helpful, and esophagoscopy progressively became a part of gastrointestinal endoscopy. By 1954, Hufford became the leading proponent of "integrative endoscopy" – utilizing the rigid esophagoscope as an introducer for a smaller semiflexible gastroscope in order to combine the two examinations, esophagogastroscopy [3, 16] (Fig. 1.7).

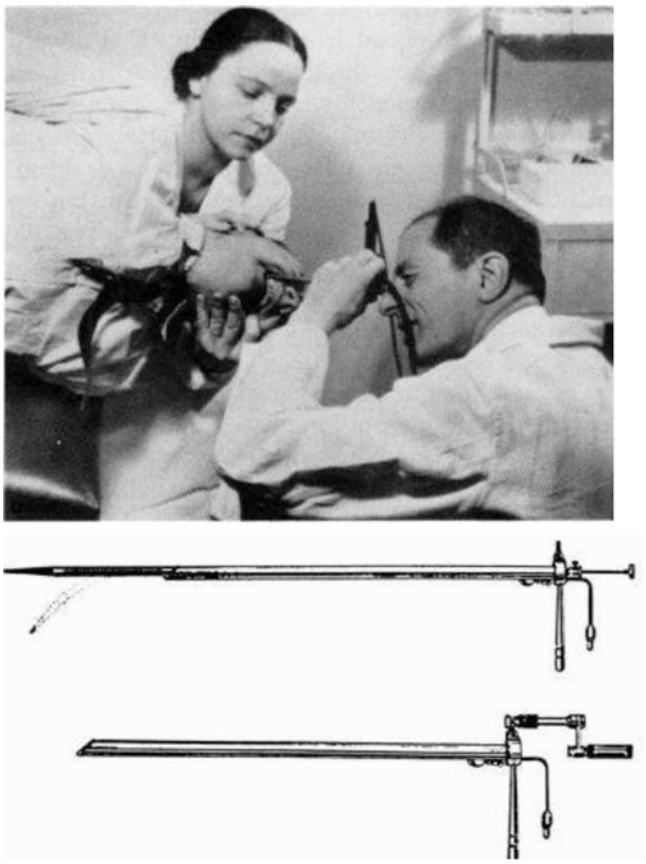

Fig. 1.7 Eder-Hufford esophagoscope 1949. Scope was representative of American rigid scopes in years prior to introduction of flexible scopes (Reprinted with permission Edmonson [3], Elsevier)

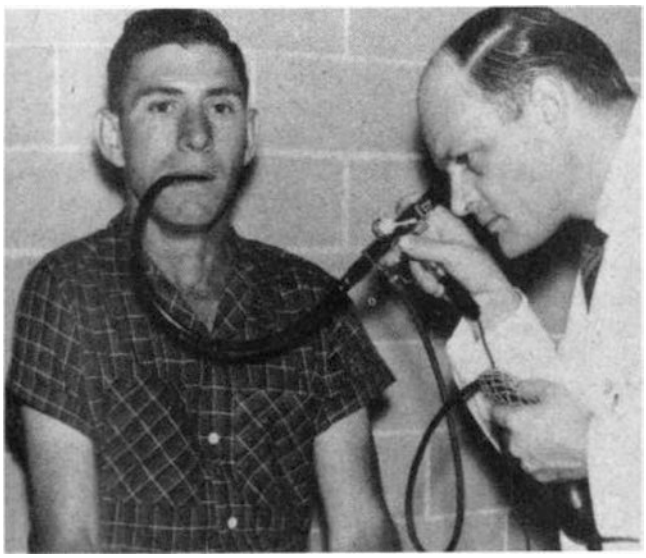

Fig. 1.8 Basil Hirschowitz – 1961. Inventor of flexible fiber-optic gastroscope demonstrates instrument on surprised patient. Hirschowitz scoped himself with instrument prior to use on patients (Reprinted with permission. Hirschowitz review article UAB Medical Center (placeholder language, real permission citation needed))

Documentation of gastric lesions could not be made photographically because of the low luminosity of the light bulbs and the large loss of light across multiple lens interfaces. Endoscopic photography first became clinically feasible in 1948 with the introduction of an apparatus for taking color transparencies through a semiflexible gastroscope [17]. In 1950, Uji, Sugiura, and Fukami working with the Olympus Corporation had developed a gastrocamera which achieved widespread use in Japan. The instrument was a miniature intragastric camera only but featured a synchronized flash and controllable tip, producing high-quality images – even by current standards [18]. The instrument was little used in the USA and was eventually overtaken by the introduction of fiber-optic instruments.

Fiber-optic endoscopy began in 1957 when gastroenterologist Basil Hirschowitz passed a prototype instrument down his own throat – followed a few days later down that of a patient. The development of a "fiberscope" began in 1954 after articles published in *Nature* by Hopkins and Kapany reported construction of a bundle of oriented glass fibers that could transmit an image along a nonlinear path [2, 19] (Fig. 1.8). In addition, Van Heel had described the need to insulate fibers from each other to provide a better image [2, 20]. Hirschowitz found that the laboratory models were only a few inches long and didn't transmit enough light to function in an endoscope. Over the next 2 years, Hirschowitz collaborated with physicists Wilbur Peters and Lawrence Curtiss at the University of Michigan. Critical to the success of the project was the invention and development of a permanent insulated glass-coated optical glass fiber by Curtiss in December 1956 – leading to the construction of a coherent bundle of coated glass fibers. This fiber bundle was then incorporated into the first fiber-optic gastroscope. In May of 1957, the invention of the fiberscope was first demonstrated as an "add-on" presentation to the American Gastroscopic Annual Meeting. Hirschowitz touted advantages over conventional scope to be (1) complete flexibility which made the instrument safer to operate and easier for the patient to tolerate; (2) better light transmission, most helpful for photography; and (3) a greater range of viewing which was said to include the duodenum [2, 12]. Initially, there was little interest among manufacturers to produce the scope – especially given their entrenched interests in their older optic technology. However, ACMI took the project and, in late 1960, released the first production model – the ACMI 4990 gastroscope. While Hirschowitz proclaimed that "the conventional gastroscope has become obsolete on all counts" [3, 21], there was skepticism within the still relatively small community of endoscopists. Many endoscopists of that time were trained to use the forward-viewing Eder-Hufford scope to inspect both the esophagus and stomach. Limitations of the initial fiberscope design included side-viewing optics which

prevented effective esophagoscopy and direct visualization during scope insertion. Furthermore, the illuminating bulb was hot, leading to the risk of thermal burns to the mucosa in addition to coagulation of secretions obscuring visualization [22]. By 1963, Hirschowitz reported a fiberscope evolved to include a controllable tip, forward-viewing optics, channels for insufflation, and aspiration and passage of accessories – including biopsy forceps. A second fiber-optic bundle was added to carry "cold light" from an external light source. By 1970, a "panendoscope" to allow visualization of the esophagus, stomach, and duodenum was introduced. Clearly, fiber-optic instruments had almost completely replaced the older lens-optic instruments as predicted 10 years earlier. Competition between Japanese and American manufacturers accelerated, and with an increasing market for endoscopic instruments, innovation flourished, leading to many additional variations of the fiberscope. By the early 1970s, one author lamented that "one could hardly purchase a new instrument and become acquainted with its use before that instrument was rendered obsolete by a new model" [3, 23].

Despite a proliferation of instruments to evaluate the esophagus and stomach, the examination of the colon remained little changed since the introduction of the rigid sigmoidoscopy by Howard A. Kelly of Johns Hopkins in 1894 [24]. With improvements in illumination design, this instrument was capable of visualizing the distal 25 cm of the colon. While the rigid scope was functional, deeper visualization was often necessary. Initial attempts to adapt the fiber-optic panendoscope to colonic examination were met with limited success. After 1960, physicians in both Japan and the USA became actively engaged in developing instruments to visualize the colon. American gastroenterologist Bergein Overholt, in conjunction with the Eder Instrument Co., developed a flexible fiber-optic sigmoidoscope and in 1967 reported a series of 40 patients at the ASGE meeting [25]. By 1969, he also reported a favorable experience with the Olympus colonoscope. The release of a longer Olympus scope in 1970 incorporated for the first time in any fiber-optic scope a four-way tip deflection. Wolf and Shinya reported a favorable series of 241 "colonofiberoscopy" examinations encountering no complications [26]. Their findings were confirmed by others. From 1975 to 1979, there were three published studies documenting nearly 75,000 cases. In 1971, William I. Wolff and Hiromi Shinya began performing colonic polyp removal with a wire snare placed through the biopsy channel of the colonoscope. By 1973, they reported a series of 303 polypectomies with few complications – bleeding in five patients – and no mortality [27].

With the availability of ever-improving fiber-optic instruments utilized by increasingly skilled endoscopists, innovation flourished. In 1968, McCune reported endoscopic cannulation of the ampulla of Vater with inadequate instrumentation [28]. Efforts to develop longer, side-viewing instruments were led by collaboration between instrument manufacturers Machida and Olympus with several groups of Japanese endoscopists. Direct observation of the papilla of Vater was described by Itari Oi and associates the following year [29]. Within a short time period, "Retrograde pancreatography and cholangiography by fiber-duodenoscope" Takagi et al. [30] and "pancreatocholedochography" Ogoshi et al. [31] were reported. Within the next 2 years, Classen [32] from Germany and Vennes [33] from the USA reported successful procedures. The endoscopes developed were capable of four-way tip control and a lever to assist cannulation – modifications necessary to produce a functional instrument. While initially developed as a diagnostic tool, with further evolution ERCP incrementally developed to play a major therapeutic role in the treatment of biliary tract disease. The addition of sphincterotomy by 1974 [34] and biliary stents [35] within another 5 years proved to be a valuable therapeutic adjunct – enhanced even further because it allowed the passage of a variety of tools (stents, balloons, lithotripters) commonly in use today. Biliary obstruction and cholangitis, which once required surgical intervention, could now be treated by a skilled endoscopist in the majority of cases.

During this same time era, advances in diagnostic imaging were occurring at a rapid pace. With modalities such as the CT scanner and external ultrasound, diagnostic capabilities expanded greatly. Endoscopy was at this time limited to luminal visualization only – while the mucosal surfaces of the gut could be visualized, submucosal and immediately adjacent structures could only be visualized by external imaging. In yet another adaptation of existing technology, ultrasonic probes were developed for use through the biopsy channel of standard endoscopes. By 1976, Lutz and Rosch reported from Germany the use of a 4 MHz Siemens ultrasonic probe – passed through the biopsy channel of an existing Olympus endoscope. In their study, the ability to differentiate pancreatic cysts from tumor was demonstrated in two patients [36]. By 1980, an ultrasonic probe with fixed-frequency transducer was incorporated into the tip of conventional fiberscope; studies in both the USA (DiMagno) [37] and Germany demonstrated the probes to have good resolution with an acoustic focus depth of up to 3 cm. Sivak and George reported their preliminary experience with EUS in 1983 [38], and by 1985 ultrasonic transducers with variable frequencies were incorporated into video scopes which were available by that time. The ability of this modality to evaluate known or suspected intramural lesions of the gut was established. With further experience and instrument refinements, indications for use expanded to the esophagus, diagnosis and staging of neoplasms (especially pancreatic and bile ducts), and study of portal hypertension, colon, and

rectum. By 1991, Wiersema et al. demonstrated the ability to perform fine needle aspiration of nodes and lesions for the diagnosis of neoplasms of the mediastinum and upper and lower gastrointestinal tract [39, 40]. The addition of Doppler technology has made the demonstration of vascular flow a valuable adjunct to the safety of tissue sampling and diagnostic accuracy. Endoscopic ultrasound was incorporated into advanced endoscopic training. Technically, the procedure remains challenging, and skill is not readily acquired as a simple adjunct to standard endoscopic skills.

The development of a charged couple device (CCD) occurred in the late 1960s. With this "electronic eye," images could be transmitted to a remote television monitor – already in widespread use. With miniaturization, the CCD was eventually applied to a colonoscope by Welch-Allyn in 1983, and by the following year, Sivak and Fleisher reported a favorable preliminary experience [41]. The image quality was felt to be comparable to that seen with fiber-optic instruments. Photographic documentation could be achieved by using a "freeze frame" feature to allow instant photographs of the video image. Competition from the Japanese manufacturers soon followed with the introduction of superior instruments by Fujinon and Olympus. Olympus was initially slow to market the new technology due to the superiority of their fiber-optic instruments at that time. However, by the mid-1980s, it had become apparent that video endoscopy was another major innovation. This prompted yet another round of rapidly improving technology. The 30 years since that time have seen progressive improvements in the quality of the image, development of lightweight flat-panel HD monitors, and the ability to produce immediate digital image and video documentation of endoscopic findings. Procedure reporting has become integrated with photo documentation and the ability to communicate directly with the electronic medical record and referring providers.

With the widespread use of endoscopy, visualization of the esophagus, stomach, duodenum, colon, and terminal ileum was commonplace. However, luminal visualization of the small intestine was limited to barium contrast studies. Endoscopic visualization of the small bowel required intraoperative enteroscopy – obviously an invasive procedure. By the mid-1980s, the sonde enteroscope was developed. This thin and very flexible balloon-tipped instrument was inserted orally and then passed through the small intestine by peristalsis only. The diagnostic examination began on scope withdrawal and allowed inspection of 50–70% of the small bowel. Unfortunately, the scope characteristics didn't allow for any therapeutic interventions [42]. By 2001, Yamamoto described "total enteroscopy with a non-surgical steerable double-balloon method" [43](Fig. 1.9). Over the next 5 years, the instrumentation and technique

Fig. 1.9 Double-balloon small bowel scope

were refined – allowing inspection of most of the small bowel utilizing combined peroral and retrograde approach. In 2007, single-balloon enteroscopy became available. Both techniques employ the use of an overtube to facilitate insertion by "pleating" the small bowel over the overtube through a series of balloon inflations and reduction maneuvers – resulting in a pleating of the small bowel like a curtain over a rod. More recently, a rotating overtube incorporating a soft-raised helix (Spirus) at the distal end has allowed for a more rapid inspection of the small intestine, utilizing standard small bowel scope [44]. Actual diagnostic yield and total procedure time appear similar to single-balloon technique [45]. Despite improvement in technique, visualization of the entire small bowel is not routinely accomplished in a single procedure. Both peroral and retrograde balloon enteroscopy may be needed for more complete visualization.

While enteroscopy allows for biopsy and therapy of small bowel abnormalities, visualization of the entire small intestine is unusual; the procedure is technically demanding and poses some risks – especially in fragile patients.*In 2001, the FDA approved use of a capsule device for imaging of the small intestine. Images are transmitted wirelessly from the capsule to a data recorder worn by the patient. The instrument consists of an 11 × 26 mm disposable plastic capsule housing a CMOS or CCD image capture system, a lens, an LED light source, and an internal battery. Data is transmitted by ultrahigh-frequency band radio telemetry (given PillCam and Olympus EndoCapsule) or "human

Fig. 1.10 Wireless capsule endoscopy permits routine visualization of the entire small intestine

body communications" (MiroCam). Currently, four different small bowel capsules are approved for use in the USA. Using these devices, visual inspection of the entire small intestine has become an integral part of evaluation for occult gastrointestinal bleeding [46] (Fig. 1.10). Modifications of this design have led to the development of capsules for visualization of the esophagus, and more recently, in 2014 the PillCam COLON was released. While inferior to direct colonoscopy, the device holds promise for evaluation of patients having prior incomplete colonoscopy exams and in patients in whom colonoscopy may be problematic [47]. Since the initial release of the small bowel capsule, modifications including the SmartPill to evaluate intestinal motility and transit times and the Bravo capsule to evaluate reflux have been developed.

Some therapeutic innovations of endoscopy are outgrowths of procedures from the past. Sclerosis of esophageal varices was first described in the otolaryngology literature in 1939 [48]. While use of the procedure was uncommon, variceal injections were performed through the rigid esophagoscope prior to the fiber-optic era [49]. Variceal banding as described by Van Stiegman in 1986 represents a further evolutionary step [50]. However, the technique of hemorrhoidal banding was described in 1958 and reported by Barron in 1963 – using a technique remarkably similar in principle to variceal band ligation of today [51]. Hemostasis with metallic clips was a common open surgical technique prior to the introduction of the earliest precursor of endoscopic hemostatic clips in 1975 [52] – a process which required several revisions over many years before the technique became a standard practice. Thermal and electrosurgical endoscopic therapies overlap with established surgical instrumentation. While the endoscopic placement of gastrostomy tubes has become a common adjunct to upper endoscopy, the gastrostomy procedure was a surgical option for many years prior to Gauderer and Ponsky's description of the technique of percutaneous endoscopic gastrostomy in 1980 [53]. Endoscopy is a useful adjunct to RFA treatment of Barrett's esophagus. Efforts at endoscopic treatment of GERD have met with varying success and at the present time are not reimbursed by most insurance carriers (Fig. 1.11).

Since the 1990s, the technology of endoscopic instruments has "matured" and may appear that progress is slowing. Endoscopic instruments have improved incrementally, but the trainee of today would likely find that the use of a scope from 1985 was operationally little different from instruments today. While change in the field of therapeutic endoscopy is inevitable, new opportunities will emerge. The era of screening colonoscopy as a mainstay in gastroenterology has likely peaked. The future may hold advances in capsule endoscopy which supplant many of the current intraluminal screening and diagnostic procedures. Common surgical procedures may become endoscopic procedures as endoscopic techniques for cutting and apposition improve. With the prevalence of reflux and obesity, endoscopic therapy will hopefully be able to target these areas. Will an endoscopic method of anti-reflux surgery become standard of care? What role will endoscopy play in the metabolic management of obesity? Will third-space endoscopy and the use of the POEM for achalasia continue to show promise? Will the third-space allow for endoscopic treatment and diagnosis of motility disorders? Will the implantation of targeted drug delivery systems evolve? Obviously, safety, efficacy, and patterns of reimbursement to providers will play a role in determining the answer to the above questions.

"Inventing the future does not simply require technological innovation but is a complex intellectual exercise that begins with the identification of true unmet needs and profound insight into disease mechanisms." Pasricha in describing "Endoscopy 20 years into the future" suggests that it may be necessary for gastroenterology to revert to its cognitive roots and start thinking about the endoscope as one of many tools it can use to solve the problems that our patients face" [54].

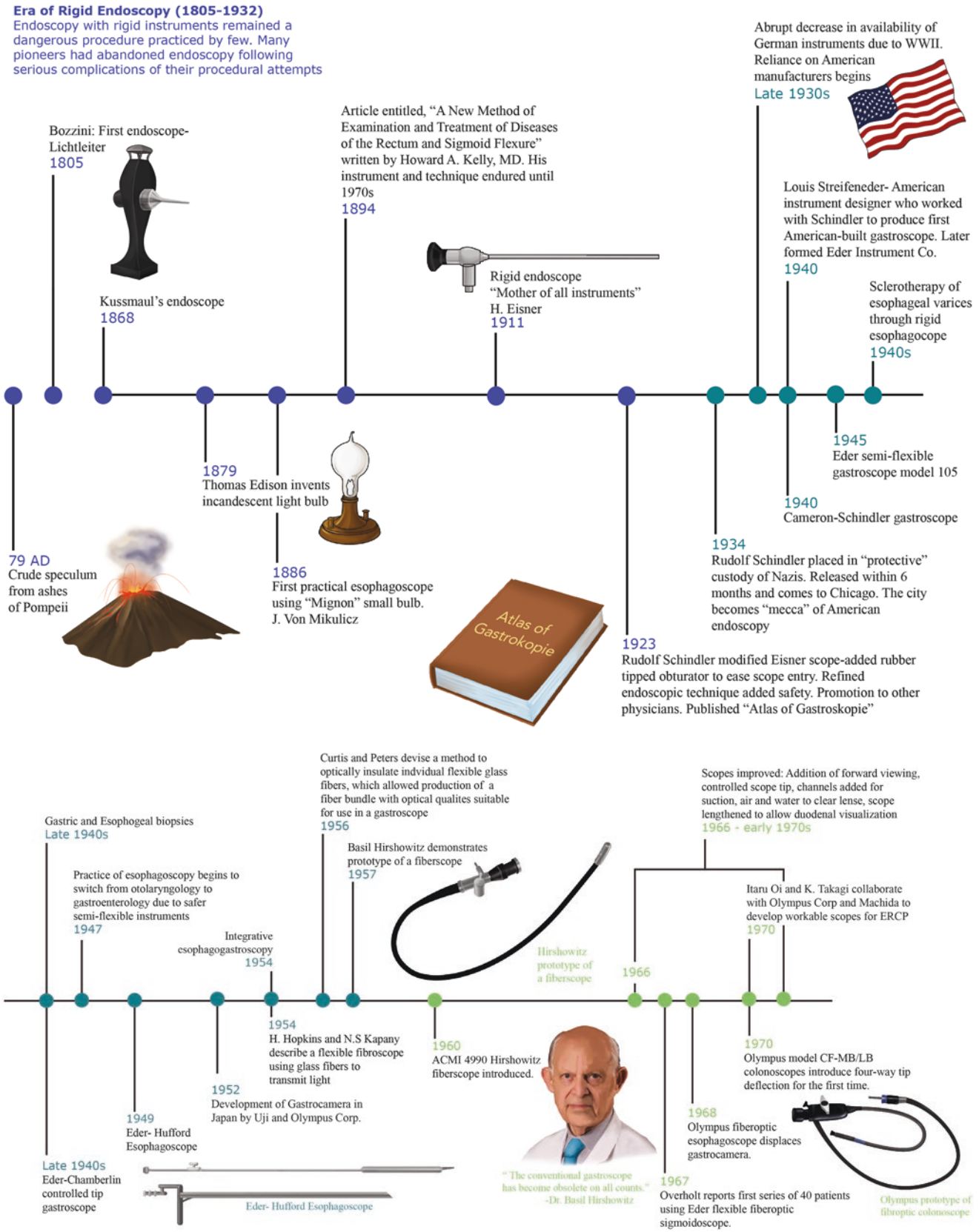

Fig. 1.11 Endoscopic Instrument Development Timelines Timeline of Endoscopic Instrument Development (Medical Illustrators: Minz Joseph MSMI, Taylor Simpson MSMI, Amanda Camp MSMI)

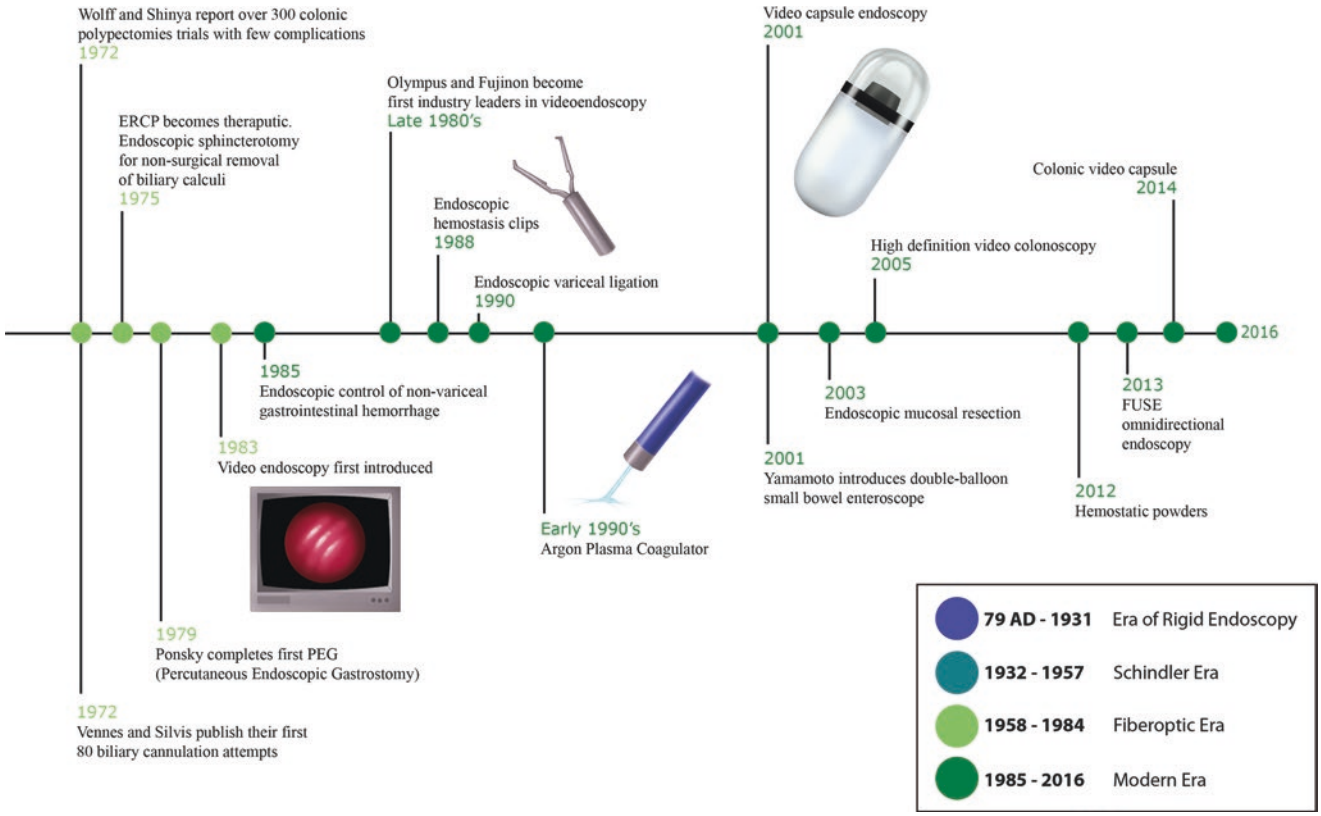

Fig. 1.11 (continued)

References

1. Sean N. Pompeian surgery and surgical instruments: The Medical News; 1895.
2. Hirschowitz B I., Development and Application of Endoscopy, Gastroenterology 1993, Feb;104(2):337–342.
3. Edmonson JM. History of the instruments for gastrointestinal endoscopy. Gastrointest Endosc. 1991;37(2):S27–56.
4. Rathert WL, Lutzmeyer W, Goddwin WE. Philip Bozzini (1793-1809) and the Lichtleiter. Urology. 1974;3:113–8.
5. Desormeaux(by translation). The endoscope and its application to the diagnosis and treatment of urinary afflictions- Lessons given at Necker Hospital. Chicago Medical Journal. 1867;24:184.
6. Walk L. The History of Gastroscopy. Clio Medica. 1966;1:209–22.
7. Bevan JA. Oesophagoscope. Lancet I. 1868;91:470–1.
8. Newell OK. The endoscopic instruments of Joseph Leiter of Vienna and the present development of endoscopy. Boston Med Surg J. 1887;117:528–30.
9. Schindler R. Gastroscopy:9.
10. Schindler R. Gastroscopy. The endoscopic study of gastric pathology. 2nd ed. Chicago: University of Chicago; 1950.
11. Benedict EB. Examination of the stomach by means of a flexible gastroscope: a preliminary report. NEJM. 1934;210:669.
12. Gerstner P. American Society of Gastrointestinal Endoscopy: a history. Gastrointest Endosc. 1991;37:S1–S26.
13. Haubrich WS. History of endoscopy. In: Sivak Jr MV, editor. Gastrointestinal endoscopy; 1987. p. 6.
14. Ray Hufford A. A new light weight, extra flexible gastroscope. Rev Gastroenterol. 1946;13:381.
15. Donald T. Chamberlain. Description of a new gastroscope. Gastroenterology. 1949;12:209–11.
16. Ray Hufford A. Integrative esophagogastroscopy. Am J Gastroenterol. 1954;22:116–25.
17. Segal HL, Watson JS. Color photography through the flexible gastroscope. Gastroenterology. 1948;10:575–85.
18. The History of Endoscopy and Olympus.
19. Hopkins HH, Kapany NS. A flexible fiberscope using static scanning. Nature. 1954;173:39–41.
20. Van Heel ACS. A new method of transporting optical images without aberrations. Nature. 1954;173:39.
21. Hirschowitz B. Endoscopic examination of the stomach and duodenal cap with the fiberscope. Lancet. 1961;277:1074–8.
22. Achord JL. The history of gastrointestinal endoscopy in Ginsberg. In: Gregory G, et al., editors. Clinical Gastrointestinal Endoscopy. p. 6.
23. Haubrich WS. Sivak Jr MV, editor. Gastrointestinal Endoscopy. p. 13.
24. Kelly HA. A new method of examination and treatment of diseases of the rectum and sigmoid flexure. Ann Surg. 1895;21:468–78.
25. Overholt BF. Flexible fiberoptic sigmoidoscopes. CA. 1969;19:80–4.
26. Wolff WI, Shinya H. Colonofiberoscopy. JAMA. 1971;217:1509–12.
27. Wolff WI, Shinya H. Polypectomy via the fiberoptic colonoscope: removal of neoplasms beyond the reach of the sigmoidoscope. N Engl J Med. 1973;288:329–32.
28. McCune WS, Shorb PE, Moscovitz H. Endoscopic cannulation of the ampulla of Vater: a preliminary report. Ann Surg. 1968;167:752–6.
29. Oi I, Takemoto T, Kendo T. Fiber duodenoscope, Direct observation of the papilla of water: A preliminary report. Endoscopy. 1970;3:101–3.

30. Takagi K, Ikeda S, Nakagawa Y, et al. Retrograde pancreatography and cholangiography by fiber duodenoscope. Gastroenterology. 1970;59:445–52.
31. Ogoshi K, Tobita Y, Hara Y. Endoscopic observation of the duodenum and pancreatocholedochography using duodenofiberscope under direct vision. Gastrointest Endosc. 1970;12:83–96.
32. Classen M, Koch H, Fruhmorgen P, et al. Results of retrograde pancreaticography. Acta Gastroenterol Jpn. 1972;7:131–6.
33. Vennes JA, Silvis SE. Endoscopic visualization of bile and pancreatic ducts. Gastrointest Endosc. 1972;18:149–52.
34. Kawai K, Akasaka Y, Murakami K, Tada M, et al. Endoscopic sphincterotomy of the ampulla of Vater. Gastrointest Endosc. 1974;20:148–51.
35. Soehendra N, Reijinders-Frederix V. Palliative bile duct drainage. A new endoscopic method of introducing a transpapillary drain. Endoscopy. 1980;12:8–11.
36. Lutz H, Rosch W. Transgastroscopic ultrasonography. Endoscopy. 1976;8:203–5.
37. DiMagno EP, Buxton JL, Regan PT, et al. Ultrasonic Endoscope. Lancet. 1980;1:629–31.
38. Sivak MV, George C. Endoscopic ultrasonography: preliminary experience. Gastrointest Endosc. 1983;29:187A.
39. Wiersema MJ, Hawes RH, Wiersema LM, et al. EUS as an adjunct to fine needle aspirate cytology of the upper and lower gastrointestinal tracts. Gastrointest Endosc. 1992;38:35–9.
40. Rex RK, Tarver RD, Wiersema M, et al. Endoscopic transesophageal fine needle aspirate of mediastinal masses. Gastrointest Endosc. 1991;37:465–8.
41. Sivak MV, Fleischer DE. Gastrointestinal. Endoscopy. 1984;30:1–5.
42. Tada M, Kawai K. Small bowel endoscopy. Scand J Gastroenterol. 1984;19:39–52.
43. Yamamoto H, Sekine Y, Saito Y. Total enteroscopy with a non-surgical steerable double-balloon method. Gastrointest Endosc. 2001;53:216–20.
44. Akerman PA, Agrawal D, Cantero D, Pangtay J. Spiral enteroscopy with the new DSB overture: a novel technique for deep perusal small-bowel intubation. Endoscopy. 2008;40:974.
45. Khashab MA, Lennon AM, Kalloo AN, et al. Gastrointestinal Endoscopy. 2010;72(4):766. Spiral vs single balloon endoscopy
46. Wireless capsule endoscopy. Technology status evaluation report. Gastrointest Endosc. 2013;78(6):805–15.
47. Capsule endoscopy of the colon. Report on emerging technology. Gastrointest Endosc. 2008;68(4):621–3.
48. Crafoord C. Surgical treatment of varicose veins of the esophagus. Acta Otolaryngol Stockh. 1939;27:422–9.
49. Patterson C, Rouse M. The injection treatment of esophageal varices. JAMA. 1946;130(7):384–6.
50. Van Stiegman NG, Cambre T, Sun JH. A new endoscopic elastic band ligating device. Gastrointest Endosc. 1986;32:230.
51. Barron J. Office ligation of hemorrhoids. Am J Surg. 1963; 195:563.
52. Hayashi T, Yonezawa M, Kawabara T. The study on staunch clip for treatment by endoscopy. Endoscopy. 1975;17:92.
53. Gauderer MW, Ponsky JL, Kzant RJ. Gastrostomy without laparotomy: a percutaneous endoscopic technique. J Pediatr Surg. 1980;15(6):872–5.
54. Pasricha PJ. Endoscopy 20 years into the future. Clin Gastroenterol Hepatol. 2013;11:119–22.

Recent Advances in Gastrointestinal Endoscopy

2

John Affronti and Andrew Lake

Responsive Insertion Technology

One manufacturer, Olympus Corp., has recently introduced what is called responsive insertion technology into their EVIS EXERA III 190 series of colonoscopies [1]. This is a combination of three proprietary technologies: variable stiffness, passive bending, and high force transmission.

Variable Stiffness

Variable stiffness functionality has been available for a number of years. Turning the handle of a colonoscope with this feature will allow manipulation of the stiffness in the colonoscope shaft (Fig. 2.1).

The mechanism of adjustable shaft stiffness is similar to that used in commercially available "through the channel" stiffening wires. These have a central cable with a surrounding metal helical coil. Tension applied to the cable compresses and stiffens the helix and colonoscope, whereas loosening has the opposite effect resulting in more flexible characteristics. The stiffening mechanism terminates 30 cm from the instrument tip so that the distal portion remains relatively floppy [2].

Some studies conclude that the variable stiffness feature by itself significantly reduces intubation time and patient discomfort [2, 3]; others do not show an advantage [4], but this may be due to the patient population studied and/or experience of the endoscopists. Moreover, when this variable stiffness component is combined with the other features described below, it appears to be advantageous [1, 5, 6].

Passive Bending

Passive bending is located in proximity to the bending section located at the distal end of the endoscope [1] (Fig. 2.2).

The passive bending portion basically has the same structure as that of the bending section, but unlike the bending section that bends through controlling it with the angulations' control knob, it will quickly bend when subject to external forces. It is characterized by a structure in which the curvature gradually increases from the bending section to the insertion tube [1] (Fig. 2.3).

(Have artist redo)

In a colonoscope equipped with a passive bending portion, the force applied by the physician will bend the passive bending portion in response to the reactive force from the colon. This will distribute the force with which the insertion tube is pushed so that the force that pushes the scope tip forward will be greater than that which pushes up the wall of the colon. That is, the force applied by the physician is physically transferred at the passive bending portion, pushing the scope tip forward [1] (Fig. 2.4).

High Force Transmission

The colonoscope insertion tube essentially has a three-layer structure consisting of a metal flex tube (the innermost layer), a mesh tube, and a polymer resin (the outermost layer). In colonoscopes with high force transmission, the characteristics of theses layers are modified so that the proximal control forces – "push," "twist," and "pull"– applied by the physician may be efficiently transmitted to the distal end of the colonoscope. This enables a fine manipulation at the proximal control section to be precisely transmitted to the insertion

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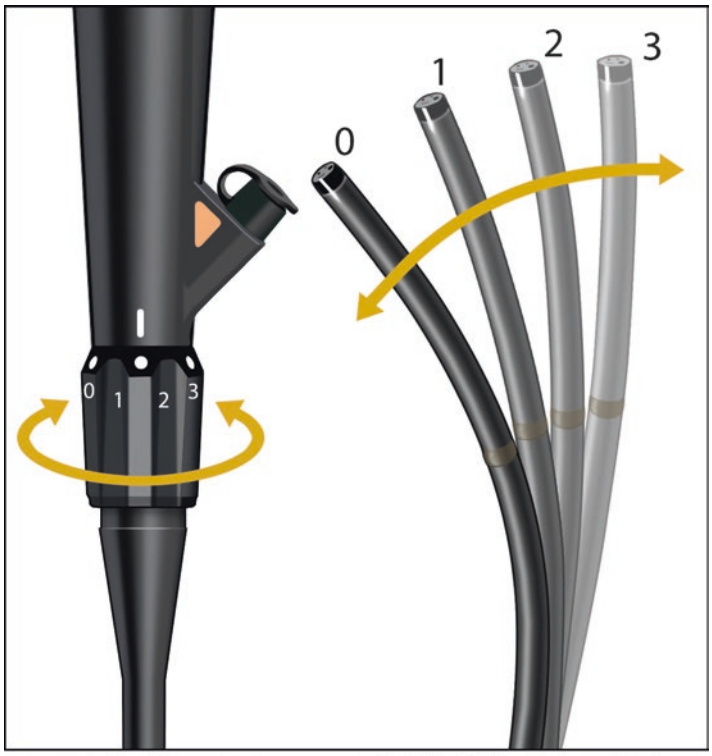

Fig. 2.1 Illustrates variable stiffness in a colonoscope shaft due to rotation of the handle

Variable stiffness of colonoscope shaft, via 'flexibility adjustment ring'

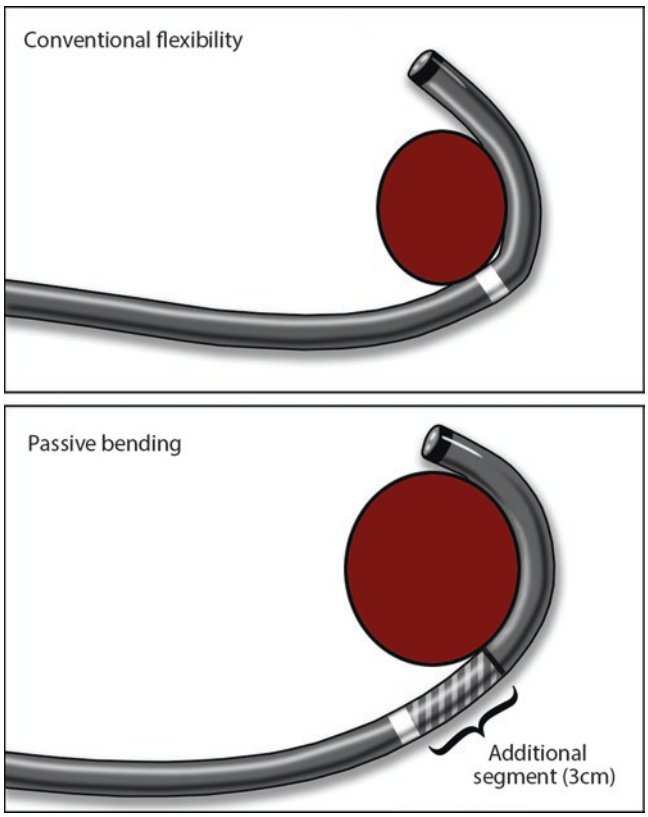

Fig. 2.2 Illustrates the *passive bending* section of the colonoscope

section so as to delicately rotate and push the tip of the colonoscope even when the insertion tube of the scope forms a loop (Fig. 2.5).

Several studies conclude that responsive insertion technology significantly reduces cecal intubation time and patient discomfort [1, 3, 5, 6].

Magnetic Endoscopic Imaging (MEI)

Electromagnets implanted along the shaft of an endoscope can be activated and deactivated in such a way as to produce magnetic fields that can be located in three-dimensional space by a detection device. This process has been in existence for years as a method for determining scope position inside the body without the use of fluoroscopy. Within the last few years, one manufacturer, Olympus, has started to incorporate electromagnets into almost all of their colonoscopes as a component of a magnetic imaging system called Scope Guide™. This second-generation system is less expensive and has a more compact detection device, and the image of the scope position that it renders is now integrated into the same endoscopy display monitor as the endoscopy image for the endoscopist (Fig. 2.6).

The beneficial impact of MEI on colonoscopy performance appears to be greatest for trainees and less experienced colonoscopists [7, 8]. However, there is also evidence that MEI can benefit experienced colonoscopists in certain

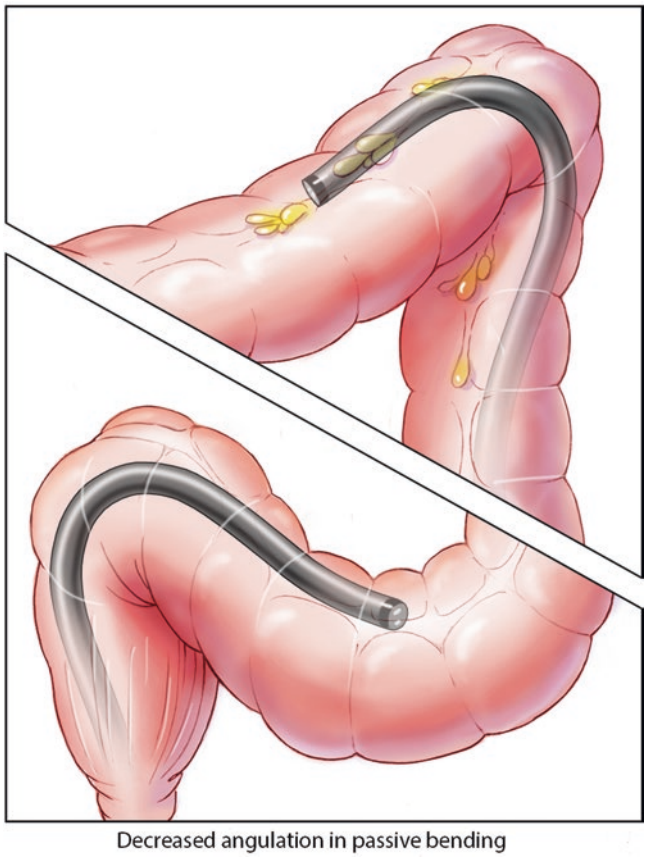

Fig. 2.3 Illustrates the gradually decreasing angulation in the passive bending section of the colonoscope toward the handle end of the instrument

patient subsets [8, 9]. Significant improvements in cecal intubation rates, insertion times, duration of colonoscope looping, number of straightening attempts, and accuracy of hand pressure were most pronounced in the trainee endoscopists studied. The experienced endoscopists had similar but less marked benefits.

Improved Endoscopic Images

The combination of advances in software and hardware has generally resulted in larger and higher-resolution endoscopic images being used today as compared with 5–10 years ago. One would think that this has had a beneficial impact on such parameters as adenoma detection rates, but any studies simply comparing the adenoma detection rate over time would have to control for so many other variables to isolate the image enhancement benefit that conclusions would be difficult to defend. Regardless, high-definition (HD) imaging certainly has the potential to improve polyp detection during colonoscopy, and all three major endoscope manufacturers (Olympus America, Center Valley, PA; Pentax Medical, Montvale, NJ; and Fujinon Inc., Wayne, NJ) produce and market HD endoscopes in the United States. Compared to standard endoscopes which produce an image signal of 100,000–400,000 pixels, HD scopes more than double the resolution with signal images with resolutions that range from 850,000 pixels to more than 1 million pixels. In addition to increased image resolution, HD scopes have the ability to perform optical zoom and can magnify an image up to 150 times, compared to only 30–35 times for standard endoscopes.

Another feature that has become available from manufacturers is dual focus technology which allows the endoscopist to adjust the depth of focus at the touch of a button. This optimizes the instrument for either close-up (within 2–6 mm) or normal viewing of the mucosa, so image clarity is maximized. Some are using this for careful examination of a lesion or post-polypectomy margins.

Some endoscope systems also now provide a pre-freeze feature which provides sharp still image capture almost all the time. The system essentially captures multiple images when the endoscopist presses a button; then the image software instantly selects the image with the clearest contrast and lines (among other parameters). This avoids the nuisance and inefficiency of multiple image capture attempts that may have had blurred motion artifact in the past.

Narrow band imaging was launched in 2005, but the new platform offers significantly brighter NBI with twice the viewable distance in the lumen, which we feel makes it much more user friendly and effective for frequent use. NBI has been widely studied and is used for targeted biopsies in Barrett's esophagus patients as well as other clinical applications. Combining such technology with the HD capabilities of these newer scopes allows for greater mucosal visualization than ever before and is gaining acceptance as a means to determine colon polyp histology endoscopically obviating the need for costly pathologic examination in some cases [10].

Improved Visualization

Despite significant advances in image quality and enhancement techniques over the past few decades, the field of view of endoscopes has changed very little. The traditional forward-viewing colonoscopy is limited to about a 170° field of view, which likely contributes to missed abnormalities such as polyps on colonoscopy, an issue reported in about a quarter of procedures [11]. Some newer endoscopes address this problem by allowing for a much wider field of view.

One such technology, full-spectrum endoscopy (Fuse) produced by EndoChoice, allows for up to 330° field of view with the colonoscope and up to 245° with the gastroscope. It accomplishes this through a proprietary design of three

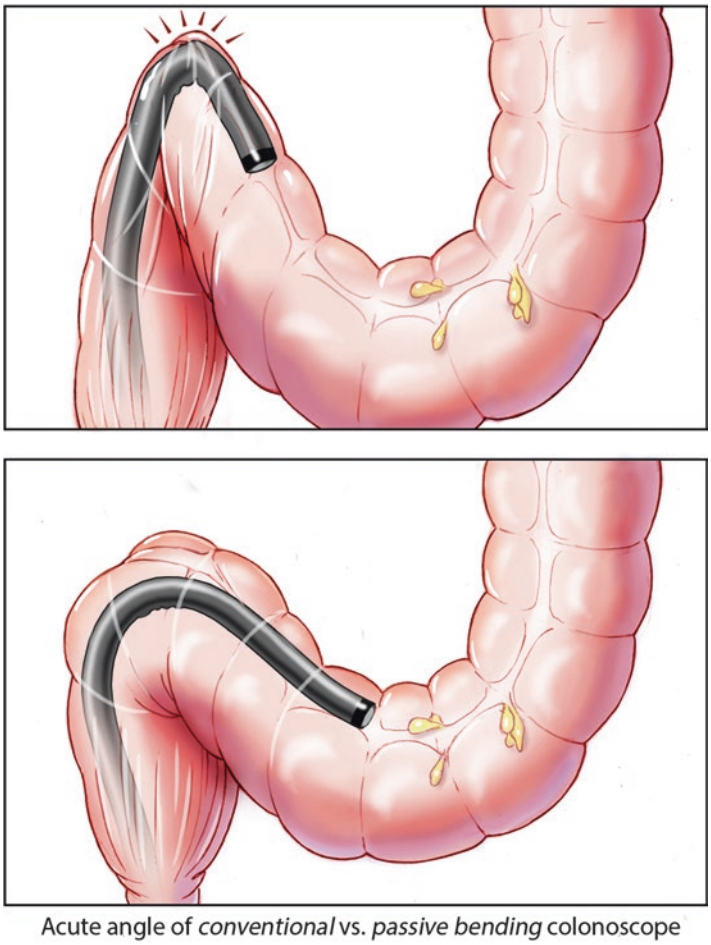

Fig. 2.4 Illustrates the comparison of a conventional colonoscope on the left with a passive bending colonoscope on the right when being pushed through an acute angle. The arrows indicate the direction of force in each illustration

lenses, two on opposing sides and one at the end of the scope, each accompanied with LED lighting (Fig. 2.7). It does this while maintaining all standard endoscope capabilities and maneuverability including full-tip deflection, a 3.8 mm working channel (colonoscope), air or CO2 insufflation, and water jet irrigation, which it is able to do secondary to additional space within the scope gained by switching from fiber-optic lighting to LED allowing for placement of more lenses. The endoscopic images are displayed on three contiguous video monitors allowing for a semi-panoramic view of the lumen.

It is important to realize that the 330° field of view is in the horizontal plane on each side of the forward view and that there are still areas above, below, and behind the forward image that are not seen perpendicular to the shaft of the scope (Fig. 2.8). These areas of unseen upper and lower area extend approximately 20–30° radially above and below the shaft of the scope behind the forward view proximal to the tip of the scope (personal communication with EndoChoice, Inc. 12/5/2015).

Even though there are unseen areas when the colonoscope is stationary, the normal instrument torqueing and movement of the colon around the colonoscope during a procedure are thought to bring these relatively small unseen areas into view.

In an international multicenter, randomized clinical trial, using a same-day, back-to-back tandem colonoscopy design, Gralnek et al. compared the adenoma miss rates of Fuse colonoscopy with standard forward-viewing colonoscopy. In total, 185 subjects (370 tandem colonoscopy examinations) completed the study with a per-lesion analysis demonstrating the adenoma miss rate was significantly lower with Fuse colonoscopy compared to standard view colonoscopy, 7.5% versus 40.8% with p value <0.0001 [11].

Taking the developments in the Fuse system a step further, Saneso Inc. has a new scope awaiting FDA approval that has five cameras to allow for 360° visualization. It has cameras coupled with LED lights located on the front, top, bottom, left, and right of the endoscope to capture images that are projected into a single HD integrated display (Fig. 2.9). The benefit of such technology has yet to be assessed, but it seems to be a promising development especially for endoscopists with lower adenoma detection rates.

Yet another technology that addresses visualization is the NaviAid G-EYE system produced by Smart Medical Systems Ltd. In this technology, a reusable balloon sheath is integrated into a standard colonoscope which is inflated upon withdrawal to depress haustral folds and thereby improve detec-

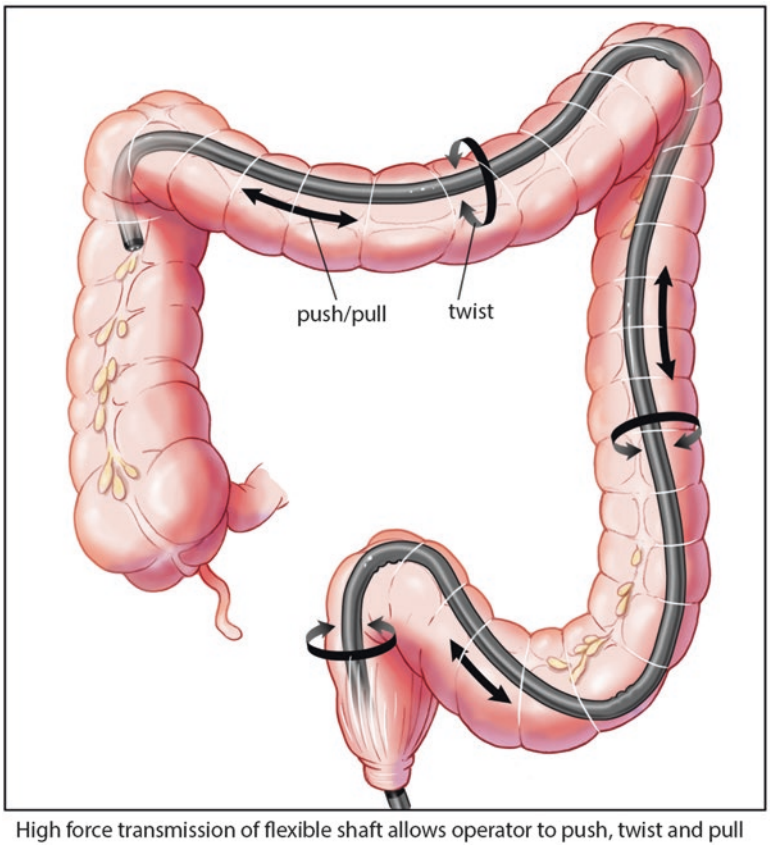

Fig. 2.5 Illustrates the ability of a colonoscope with high force transmission to transmit torque and pushing forces throughout the instrument when the configuration of the colonoscope includes acute angles

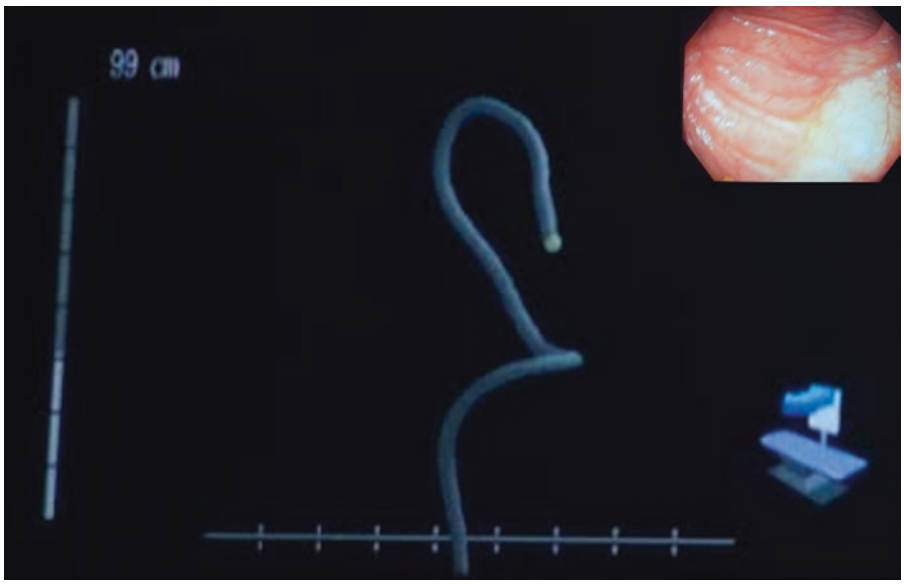

Fig. 2.6 Illustrates a magnetic endoscopic imaging system rendering the configuration of a colonoscope (here maximized) inside the patient along with the endoscopic view (here minimized) during a colonoscopy

tion of polyps between folds. While similar products are available as attachments that can be placed on the end of the scope and are collapsed when inserting and then fan out when withdrawing, this is the first of this type that is incorporated into a scope. In a prospective randomized trial, using same-day back-to-back endoscopy, the adenoma miss rate for balloon colonoscopy was significantly lower than that of standard colonoscopy (7.5% vs. 44.7%). This study also showed the detection of additional adenomas by balloon colonoscopy was significant (81%); however, this was a small study with only about 60 patients in each group, and further conformation is needed [12].

Developing and Notable Technologies

There are several scopes in development that change the basic structure of the endoscope and how it is advanced. From a mechanical perspective, the standard endoscope consists of a long and fairly stiff tube with a steerable head, which provides a balance between being too stiff and causing trouble maneuvering turns or too complaint and forming excessive loops. These new scopes abandon the inherent stiffness of the endoscope and are essentially flexible tubes that can be stiffened later to retain their shape. NeoGuide™ from NeoGuide Systems, Inc. is one such device and at this point is the only one in the clinical trial stage. The NeoGuide™ consists of a 173-cm-long endoscope composed of 16 8-cm-long independent vertebrae. Each segment can be directed to assume a right, left, up, or down circular curve including a combination of such motions. It is inserted like a standard endoscope, during which time the position and angle of the scope tip are encoded into a computer algorithm to direct each successive vertebra to take the same shape that the tip had at a given insertion depth. This avoids the pushing against the gastrointestinal wall used to maneuver in standard endoscopy and thus may cause less discomfort with insertion. The mechanical valves that control insufflation, suction, or water irrigation are the same as in conventional endoscopes and biopsies, and therapeutic maneuvers can be performed conventionally as well by switching to passive mode where the shape and stiffness become like a standard endoscope [13].

Fig. 2.7 Shows an angled view of the tip of the Fuse endoscopes with the *upper* scope being the colonoscopy and the *lower* the gastroscope. Notice the *yellow* LED lights as well as the *white* lenses on the distal tip of the scope and the side. An additional side lens is located on the opposite side of the scope

Another development in the past few years is not an endoscope at all but rather a new and improved wireless capsule used exclusively for colonoscopy, the PillCam Colon capsule (Given Imaging, Yokneam, Israel). Compared to the well-known small bowel capsule, the colon capsule is slightly larger at 11 × 32 mm, captures video on both ends, provides a wider angle of view at 21%, and takes twice as many frames per second at four. Its sensitivity for detecting significant polyps (polyps ≥6 mm or >3 polyps >3 mm) or larger polyps (>10 mm) has been reported at 89% and 88%, respectively, which is comparable to other colon cancer screening modalities [14]. The main drawback is that it requires a good

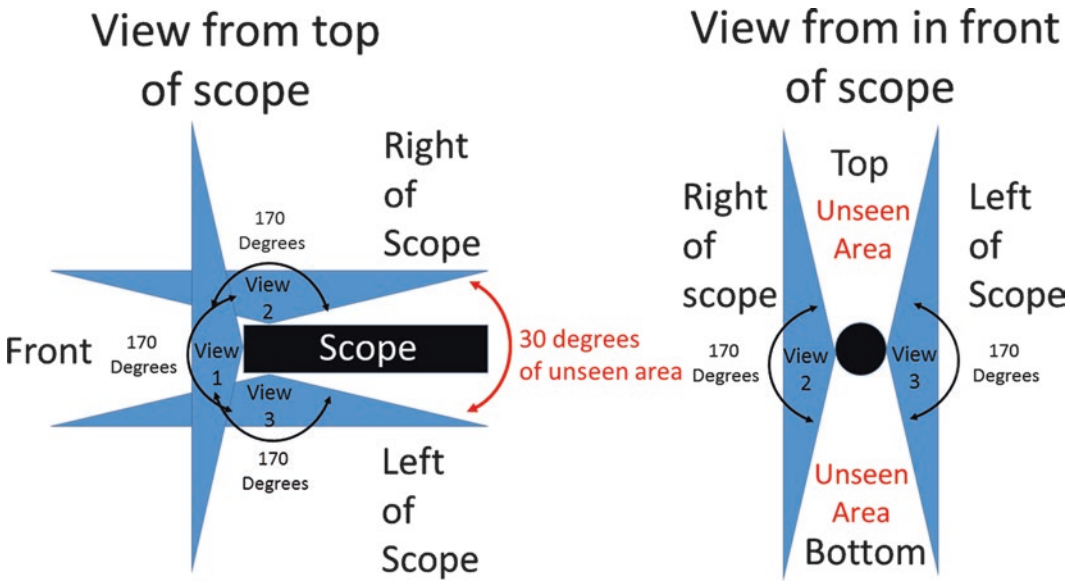

Fig. 2.8 Illustrates the views of the full-spectrum colonoscopy (FUSE) instrument. *View 1* is forward, *view 2* is right, and *view 3* is left. The *unseen area* that exists behind the forward view above and below the scope shaft is also labeled

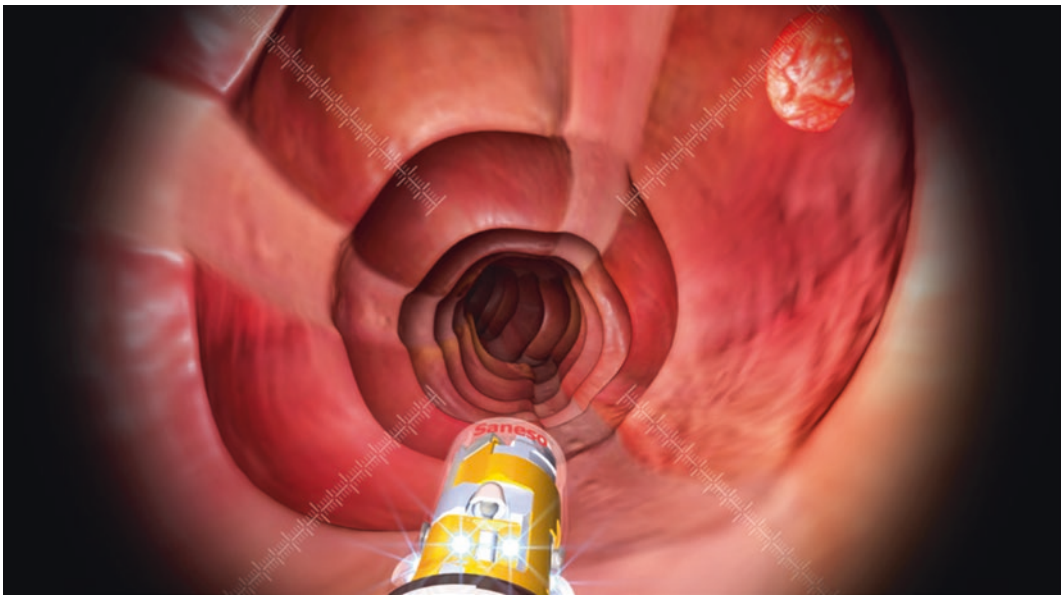

Fig. 2.9 Illustrates the integrated view of the five images captured by the endoscope using Saneso technology

bowel prep to allow adequate visualization, which can be a significant issue in elderly patient or those with significant comorbidities who would be more likely to use such a noninvasive test. Where this really seems to have a niche role for incomplete colonoscopy where it can be performed immediately after the colonoscopy as the bowel is already prepped?

Conclusion

Looking at the recent advances in endoscopic equipment, it is hard to tell what further developments the future may bring. Despite this, the endoscopes of the future will likely retain the basic structure of the current endoscopes but will be easier to operate and will allow one to make most diagnoses endoscopically. With such abilities, the focus in further developments is likely to be tailored to therapeutic interventions which may someday replace surgical procedures.

References

1. Saito Y, Kimura H. Responsive insertion technology. Dig Endosc. 2011;23(Suppl 1):164–7.
2. Brooker JC, Saunders BP, Shah SG, et al. A new variable stiffness colonoscope makes colonoscopy easier: a randomised controlled trial. Gut. 2000;46(6):801–5.
3. Yoshikawa I, Honda H, Nagata K, et al. Variable stiffness colonoscopes are associated with less pain during colonoscopy in unsedated patients. Am J Gastroenterol. 2002;97(12):3052–5.
4. Shumaker DA, Zaman A, Katon RM. A randomized controlled trial in a training institution comparing a pediatric variable stiffness colonoscope, a pediatric colonoscope, and an adult colonoscope. Gastrointest Endosc. 2002;55(2):172–9.
5. Cuesta R, Sola-Vera J, Uceda F, et al. Does "responsive insertion technology" improve practice of colonoscopy? Results of a randomized study. Scand J Gastroenterol. 2014;49(3):355–61.
6. Prieto-de-Frias C, Munoz-Navas M, Carretero C, et al. Comparative study of a responsive insertion technology (RIT) colonoscope versus a variable-stiffness colonoscope. Rev Esp Enferm Dig. 2013;105(4):208–13.
7. Haycock A. Magnetic Endoscopic Imaging. Up to date 2013. Accessed 18 Sept 2015.
8. Shah SG, Brooker JC, Williams CB, et al. Effect of magnetic endoscope imaging on colonoscopy performance: a randomised controlled trial. Lancet. 2000;356(9243):1718–22.
9. Cheung HY, Chung CC, Kwok SY, et al. Improvement in colonoscopy performance with adjunctive magnetic endoscope imaging: a randomized controlled trial. Endoscopy. 2006;38(3):214–7.
10. Hassan C, Repici A, Zullo A, et al. New paradigms for colonoscopic management of diminutive colorectal polyps: predict, resect, and discard or do not resect? Clin Endosc. 2013;46(2):130–7.
11. Gralnek IM, Siersema PD, Halpern Z, et al. Standard forward-viewing colonoscopy versus full-spectrum endoscopy: an international, multicentre, randomised, tandem colonoscopy trial. Lancet Oncol. 2014;15:353–60.
12. Halpern Z, Gross SA, Gralnek IM, et al. Comparison of adenoma detection and miss rates between a novel balloon colonoscope and standard colonoscopy: a randomized tandem study. Endoscopy. 2015;47(4):238–44.
13. Obstein KL, Valdastri P. Advanced endoscopic technologies for colorectal cancer screening. World J Gastroenterol. 2013;19(4):431–9.
14. Eliakim R, Yassin K, Niv Y, et al. Prospective multicenter performance evaluation of the second-generation colon capsule compared with colonoscopy. Endoscopy. 2009;41:1026–31.

Endoscopic Management of Foreign Bodies

3

Parit Mekaroonkamol and Saurabh Chawla

Introduction

Foreign body ingestion including food impaction is one of the most common gastrointestinal emergencies that can lead to serious complications and occasionally death if left untreated. There are over 100,000 cases of foreign body ingestion with approximately 1500 deaths reported each year in the United Sates [1–3]. Even though most ingested foreign bodies pass spontaneously, in 10–20% of the patients they may not, increasing the risk for perforation, and may require intervention [4–8]. Fortunately, with nearly 95% success rate of endoscopic treatment, surgery is rarely needed [9, 10]. Therefore, early recognition of high-risk cases and timely endoscopic intervention are the cornerstone of management in patients presenting with foreign body ingestion. This chapter summarizes the approach, techniques, and existing evidence on endoscopic management of foreign body ingestion.

Clinical Presentation

Foreign body ingestion commonly occurs in children with a peak incidence between 6 months and 6 years old [1, 2, 11, 12]. These are usually true foreign body ingestions occurring accidentally with common household objects such as button batteries, magnets, coins, and toys [1, 13]. Adult cases are not uncommon and contribute to 10–20% of all foreign body ingestions [2, 14]. Unlike children, food bolus impaction is the most common type of foreign body in adults with most instances occurring in patients older than 40 years [5, 15]. Young adults who present with food bolus impaction should raise concern for underlying eosinophilic esophagitis which has been reported to account for up to one-third of all food impaction cases [4, 16]. Patients at increased risk of food impaction and foreign body ingestion include edentulous patients, those with underlying esophageal pathology (such as eosinophilic esophagitis, achalasia, esophageal webs, and rings), abnormal esophageal anatomy (including those with prior gastroesophageal surgery), patients with psychiatric disorders, and those with transient or permanent mental impairment (intoxication or dementia) [5, 12, 15, 17–19]. Foreign bodies in the small bowel usually have a delayed presentation after oral ingestion and are rarely emergent. Small bowel obstruction occurs when impaction occurs in regions of luminal narrowing in the intestinal lumen such as ileocecal valve or proximal to small bowel strictures from disease or therapy (surgical or radiation). Rectal or colonic foreign bodies are more commonly a result of deliberate or malicious insertion though rarely swallowed objects that have transited through the small bowel may become symptomatic after getting stuck in the rectum. Intentional ingestion or rectal insertion can be seen in those who have secondary gain such as incarcerated inmates, drug mules, body packers, and psychiatric patients [20, 21].

When the foreign body is in the upper gastrointestinal tract, presenting symptoms include dysphagia, inability to tolerate secretion, chest discomfort, gagging, vomiting, wheezing, stridor, or blood-stained saliva [4, 13, 18]. However, almost half of the patients can be asymptomatic [13]. Sharp objects, corrosive battery discs, or prolonged retention of a foreign body in the esophagus may cause esophageal perforation. Esophageal perforation may be localized or may cause frank extravasation into the mediastinum and should be suspected in patients presenting with subcutaneous emphysema, severe chest pain, neck swelling, erythema, and/or a sepsis-like picture [4]. Foreign bodies in lower gastrointestinal tract are more prevalent in men [22, 23]. Patients can present with rectal discomfort, abdominal pain, rectal bleeding, painful defecation, constipation, and obstructive symptoms. Fever and sepsis may be presenting features if the object perforates the intestinal lumen [24, 25].

A thorough history should focus on prior episodes of food bolus impaction, any risk factors to underlying esophageal

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pathology (smoking history, weight loss, dysphagia, asthma, food allergy, etc.), timing of ingestion, type of foreign body (if known), and history of rectal injury. Attention should be paid to the neck, throat, lung, and abdominal examination. Hemodynamic instability, subcutaneous emphysema, or the presence of crepitation in the neck or chest, stridor, and peritoneal signs should prompt an urgent radiologic evaluation to rule out visceral organ perforation in gastrointestinal tract.

Management

With advances in endoscopic instruments and techniques, endoscopy has become the mainstay for the management of gastrointestinal foreign bodies. However, patients can have myriad presentations after foreign body ingestion or food impaction, and therefore management needs to be individualized for each patient. At presentation, a careful history should be obtained to ascertain the nature and number of ingested foreign bodies, and attention should be paid to the patient's ability to tolerate secretions, the presence of respiratory distress, and also for signs of complications like free or localized perforation as discussed in the prior section.

Early endotracheal intubation for airway protection should be obtained if possible for signs of respiratory distress or inability to swallow secretions. Cross-sectional imaging is often very useful in planning further therapy and should be sought in patients who are otherwise stable. In patients where perforation by the foreign body is suspected, early surgery consult, and antimicrobial use may be considered prior to embarking on endoscopic therapy.

In some instances, other specialties and ancillary services, like psychiatry, mental health workers, social workers, and law enforcement, may need to be involved, and attention should be paid to careful documentation and obtaining proper consent prior to start of endoscopic therapy.

Endoscopic therapy in different instances may differ in terms of timing, use of sedation, endoscopic instruments, and techniques. These are further detailed in the following section.

Role of Imaging

Plain radiographs and CT cross-sectional imaging are the radiologic modalities of choice for initial evaluation of foreign bodies in GI tract. They are easy to perform and readily available and provide information regarding shape, size, location, and number of the foreign bodies [4, 26]. However, they may not detect radiolucent objects, and the use of CT scan may be limited when a metal object, which can produce beam-hardening artifacts, is also present [4, 26, 27].

For imaging evaluation, it is recommended that the whole gastrointestinal tract from the nasopharynx to anus (not just the abdominal film) should be included as the history of timing of ingestion and the number of ingested objects are often times not reliable [28, 29]. When a plain radiograph is selected, both anteroposterior and lateral films should be obtained. This is particularly helpful for localizing the object (esophagus vs. trachea) and differentiating between a coin and a disc battery in the esophagus [1, 30]. As opposed to a sharp-edged single-layer coin, a disc (or button) battery has a bilaminar structure; thus a reduced density "double ring" or a "halo sign" can be seen in the anteroposterior view, while a two-layer edge or a "step-off sign" can be seen in the lateral view [1, 31]. Coronal (circular object facing frontally on the anteroposterior film) and sagittal orientation of the object can be suggestive of its location. When the coin is oriented in the coronal plane, it is more likely to be in the esophagus, and a sagittal-oriented coin is, vice versa, more likely to be in the trachea [32, 33]. However, this is not always true and the reverse has been reported [34, 35]. Therefore, a lateral film (or, in some occasions, a CT scan) is needed to help precisely localize the object [1, 35].

Battery, steak bone, coins, pins, needles, staples, and other common ingested objects are radiopaque, whereas chicken bone, fish bone, wood, plastic, glass, and thin metal objects may not be seen on the plain radiograph or CT scan [18, 26]. Therefore, a negative radiologic study does not exclude the presence of foreign body, and endoscopic evaluation is still warranted especially when sharp objects are ingested or when the patient has persistent symptoms [4, 36].

Another important function of radiologic imaging is to help exclude any complication such as perforation, obstruction, or aspirated objects before proceeding with endoscopy. It is also recommended before any rectal examination or attempts to manually remove a foreign body in the rectum to exclude any sharp objects that can potentially harm the examiner [37].

Any study using oral contrast is relatively contraindicated due to risk of aspiration and its interference with subsequent endoscopic evaluation. Magnetic resonance imaging (MRI) usually has a very limited role in these situations due to the possibility of an unknown metal object in the body that can be harmful during an MRI and also the long turnaround time of the study [4, 36].

It is important to note that a radiologic work-up is not required prior to endoscopy when the history is reliable and there are little signs or symptoms to suggest perforation in patients with non-bony food bolus impaction [4].

Timing of Endoscopy

Appropriate timing of endoscopic intervention is determined on a case-by-case basis based on the risk of complications from a given foreign body which may include aspiration, transmural erosion, perforation, fistula formation, and luminal obstruction [4, 18]. These risks are dependent on the nature,

size, and shape of the ingested object, the expected location of obstruction, the time elapsed since ingestion, and the overall clinical stability of the patient [4, 38–40]. As opposed to adults, risk assessment in pediatric patients is more difficult due to their body size and less reliable history; thus, endoscopic removal is usually preferred over expectant management in this population [1].

The American Society of Gastrointestinal Endoscopy (ASGE) has published a guideline recommending an "emergent" procedure for patients with complete esophageal obstruction who cannot tolerate secretions, patients with sharp objects in the esophagus, and patients with disc batteries lodged in the esophagus. Blunt objects in the esophagus, patients with incomplete esophageal obstruction, or long (>6 cm) objects in the stomach or duodenum required "urgent" endoscopy, while coins in the esophagus and small blunt objects (defined as objects shorter than 6 cm in length and smaller than 2.5 cm in diameter) including batteries in the stomach can be deferred to "nonurgent" timing (Table 3.1) [4].

However, the time frame of emergent versus urgent endoscopic intervention in foreign body removal is a matter of debate. For upper gastrointestinal bleeding, the definition of "emergent" procedure is better defined [41–43]. Considering an average duration of 4–6 h of normal gastric passage, we define "emergent" endoscopy as within 6 h in our practice, while urgent endoscopy can be performed within 24 h.

Table 3.1 Timing of endoscopy for foreign body removal [1, 4]

	Patients who cannot tolerate secretion
Emergent endoscopy (within 6 h)	Sharp object in the esophagus
	Disc battery in the esophagus
Urgent endoscopy (6–24 h)	Blunt foreign body in the esophagus
	Food bolus impaction in the esophagus without complete obstruction
	Sharp foreign body in the stomach or duodenum
	Long object (>6 cm) that has not yet passed proximal duodenum
	Magnet within endoscopic reach
Nonurgent endoscopy (can be observed for more than 24 h)	Coins that have remained in the esophagus longer than 24 h (sooner if the patient is symptomatic)
	Large (>2.5 cm) blunt object in the stomach
	Battery (either cylindrical or disc type) that has remained in the stomach longer than 48 h (sooner if patient is symptomatic)
	Any symptomatic pediatric patients with blunt foreign body within endoscopic reach

Although the risk of perforation from a foreign body that has already passed the esophagus is very low (less than 1%), this risk increases significantly up to 35% when the object is sharp or pointed. The most common perforation site is at ileocecal valve which is the narrowest part of the small intestine [12, 44, 45]. Therefore, any sharp object within endoscopic reach should be retrieved when possible; otherwise, serial imaging should be performed to ensure safe passage of the foreign body [4, 46, 47].

Important Considerations [4, 18, 26, 48–50]

Not all bones and metals are radiopaque
Small fish bone, chicken bone, thin metal, aluminum, wood, and glass are unlikely to be seen radiologically
MRI can be used to detect radiolucent objects. However, it is contraindicated if any metal is suspected
Avoid luminal contrast study as it can obscure endoscopic view and increase risk of aspiration

Practical Considerations Before Endoscopy

Clinical scenario	Management options
Patients with compromised non-secured airway	Consider ENT evaluation vs. tracheal intubation prior to endoscopy
Patients who have co-ingestion with other corrosive or caustic agent	Consider imaging evaluation to rule out perforation Consider ENT evaluation to rule out upper airway injury
Patients with severe chest pain, hemodynamic instability, high-grade fever, subcutaneous emphysema, signs of peritonitis	Consider imaging evaluation to rule out perforation Empiric antibiotics if there is clinical sepsis with high suspicion for perforation
Patients with active suicidal idea, combative behavior, prisoners with suspected secondary gain	Consider psychiatric evaluation Exercise appropriate security measures, i.e., per protocol restraints, presence of security officer or 1:1 observation, limit patient's accessibility to sharp objects, etc. Appropriate documentation of consent per protocol
Pediatric patients <60 lbs body weight	Consider using pediatric gastroscope Consult pediatric anesthesiologist and pediatric gastroenterologist
Multiple foreign bodies, large foreign body, sharp foreign body, expect long procedure, patient who cannot tolerate secretion or with high risk of aspiration	Consider using an overtube Consider tracheal intubation

Preparation Before Endoscopy

- *Mode of Sedation*

  Decision on the mode of sedation should be individualized for the patient and made after a multidisciplinary discussion between gastroenterology, anesthesiology, emergency medicine, and intensive care as appropriate. In most cases, conscious sedation is safe and acceptable for endoscopic removal of foreign bodies. However, in special situations when it is anticipated that the procedure may be prolonged or foreign body extraction may be difficult, general anesthesia with elective endotracheal intubation should be considered. These circumstances include, but are not limited to, a large foreign body, multiple foreign bodies, foreign body with more than one pointed or sharp ends, and foreign bodies in challenging position. Selective patients with high intra-procedural risk, such as those with complete esophageal obstruction, those with multiple comorbidities, and small children, may also be considered for tracheal intubation under general anesthesia [1, 4, 18, 49]. If endotracheal intubation is not undertaken, patient should be placed in Trendelenburg position to minimize the risk of accidental dislodgment of the foreign body into the trachea [12, 36, 46, 51].

- *Endoscopes*

  A flexible standard gastroscope is the most commonly used tool for foreign body removal in the upper gastrointestinal tract. A rigid endoscope or laryngoscope may occasionally be considered when foreign body is lodged in proximal esophagus [52, 53]. This can be particularly useful when sharp objects are retained in the hypopharynx [54]; however, it carries a higher risk of perforation and may require an otolaryngologist or an endoscopist experienced in the use of rigid scopes [37, 52, 55].

  Other endoscopes such as single- or double-channel therapeutic gastroscopes, pediatric gastroscopes, enteroscopes, etc. are alternate options in special circumstances dependent on size and position of the foreign body, degree of luminal obstruction, or habitus of the patient [4, 56]. In general, standard adult gastroscope can be safely used for children weighing more than 10 kg (22 lbs) [57]. Pediatric or ultrathin gastroscope with insertion tube diameter of less than 6 mm should be used for pediatric patients younger than 1 year old or weigh less than 5 kg (11 lbs) [18]. Sigmoidoscope and colonoscope may be used for foreign bodies in lower gastrointestinal tract, while enteroscopes can be used to reach further into the small bowel. Occasionally specialized techniques like single or double balloon-assisted or spiral enteroscopy may be used to retrieve foreign bodies from mid and distal small bowel.

  Endoscopes vary from different manufacturers/models and are available in variable diameter (4.9–13.7 mm), length (925–2000 mm), number of channels, and channel size (2.0–4.2 mm) [58] as shown in Table 3.2. It is important to confirm the compatibility between each retrieval device and the endoscope being used prior to start of the procedure.

- *Retrieval Devices*

  Even though the successful endoscopic removal of foreign body largely depends on the nature and location of the foreign body and endoscopist's maneuverability of the scope [59, 60], proper selection of retrieval device is equally important. There are multiple available instruments or devices for foreign body removal as shown in Table 3.3. Selection of the appropriate device to be used depends on the size, shape, number, and location of the foreign body being retrieved and also the endoscopist's preference [46, 47]. Most devices can be used in standard upper endoscopes with a channel size of 2.8 mm. Only a few devices with extra wide opening angle and width are designed specifically for therapeutic scopes which have a larger channel size (3.2 or 3.7 mm).

  Available retrieval devices may vary among each endoscopy unit, and it is essential to know which instrument is available to the endoscopist. The endoscopy unit should keep a diverse array of retrieving devices and have, at least, alligator forceps, rat tooth forceps, prong grasping forceps, snare, Dormia basket, Roth Net, protector hood, and an overtube [4, 36, 46].

Aside from commonly used devices mentioned in Table 3.3, there are other accessory endoscopic instruments with different configurations, sizes, and rotatable function

Table 3.2 Endoscope specifications [58]

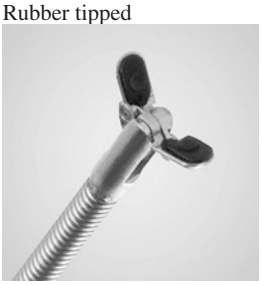
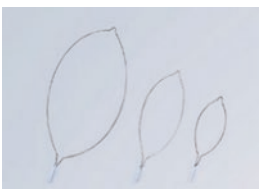
Scope type	Scope length (mm)	Scope diameter (mm)	Working channel (mm)
Standard adult gastroscope	1030–1100	8.8–9.8	2.4–2.8
Therapeutic gastroscope (dual channel)	1030–1100	11.3–12.8	2.8/3.7–6.0
Pediatric (ultrathin) gastroscope	1050–1100	4.9–5.9	2.0–2.2
Adult colonoscope	1330–1700	12.8–13.2	3.7–4.2
Therapeutic colonoscope (dual channel)	1330–1700	13.2–13.7	2.8–3.2/3.7–4.2
Pediatric colonoscope	1330–1700	11.1–11.8	3.2
Enteroscope	1520–2000	8.5–11.6	2.2–3.8
Sigmoidoscope	700–790	11.3–12.8	3.2–4.2

Table 3.3 Commonly used retrieving devices [46, 47, 59, 61, 62]

Retrieval devices	Design	Available configuration	Utility advantage	Limitation
Standard biopsy forceps 	Small jaw forceps with a needle spike between the opposing jaws	Biopsy cup jaws may be round, oval, elongated, fenestrated or non-fenestrated, and smooth or serrated	Used mainly for tissue sample Can retrieve only small object such as pin or needle	Insecure grasp, small opening angle, and narrow width. Not suitable for most foreign body removal
Rat tooth 	Opposing teeth at the tips for more reliable grasp	Available opening width: 3.0–19.5 mm Available length: 120–230 cm	Ideal for soft object, stent removal, finer tissue handling than alligator and shark tooth	May not have reliable grip on a large hard object
Shark tooth 	Similar to rat tooth design with larger jaws. Some are also equipped with small backward-angled teeth (toward the handle) along the length of the jaw	Available opening width: 4.7 mm Available length: 165 cm	Suitable for flat hard object, i.e., a coin	Not designed to be used with a colonoscope Maximum opening width is 4.7 mm
Alligator 	Small teeth along the length of the jaw	Available opening width: 7.5 and 11.3 mm Available length: 165 and 230 cm	Suitable for various surfaced foreign bodies including a flat hard object such as a coin	Limited jaw length
Rat tooth-alligator 	Combined opposing distal teeth and smaller teeth along the jaw	Available opening width: 11.3–19.5 mm Available length: 120 and 230 cm	Very secure grip. Some designs are fully rotatable	Not suitable for round slippery object

(continued)

Table 3.3 (continued)

Retrieval devices	Design	Available configuration	Utility advantage	Limitation
Rubber tipped 	Attached rubber on the opposing jaws	Available opening width: 4.8 mm Available length: 190 cm	Most secure grip of small thin object such as pin, needle, nails, and blade	Short jaws. No distal teeth. Cannot be used for large object. It is not designed to be used with a colonoscope
Tripod forceps 	A pronged grasping forceps with three arms. There is a small rounded hook at the tip of each arm. A built-in proximal flushing port allows irrigation of object inside the prong	Available opening width: 20 mm Available length: 165 and 230 cm	Long prong with wide opening angle. Suitable for soft object. It is usually used for a large, blunt, or round foreign body	Pliable prongs do not give a reliable grip for a hard heavy object or impacted foreign bodies. Cannot close the device too tightly as the prong could bend or break
Pentapod forceps 	A pronged grasping forceps with five arms. There is a small rounded hook at the tip of each arm. A built-in proximal flushing port allows irrigation of object inside the prong	Available opening width: 20 mm Available length: 165 and 230 cm	Long prong with wider opening angle than a tripod when fully opened. Suitable for a large blunt or round foreign body	Pliable prongs do not give a reliable grip for a hard heavy object or impacted foreign bodies. Cannot close the device too tightly as the prong could bend or break
Four-wire basket 	Retractable wires forming a helical sphere configuration. Originally invented to retrieve ureteral stone	Available opening width: 22, 32, and 35 mm. Largest size: 3.5 × 6 cm. Available length: 120–240 cm Also available in 3, 4, 6, and 8 wires The wire can be soft (braided) or stiff (solid)	Provide a four-dimensional grasp. Suitable for round and slippery object or long (>6 cm) object. Some models also have a rotatable function	Not suitable for small, thin objects that can fall through the wires
Snare 	Different shapes of snare loops are mainly designed for the benefit of polypectomy. When used for foreign body removal, the size of the fully opened loop matters the most	Available opening width: 10–33 mm. Largest size: 3.5 × 6 cm Available length: 105–240 cm Also available in crescent, oval, and hexagonal shape	Easy to use. Spiral wire design provides firmer grip and minimal slippage. Suitable for long object	Provide only two-dimensional grasp Not suitable for round slippery object

(continued)

Table 3.3 (continued)

Retrieval devices	Design	Available configuration	Utility advantage	Limitation
Retrieval net (Roth Net®) 	Similar to snare device but with a soft flexible mesh attached to the noose of the snare forming a concave compartment for retrieval purpose	Commonly used shape and size are oval 3 × 6 cm for adult and 2 × 4.5 cm for pediatric cases. 4 × 5.5 cm octagonal net is specifically designed for food bolus. Octagonal shape allows the net to be fully opened in narrow lumen without losing its form. 4 × 8 cm hexagonal net is used for a very large object Available length: 160 and 230 cm	Suitable for small round slippery object such as disc battery, to retrieve multiple small objects at once, food bolus, or large objects that are difficult to grasp	Cannot be used for long object that does not fit in the net pocket

Images courtesy of Olympus, Roth Net ® -US Endoscopy

from many manufacturers that may be used for foreign body removal. For example, W-shape alligator forceps has longer jaws to grasp larger objects, Pelican-type forceps has an opposing cup to collect the sample in the cup, and certain type of rat tooth-alligator forceps can rotate in vivo. A Twin Grasper forceps (Ovesco Endoscopy AG) was originally designed for tissue approximation before endoscopic closure. It has a separate handle to independently control each jaw of the forceps making it an ideal tool to grasp a big pliable foreign body and "fold" it to a smaller piece. It is available in 165 and 230 cm length and requires a minimum of 3.2 mm working channel. Foreign bodies in proximal esophagus or in oropharyngeal area are usually handled by an otolaryngologist. If a rigid endoscope is used for removal, a Magill forceps can aid the retrieval.

Majority of the foreign bodies can be safely retrieved using basic, universally available devices such as a snare or rat tooth forceps [17, 63, 64]. However, difficulty of the case, cost, and the technician's and the endoscopist's familiarity to the device should also factor into the consideration for instrument selection.

- *Protector Hood*

  A protector hood is an inverted bell-shape device that is used to protect the esophagus, cardia, and posterior pharynx from sharp or pointed object during retrieval [46, 65]. It is easy to assemble and use. It is preloaded with its narrow part attached to the tip of the scope with the base of the hood (the wide end) pointing toward the shaft. During advancement of the scope, the

hood will stay backward (the wide end pointing backward) and allow normal visualization; however, when the scope is withdrawn pass the gastroesophageal junction, the hood will be "flipped" back to cover the foreign body. It is important for the endoscopist to grasp and pull the foreign body back to the tip of the scope as close as possible to ensure that all pointed tips and sharp ends are covered within the hood. Since flipping of the hood requires tension at lower esophageal sphincter, it cannot be used for foreign bodies in the esophagus. Even though it is recommended to be used after pushing the foreign body into the stomach first, using this device should be avoided when dealing with sharp objects in the esophagus, as these objects should not be pushed into the stomach [4, 46, 47].

- *Overtube Placement*

  An overtube is an accessory device used to create a safe conduit from the oral cavity to the esophagus or stomach allowing repeated passage of the endoscope while protecting the mucosa of the gastrointestinal tract and preventing aspiration [5, 66–69]. It is a sleeve-like tube made with a semirigid plastic that is reinforced with metal coil to prevent luminal collapse. The distal end of the tube is however soft and flexible with tapered tip to a diameter similar to the scope. Both inner and outer tubes are transparent to allow full visualization of the mucosa. When fully assembled, the external end of the outer tube is closed with a sealed cap to allow insufflation [46, 47, 66]. The overtube discussed in this chapter refers to only the overtube used for foreign body removal, not the ones used to assist deep enteroscopy.

  Overtube is particularly helpful when removing sharp objects, large (>2.5 cm) round object, long objects (>6 cm), or disc batteries [70]. It comes in different lengths and sizes. A short tube (23 and 25 cm) is for the protection of the hypopharynx during extraction of esophageal foreign body, while a long tube (50 cm) is meant to be fully inserted into the stomach to also protect the esophagus and gastroesophageal junction. Overtubes also come in different diameters for standard and therapeutic gastroscopes.

  A two-tube system with air cap allows effective air insufflation and minimizes the risk of entrapped mucosa between the outer tube and the scope. Insertion requires appropriate technique with gentle manipulation as noted below. Mucosal pinching can cause mucosal abrasion, tear, or even perforation [71, 72]. Common sites of trauma are at the hypopharynx and esophagus. Other reported complications include variceal rupture, pneumomediastinum, transient vocal cord paralysis, overtube separation from the bite block, and tracheal compression [72–76]. Airway must be closely monitored, while patient has an overtube inserted (Figs. 3.1, 3.2, 3.3, and 3.4) [47, 66].

Fig. 3.1 Esophageal and gastric Guardus® overtubes (Images courtesy: US Endoscopy)

Fig. 3.2 Esophageal and gastric Guardus® overtubes (Images courtesy: US Endoscopy)

Indication to Use an Overtube

- Sharp, pointed object
- Large (>2.5 cm) round object
- Long (>6 cm) object
- Disc battery
- Large food bolus or bezoars
- Fragmented or complex-shape object that may require frequent endoscopic insertion

Fig. 3.3 Esophageal and gastric Guardus® overtubes (Images courtesy: US Endoscopy)

Practical Tips on Overtube Insertion

- Make sure that the diameter of the overtube is compatible with the diameter of the endoscope. There should be no gap between the tube and the scope.
- Generous lubrication on both inner and outer tube.
- Use a large (>60 Fr) bite block.
- To slide the tube down to a desired location, hold the scope straight and use a slightly rotating motion to gently insert the tube.
- If excessive resistance is met, readjust the scope position and use extra lubricant.
- Every time the tube needs to be pushed in, reinsert the scope along with the inner tube to avoid trapping of mucosa between the tube and the scope.
- Exercise extra care when inserting the tube in patients with short or fixed neck.

Endoscopic Techniques

The type and location of the foreign body are the most important factors to consider while deciding which instrument and endoscopic technique are to be used. Common anatomical areas of foreign body impaction are regions with anatomical narrowing, pathologic stricture, or acute angulation. These areas include cricopharyngeus muscle or upper esophageal sphincter (usually at 15–17 cm from the incisor), aortic crossover at the mid esophagus (usually at 22–24 cm from the incisors), gastroesophageal junction (usually at 38–40 cm from the incisor), pylorus, duodenal sweep, ileocecal valve, rectosigmoid junction, and anus [26, 27, 77–79]. Upper esophageal sphincter is the most common site of

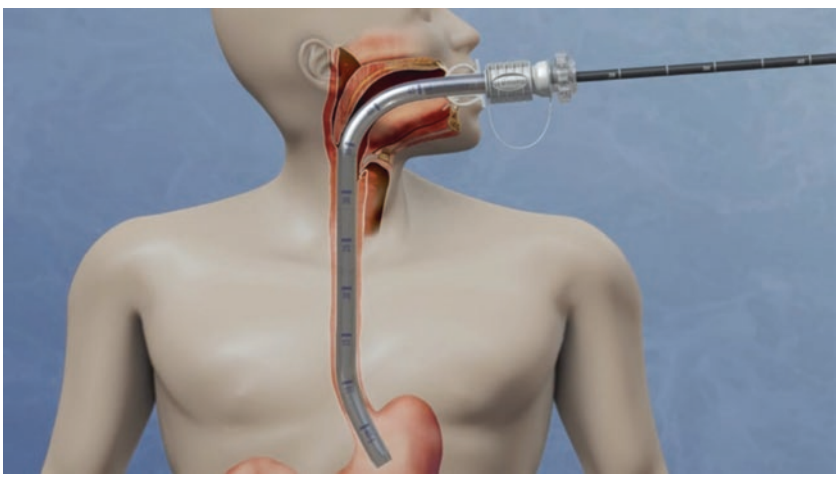


Fig. 3.4 Illustration of Guardus® overtube insertion (Image Courtesy: US Endoscopy)

impaction in pediatric patients as this area is significantly smaller than in adults [37, 54, 77, 80].

When possible, it is recommended to simulate grasping a similar target using the selected device ex vivo before the actual procedure [4, 12, 47, 81]. This practice allows the endoscopist to gauge the difficulty of the procedure, help in selecting appropriate device, and familiarize the technician with the equipment. The need for endoscopic intervention is by far more common for foreign bodies in upper gastrointestinal tract. However, it is sometimes required in lower gastrointestinal tract when the object passes beyond the ileocecal valve and is within the reach of a colonoscope. The endoscopic techniques are similar in concept and are largely dependent on the size, shape, number of the foreign bodies, and selected equipment to be used. Detailed endoscopic approaches to common foreign bodies are discussed here.

Approach to Common Foreign Bodies

- *Food Bolus Impaction*

  For adult patients in western countries, esophageal food bolus impaction is the most common type of foreign body obstruction reported [4, 5, 12]. More than half of these patients have underlying esophageal pathology, most commonly from a Schatzki's ring, peptic strictures, and eosinophilic esophagitis [15, 16, 19, 45, 82]. Therefore, special care must be taken before advancing the bolus in the esophagus or when attempting dilation after prolonged impaction. Other possible underlying cause includes external compression, post-surgical complications like anastomotic strictures or fundoplication wrap, motility disorders, or esophageal cancer.

  Despite conflicting data on its effectiveness [83–86], glucagon (1 mg intravenously in a single dose) remains the first-line medical therapy for patients with food impaction with intent to relax lower esophageal sphincter allowing the bolus to pass; however, it should not delay endoscopic intervention [4]. After glucagon fails to dislodge the food bolus, endoscopic intervention is warranted.

  Food bolus can be extracted or advanced into the stomach endoscopically. "Pushing" technique, which was once contraindicated due to concerned risk of perforation [36, 45, 81], is now an acceptable approach to advance the food bolus as long as only gentle pressure is applied [15, 87]. When possible, an evaluation of the esophagus distal to the impaction should be performed first. This may be achieved by an ultrathin endoscope. The reported success of push technique is as high as 90% with minimal complications [18, 63]. Fragmentation of the food bolus using a snare or forceps may be required if significant resistance is met before gentle "push" can be successfully performed [4].

  A snare, a retrieving net, and grasping forceps are commonly used to break, soften, and remove the impacted food bolus in either an en bloc or a piecemeal fashion, preferably through an overtube [4]. A clear plastic cap, similar to the ones used for variceal banding, can be used to assist food bolus removal. It is preloaded onto the tip of the endoscope to secure the small soft food residue in the lumen of the cap [88].

  Once the foreign body is removed, the underlying esophageal mucosa should be carefully evaluated. In a setting of underlying esophageal ring or web, dilation can be safely performed in the same session as long as there is no significant mucosal damage [15, 16]. Biopsy of the mid and distal esophagus should be performed to rule out eosinophilic esophagitis even if the mucosa appears normal as its prevalence can be as high as 33% (Fig. 3.5) [16].

- *Sharp or Pointed Objects*

  Even though majority of the foreign bodies can pass spontaneously without any incidence, sharp objects carry higher risk of complications of up to 35% [89, 90]. The risk is particularly higher when the foreign body is in proximal esophagus [91]. Once past the esophagus, the risk of perforation is highest at the ileocecal valve [4, 12]. Therefore, sharp foreign bodies in the upper gastrointestinal tract are considered gastrointestinal emergencies, and endoscopy is warranted regardless of a negative radiologic work-up or even when the object has already passed into the stomach [4, 18]. Common

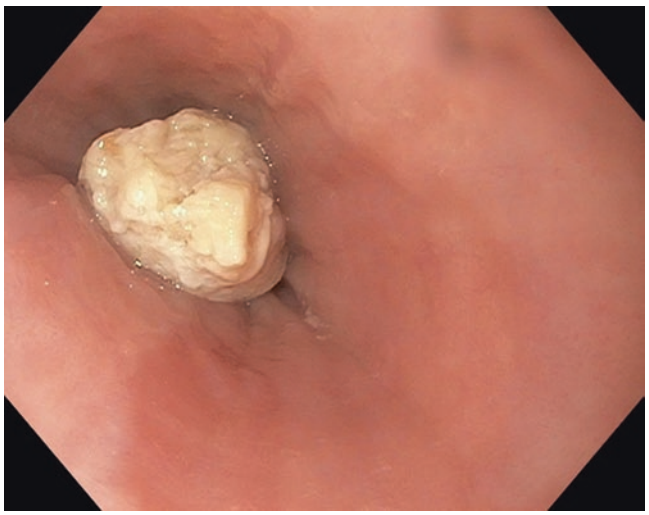


Fig. 3.5 Food bolus obstructed in the esophagus in patient with eosinophilic esophagitis

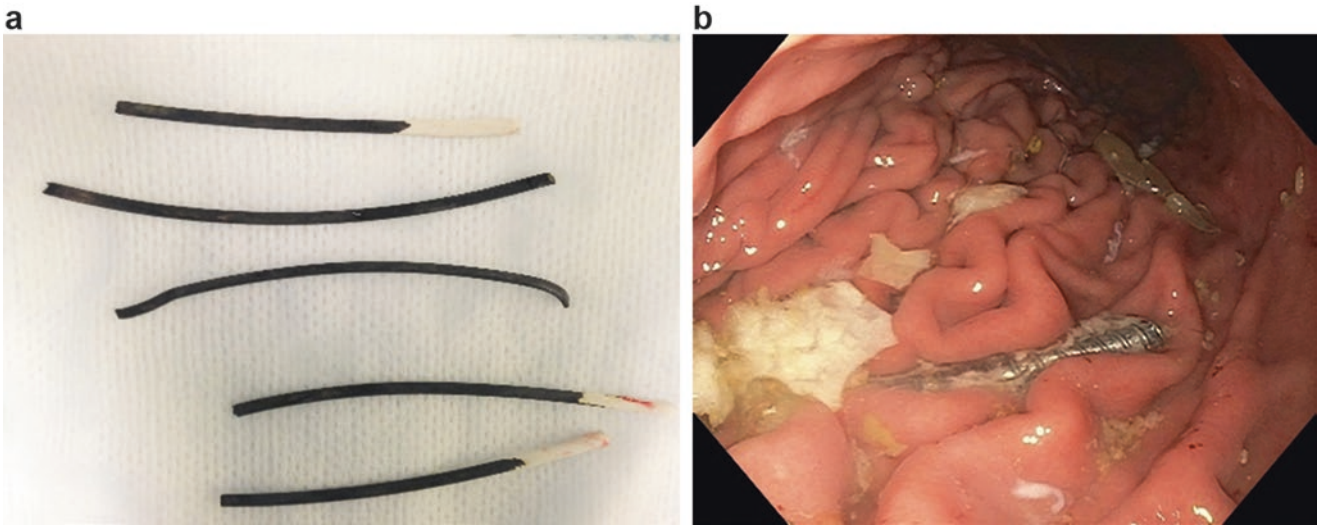


Fig. 3.6 (**a**) Sharp broken wire fragments recovered from the stomach, (**b**) long metal screw in the stomach

sharp foreign bodies include fish bones, chicken bones, pins, needles, and straightened paper clips.

To minimize the risk of mucosal injury during retrieval of sharp objects, an overtube or a protective hood is preferred. Forceps and retrieval nets are commonly used. A rubber tip forceps is ideal to grasp a small thin pointed object like a pin or a needle, while a rat tooth-alligator forceps is suitable for larger object like a chicken bone or paper clip [47]. The sharp or point end of the object should always "trail" and not lead during extraction [8, 47, 65, 67].

If the object passes beyond the reach of endoscope, a daily radiograph should be performed to ensure a safe passage of the object out of the body [8, 12]. Once the object is in the left side of the colon, an unprepped flexible sigmoidoscopy may be performed to retrieve the object in order to avoid any rectal or sphincter injury. If the object does not progress within 3 days or advancing with pointed end, surgical intervention should be considered (Fig. 3.6) [4, 9].

- *Long Objects*

Long objects are defined as those longer than 6 cm in adults, longer than 5 cm in children older than 1 year old, and longer than 3 cm in children less than 1 year old. It is also considered "bulky" if it is larger than 2.5 cm such as toothbrush, pen, spoon, and battery [4, 18, 91, 92]. These long foreign bodies tend to have difficulty passing the duodenal sweep and ileocecal valve with a perforation risk as high as 35% [6, 45]. They should be removed if they are within endoscopic reach and preferably before passing through the pylorus to minimize the risk of perforation and obstruction [4, 18, 91].

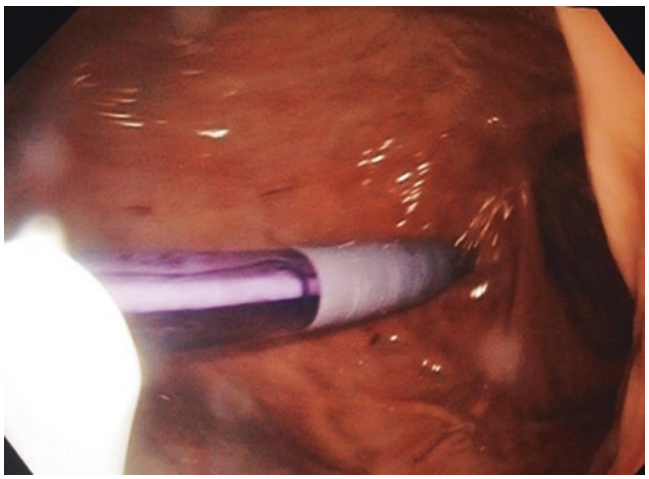


Fig. 3.7 Long ballpoint pen in the stomach of patient

A snare or a basket over a long (>45 cm) overtube is usually a preferred method [4, 9, 18]. However, in order for the foreign body to pass through the overtube, it must align to the tube in longitudinal axis. The retrieval device should grasp the end of the foreign body, rather than the middle, but not too distal that it may slip off. Rearranging the axis of the object can be difficult when it is very long. In these challenging cases, using two snares via a double-channel therapeutic gastroscope to maneuver the object into a desired position is an option (Fig. 3.7) [64, 93].

- *Short Blunt Objects*

The most common ingested blunt foreign body is a coin, particularly in toddlers and small children [12, 91, 94]. Even though majority of coins can pass spontaneously

and patients are asymptomatic [18, 92, 95], coins in the proximal esophagus and in children are less likely to pass due to the small luminal caliber of their esophagus, thus requiring endoscopic intervention [40, 95]. Location and patient's tolerance determine the timing of endoscopy. As long as the patient is asymptomatic, coins in the esophagus can be observed for 24 h, while coins in the stomach and small bowel can be observed with serial imaging for up to 4 weeks (unless the object stays at the same site for more than 3 days) [4, 18, 91].

American pennies, however, may be made of zinc, which is corrosive. Ingested pennies, therefore, carry higher risk of tissue damage and esophageal perforation, prompting a more urgent intervention when needed [96–98].

A retrieval net is a preferred device as it can grasp the coin securely with minimal risk of losing the coin into the airway during extraction [18, 92]. A rat tooth forceps, alligator forceps, or prong grasper are alternative options, especially when the lumen is tight and the net cannot engulf the whole coin [9, 18, 91].

Round small objects with smooth surfaces such as beads, pearls, and buttons are best retrieved with a net or a basket. When possible, a gentle manipulation or a push into the stomach will allow larger room for endoscopic intervention [9, 91]. They can be observed with serial imaging up to 4 weeks if they have passed into the stomach and up to 1 week if distal to duodenum [4, 12, 36]. If the object fails to progress and is not within endoscopic reach, surgical evaluation is warranted.

Video capsule retention occurs in 1.4% of all cases, most commonly occurring in patients with underlying small bowel stricture or diverticular disease [99–101]. The challenge in these instances is in reaching the site of retention rather than retrieving the capsule. A snare and a retrieving net are available in 230–240 cm length, which is compatible with small bowel enteroscope, and are most commonly used in this situation [91]. In stricturing Crohn's disease, corticosteroid may be attempted first to reduce the inflammation of the affected segment of the small bowel, hoping to dislodge the capsule without any endoscopic intervention [91]. Surgery is sometimes inevitable when the impacted site is not reachable endoscopically [100]. The use of self-dissolving patency capsules prior to video capsule endoscopy (VCE) in patients with suspected stricturing small bowel disease may help to identify potential sites of luminal narrowing. These patients are at high risk of obstruction with the video capsule, and therefore alternate small bowel imaging modalities may be used for them (Fig. 3.8).

- *Batteries and Magnets*

  Common household batteries are of two main types: the disc battery and the cylindrical battery. An ingested disc battery can be lethally harmful due to its corrosive properties and possibility of electrical injury. Children are particularly at risk due to a small esophageal lumen [102]. When both poles of the battery are in contact with esophageal mucosa, electrical conduction can cause significant burn to the gastrointestinal tract. Moreover, alkaline fluid and metallic component inside the battery (such as sodium hydroxide, potassium hydroxide, zinc oxide, mercuric oxide, silver oxide, zinc oxide, and lithium oxide) can cause severe

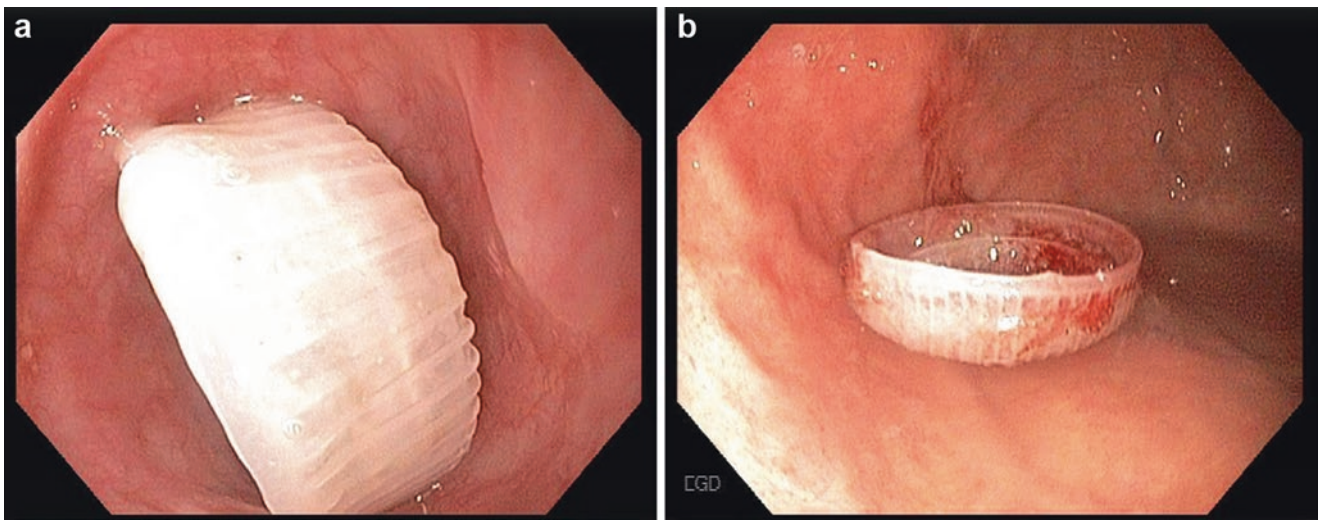


Fig. 3.8 (**a**, **b**) Swallowed bottle cap impacted in the esophagus, retrieved after gently pushing it into the stomach (Image Courtesy: Dr. Emad Qayed)

caustic and chemical injury leading to liquefaction necrosis and esophageal perforation [9, 91]. Absorption of such chemicals leading to mercury toxicity has also been reported [102–105]. Ulceration and necrosis can occur rather quickly, even within 6–8 h after ingestion [28, 106]; therefore, disc battery in the esophagus requires emergent endoscopic intervention. Once batteries pass into the stomach, they are less harmful and can be observed up to 48 h for spontaneous passage [4, 18]. For this reason, self-induced emetic is strongly discouraged as it can cause the battery to migrate from the stomach back into the esophagus. Cylindrical battery ingestion is less common and is also less hazardous [102], but it should still be retrieved if retained in the stomach for longer than 48 h [4].

High-power magnets, made of neodymium, are common household objects and may also be present in children toys [107]. They can present with life-threatening injuries when ingested. It is especially alarming when more than two magnets or a magnet and other metallic foreign body are ingested. The magnetic force between the two can entrap segments of bowel especially when ingested at different times, leading to pressure wall necrosis, fistulization, and perforation, or it can disrupt peristalsis leading to volvulus, intussusception, and obstruction [4, 18, 108–112]. Unfortunately, history regarding the number of foreign body is not always reliable in patients who intentionally ingest the magnet, and assuming that there is only one ingested magnet has led to serious morbidity and mortality in the past [108, 113]. It is therefore recommended that endoscopic retrieval should be attempted even if history and radiologic work-up suggest only one magnet in the gastrointestinal tract [113].

Due to the small size and round thin shape of disc battery and magnet, a retrieval net or a basket is usually an instrument of choice. However, a snare is more appropriate for a cylindrical battery or a long magnet [4, 59, 91].

- *Narcotic Packers*

  A body packer or a drug mule may conceal illicit drugs (usually heroin or cocaine) by wrapping it in latex container such as condom and swallowing the packet or putting it in the rectum. History is, not surprisingly, of little use as the patients tend to lie about the nature of ingested foreign body. Plain radiograph showing a halo sign (oval or round densities surrounded by a gas halo) has a sensitivity of up to 90% [114]. However, both CT and plain radiograph can be falsely negative if the drug is in liquid form [115]. A body packer tends to have multiple packets with 3–5 g of drug in each packet [9]. High index of suspicion is essential in making the correct diagnosis. Patients in high drug trafficking regions who do not give a reliable history should raise the clinician's suspicion to prompt radiologic work-up before proceeding with endoscopy [116]. It is important to note that body packers have been reported in both adult and children [117].

  Endoscopic intervention is contraindicated due to the fear of ruptured and/or leaked content causing rapid absorption and fatal drug overdose [4, 18, 91, 118]. Signs and symptoms of cocaine intoxication include tachycardia, mydriasis, diaphoresis, agitation, hyperthermia, hypertension, chest pain, myocardial infarction, seizure, and ventricular fibrillation, while lethargy, respiratory depression, pinpoint pupils, and constipation can be seen in heroin toxicity [119]. The packet itself can also cause bowel obstruction.

  If the patient is asymptomatic, gentle gastrointestinal purge with close monitoring may be attempted initially [4, 18]. Polyethylene glycol at a rate of 2 L per hour, metoclopramide 10 mg every 6 h intravenously, or erythromycin 500 mg every 6 h intravenously are all safe purgatives in these situations [114, 120, 121]. Surgical intervention is warranted if the packet fails to progress, leaks, ruptures, or if the patient develops intoxicated symptoms or obstructive symptoms [4, 9, 122].

Practical Considerations

- Never lead with a sharp end, have it trail.
- Never extract narcotic packet endoscopically.
- Never leave a foreign body in GI tract without follow-up.
- Never leave airway unprotected.

Foreign Body Removal from Lower Gastrointestinal Tract

The rectum is the most common site of foreign body in lower gastrointestinal tract as majority of the cases are results of transanal insertion rather than oral ingestion [77, 123]. Other common sites are ileocecal valve, hepatic flexure, and splenic flexure where the colon is angulated and a long object might get impacted [77]. Common objects are erotogenic stimulants, long cylindrical household objects, bottles, light bulbs, illegal drugs (in body packer or drug mules), thermometers, and suppository medications [22, 23, 124, 125]. They are usually long and unable to navigate

through the anorectal angle [126]. While up to two-thirds of rectal foreign bodies can be removed transanally by manual manipulation or forceps extraction under local anesthesia [23, 127], foreign bodies proximal to rectosigmoid junction are more likely to require endoscopic intervention or surgery [22, 25, 77, 128]. There is usually no urgent need for surgical intervention in most cases, such as in small blunt foreign bodies in an asymptomatic patient. These patients can be observed until the object moves distally to the rectum where the extraction is easier [126]. If there is no progression over the course of 72 h, endoscopic or surgical intervention is indicated [77, 128].

Imaging study (either a plain radiograph or CT scan) should precede a digital examination and any attempt to manually remove the object. This is to exclude any sharp object that can potentially harm the examiner and also any preexisting perforation that can be worsened by removal attempts [37]. When necessary, attempts of transanal removal should be performed by a gastroenterologist or a colorectal surgeon [125]. A low-lying object (in rectal vault below rectosigmoid junction) can usually be extracted using an anoscope with bimanual manipulation [77, 124, 128].

If transanal digital removal and bimanual manipulation fail, a flexible sigmoidoscopy is warranted. A polypectomy snare and a grasping forceps are the commonly used tools [124]. If the object is smooth cylindrical shape with no edge, a snare is more suitable [77]. Once the object is firmly grasped, the real challenge is maneuvering it through the curvature of rectosigmoid junction and preventing sphincter injury during transanal extraction. A proctoscope or a retractor under full relaxation of anal sphincter either by local or general anesthesia can be used to facilitate extraction and protect the sphincter muscle [77, 124, 128]. Careful maneuvering should be exercised not to "pull out" if the significant resistance is met. It may not be possible for a long object to be extracted without extraluminal manipulation [25]. If endoscopic removal fails, surgical evaluation is warranted [77, 124, 128]. After a successful extraction, a repeat flexible sigmoidoscopy is recommended to evaluate for any mucosal laceration, subtle perforation, or signs of hemorrhage [23, 129]. If significant mucosal injury is found, the patient should be closely observed with serial abdominal examination and imaging study as appropriate [77].

Keys to Successful Endoscopic Retrieval of Foreign Body

- Clear indication.
- Proper timing.
- Know your equipment.
- Practice makes perfect.

Complications

Acute complications of foreign bodies in gastrointestinal tract include pressure necrosis, gastrointestinal bleeding, perforation, bowel obstruction, airway compromise, and cardiac tamponade [9, 18, 130–134]. The risk is higher when the foreign body is sharp and located in the esophagus [12, 44, 45]. Long-term complications include stricture and fistula formation such as tracheoesophageal fistula and aortoenteric fistula [135–137]. The strongest predictor of complications is the duration of lodgment. The risk is significantly higher when the food is lodged in one location for longer than 24 h [132]. For foreign bodies that can transit pass the colon and into the rectum, grade I rectal trauma is the most common lower gastrointestinal tract injury [25].

Conclusions

Foreign bodies in the gastrointestinal tract can often be managed conservatively or endoscopically. Though majority of the foreign bodies can pass spontaneously, it is important to recognize situations in which patients are at high risk of developing complications. Thorough history taking and radiologic evaluation can help triage patients into those who require emergent, urgent, nonurgent endoscopic intervention or just conservative management. The proper use of protective devices, careful selection of retrieval instruments, and skillful endoscopic technique with ex vivo practice are the keys to successful and safe extraction.

References

1. Kramer RE, Lerner DG, Lin T, et al. Management of ingested foreign bodies in children: a clinical report of the NASPGHAN endoscopy committee. J Pediatr Gastroenterol Nutr. 2015; 60(4):562–74.
2. Wyllie R. Foreign bodies in the gastrointestinal tract. Curr Opin Pediatr. 2006;18(5):563–4.
3. Devanesan J, Pisani A, Sharma P, Kazarian KK, Mersheimer WL. Metallic foreign bodies in the stomach. Arch Surg. 1977;112(5):664–5.
4. Ikenberry SO, Jue TL, Anderson MA, et al. Management of ingested foreign bodies and food impactions. Gastrointest Endosc. 2011;73(6):1085–91.
5. Mosca S, Manes G, Martino R, et al. Endoscopic management of foreign bodies in the upper gastrointestinal tract: report on a series of 414 adult patients. Endoscopy. 2001;33(8):692–6.
6. Palta R, Sahota A, Bemarki A, Salama P, Simpson N, Laine L. Foreign-body ingestion: characteristics and outcomes in a lower socioeconomic population with predominantly intentional ingestion. Gastrointest Endosc. 2009;69(3):426–33.
7. Pellerin D, Fortier-Beaulieu M, Gueguen J. The fate of swallowed foreign bodies: experience of 1250 instances of sub-

diaphragmatic foreign bodies in children. Prog Pediatr Radiol. 1969;2(2):286–302.
8. Smith MT, Wong RK. Foreign bodies. Gastrointest Endosc Clin N Am. 2007;17(2):361–82.
9. Sugawa C, Ono H, Taleb M, Lucas CE. Endoscopic management of foreign bodies in the upper gastrointestinal tract: a review. World J Gastrointest Endosc. 2014;6(10):475–81.
10. Yao CC, Wu IT, Lu LS, et al. Endoscopic management of foreign bodies in the upper gastrointestinal tract of adults. Biomed Res Int. 2015;2015:658602.
11. Panieri E, Bass D. The management of ingested foreign bodies in children-a review of 663 cases. Eur J Emerg Med. 1995;2(2):83–7.
12. Webb WA. Management of foreign bodies of the upper gastrointestinal tract: update. Gastrointest Endosc. 1995;41(1):39–51.
13. Arana A, Hauser B, Hachimi-Idrissi S, Vandenplas Y. Management of ingested foreign bodies in childhood and review of the literature. Eur J Pediatr. 2001;160(8):468–72.
14. Watson WA, Litovitz TL, Rodgers GC Jr, et al. 2004 Annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med. 2005;23(5):589–666.
15. Longstreth GF, Longstreth KJ, Yao JF. Esophageal food impaction: epidemiology and therapy. A retrospective, observational study. Gastrointest Endosc. 2001;53(2):193–8.
16. Kerlin P, Jones D, Remedios M, Campbell C. Prevalence of eosinophilic esophagitis in adults with food bolus obstruction of the esophagus. J Clin Gastroenterol. 2007;41(4):356–61.
17. Katsinelos P, Kountouras J, Paroutoglou G, Zavos C, Mimidis K, Chatzimavroudis G. Endoscopic techniques and management of foreign body ingestion and food bolus impaction in the upper gastrointestinal tract: a retrospective analysis of 139 cases. J Clin Gastroenterol. 2006;40(9):784–9.
18. Magalhães-Costa P, Carvalho L, Rodrigues JP, et al. Endoscopic management of Foreign bodies in the upper gastrointestinal tract: an evidence-based review article. GE Portuguese J Gastroenterol. 2016;23(3):142–52.
19. Sperry SL, Crockett SD, Miller CB, Shaheen NJ, Dellon ES. Esophageal foreign-body impactions: epidemiology, time trends, and the impact of the increasing prevalence of eosinophilic esophagitis. Gastrointest Endosc. 2011;74(5):985–91.
20. Evans DC, Wojda TR, Jones CD, Otey AJ, Stawicki SP. Intentional ingestions of foreign objects among prisoners: A review. World J Gastrointest Endosc. 2015;7(3):162.
21. O'Sullivan S, Reardon C, McGreal G, Hehir D, Kirwan W, Brady M. Deliberate ingestion of foreign bodies by institutionalised psychiatric hospital patients and prison inmates. Ir J Med Sci. 1996;165(4):294–6.
22. Kurer MA, Davey C, Khan S, Chintapatla S. Colorectal foreign bodies: a systematic review. Color Dis. 2010;12(9):851–61.
23. Goldberg JE, Steele SR. Rectal foreign bodies. Surg Clin N Am. 2010;90(1):173–84.
24. Caliskan C, Makay O, Firat O, Can Karaca A, Akgun E, Korkut M. Foreign bodies in the rectum: An analysis of 30 patients. Surg Today. 2011;41(6):795–800.
25. Rodríguez-Hermosa JI, Codina-Cazador A, Ruiz B, Sirvent JM, Roig J, Farrés R. Management of foreign bodies in the rectum. Color Dis. 2007;9(6):543–8.
26. Lee JH, Kim HC, Yang DM, et al. What is the role of plain radiography in patients with foreign bodies in the gastrointestinal tract? Clin Imaging. 2012;36(5):447–54.
27. Gayer G, Petrovitch I, Jeffrey RB. Foreign objects encountered in the abdominal cavity at CT. Radiographics Rev Public Radiol Soc N Am Inc. 2011;31(2):409–28.
28. Maves MD, Carithers JS, Birck HG. Esophageal burns secondary to disc battery ingestion. Ann Otol Rhinol Laryngol. 1984;93(4):364–9.
29. Rumack BH, Rumack CM. Disk battery ingestion. JAMA. 1983;249(18):2509–11.
30. Bernstein JM, Burrows SA, Saunders MW. Lodged oesophageal button battery masquerading as a coin: an unusual cause of bilateral vocal cord paralysis. Emerg Med J. 2007;24(3):e15–-e15.
31. Maves M, Lloyd T, Carithers J. Radiographic identification of ingested disc batteries. Pediatr Radiol. 1986;16(2):154–6.
32. Conners GP, Hadley JA. Esophageal coin with an unusual radiographic appearance. Pediatr Emerg Care. 2005;21(10):667–9.
33. Jackson C, Jackson CL. Diseases of the air and food passages of foreign body origin. Philadelphia/London: Wiley Online Library; 1936.
34. Raney LH, Losek JD. Child with esophageal coin and atypical radiograph. J Emerg Med. 2008;34(1):63–6.
35. Schlesinger AE, Crowe JE. Sagittal orientation of ingested coins in the esophagus in children. AJR Am J Roentgenol. 2011;196(3):670–2.
36. Ginsberg GG. Management of ingested foreign objects and food bolus impactions. Gastrointest Endosc. 1995;41(1):33–8.
37. Stack LB, Munter DW. Foreign bodies in the gastrointestinal tract. Emerg Med Clin North Am. 1996;14(3):493–522.
38. Bendig DW, Mackie GG. Management of smooth-blunt gastric foreign bodies in asymptomatic patients. Clin Pediatr. 1990;29(11):642–5.
39. Hachimi-Idrissi S, Corne L, Vandenplas Y. Management of ingested foreign bodies in childhood: our experience and review of the literature. Eur J Emerg Med. 1998;5(3):319–24.
40. Soprano JV, Mandl KD. Four strategies for the management of esophageal coins in children. Pediatrics. 2000;105(1):e5–e5.
41. Sarin N, Monga N, Adams PC. Time to endoscopy and outcomes in upper gastrointestinal bleeding. Can J Gastroenterol. 2009;23(7):489.
42. Tai C-M, Huang S-P, Wang H-P, et al. High-risk ED patients with nonvariceal upper gastrointestinal hemorrhage undergoing emergency or urgent endoscopy: a retrospective analysis. Am J Emerg Med. 2007;25(3):273–8.
43. Targownik LE, Murthy S, Keyvani L, Leeson S. The role of rapid endoscopy for high-risk patients with acute nonvariceal upper gastrointestinal bleeding. Can J Gastroenterol. 2007;21(7):425.
44. Davidoff E, Towne J. Ingested foreign bodies. N Y State J Med. 1975;75(7):1003–7.
45. Vizcarrondo FJ, Brady PG, Nord HJ. Foreign bodies of the upper gastrointestinal tract. Gastrointest Endosc. 1983;29(3):208–10.
46. Bounds BC. Endoscopic retrieval devices. Tech Gastrointest Endosc. 2006;8(1):16–21.
47. Diehl DL, Adler DG, Conway JD, et al. Endoscopic retrieval devices. Gastrointest Endosc. 2009;69(6):997–1003.
48. Ayantunde AA, Oke T. A review of gastrointestinal foreign bodies. Int J Clin Pract. 2006;60(6):735–9.
49. Chiu Y-H, Hou S-K, Chen S-C, et al. Diagnosis and Endoscopic Management of Upper Gastrointestinal Foreign Bodies. Am J Med Sci. 2012;343(3):192–5.
50. Telford J. Management of ingested foreign bodies. Can J Gastroenterol Hepatol. 2005;19(10):599–601.
51. Neustater B, Barkin JS. Extraction of an esophageal food impaction with a Roth retrieval net. Gastrointest Endosc. 1996;43(1):66–7.
52. Gmeiner D, Von Rahden B, Meco C, Hutter J, Oberascher G, Stein H. Flexible versus rigid endoscopy for treatment of foreign body impaction in the esophagus. Surg Endosc. 2007; 21(11):2026–9.
53. Herranz-Gonzalez J, Martinez-Vidal J, Garcia-Sarandeses A, Vazquez-Barro C. Esophageal foreign bodies in adults. Otolaryngol Head Neck Surg Official J Am Acad Otolaryngol Head Neck Surg. 1991;105(5):649–54.
54. Cheng W, Tam P. Foreign-body ingestion in children: experience with 1,265 cases. J Pediatr Surg. 1999;34(10):1472–6.

55. Berggreen PJ, Edwyn Harrison M, Sanowski RA, Ingebo K, Noland B, Zierer S. Techniques and complications of esophageal foreign body extraction in children and adults. Gastrointest Endosc. 1993;39(5):626–30.
56. Kim J, Kim S, Kim J, et al. Management of foreign bodies in the gastrointestinal tract: an analysis of 104 cases in children. Endoscopy. 1999;31(4):302–4.
57. Barth BA, Banerjee S, Bhat YM, et al. Equipment for pediatric endoscopy. Gastrointest Endosc. 2012;76(1):8–17.
58. Varadarajulu S, Banerjee S, Barth BA, et al. GI endoscopes. Gastrointest Endosc. 2011;74(1):1–6. e6.
59. Faigel DO, Stotland BR, Kochman ML, et al. Device choice and experience level in endoscopic foreign object retrieval: an in vivo study. Gastrointest Endosc. 1997;45(6):490–2.
60. Llompart A, Reyes J, Ginard D, et al. Endoscopic management of foreign bodies in the esophagus. Results of a retrospective series of 501 cases. Gastroenterol Hepatol. 2001;25(7):448–51.
61. Barkun A, Liu J, Carpenter S, et al. Update on endoscopic tissue sampling devices. Gastrointest Endosc. 2006;63(6):741–5.
62. Carpenter S, Petersen BT, Chuttani R, et al. Polypectomy devices. Gastrointest Endosc. 2007;65(6):741–9.
63. Chaves D, Ishioka S, Felix V, Sakai P, Gama-Rodrigues J. Removal of a foreign body from the upper gastrointestinal tract with a flexible endoscope: a prospective study. Endoscopy. 2004;36(10):887–92.
64. Li Z-S, Sun Z-X, Zou D-W, Xu G-M, Wu R-P, Liao Z. Endoscopic management of foreign bodies in the upper-GI tract: experience with 1088 cases in China. Gastrointest Endosc. 2006;64(4):485–92.
65. Bertoni G, Sassatelli R, Conigliaro R, Bedogni G. A simple latex protector hood for safe endoscopic removal of sharp-pointed gastroesophageal foreign bodies. Gastrointest Endosc. 1996;44(4):458–61.
66. Tierney WM, Adler DG, Conway JD, et al. Overtube use in gastrointestinal endoscopy. Gastrointest Endosc. 2009;70(5):828–34.
67. Bertoni G, Pacchione D, Sassatelli R, Ricci E, Mortilla MG, Gumina C. A new protector device for safe endoscopic removal of sharp gastroesophageal foreign bodies in infants. J Pediatr Gastroenterol Nutr. 1993;16(4):393–6.
68. Brady P. Esophageal foreign bodies. Gastroenterol Clin N Am. 1991;20(4):691–701.
69. Rogers BG, Kot C, Meiri S, Epstein M. An overtube for the flexible fiberoptic esophagogastroduodenoscope. Gastrointest Endosc. 1982;28(4):256–7.
70. Wells CD, Fleischer DE. Overtubes in gastrointestinal endoscopy. Am J Gastroenterol. 2008;103(3):745–52.
71. Berkelhammer C, Madhav G, Lyon S, Roberts J. “Pinch” injury during overtube placement in upper endoscopy. Gastrointest Endosc. 1993;39(2):186–8.
72. Holderman WH, Etzkorn KP, Patel SA, Harig JM, Watkins JL. Endoscopic findings and overtube-related complications associated with esophageal variceal ligation. J Clin Gastroenterol. 1995;21(2):91–4.
73. Jeffries M, Scheiman J. Overtube separation. Gastrointest Endosc. 1998;47(5):435–6.
74. Levy R, Kaur S, Uzer M. Separation of an overtube from the bite block during band ligation of esophageal varices. Gastrointest Endosc. 1997;46(1):66–8.
75. Dinning JP, Jaffe PE. Delayed presentation of esophageal perforation as a result of overtube placement. J Clin Gastroenterol. 1997;24(4):250–2.
76. El-Newihi H, Mihas A. Esophageal perforation as a complication of endoscopic overtube insertion. Am J Gastroenterol. 1994;89(6):953–4.
77. Anderson KL, Dean AJ. Foreign bodies in the gastrointestinal tract and anorectal emergencies. Emerg Med Clin North Am. 2011;29(2):369–400.
78. Roberts JR. Hedges JR. Elsevier Health Sciences: Clinical procedures in emergency medicine; 2009.
79. Pavlidis TE, Marakis GN, Triantafyllou A, Psarras K, Kontoulis TM, Sakantamis AK. Management of ingested foreign bodies. How justifiable is a waiting policy? Surg Laparosc Endosc Percutan Tech. 2008;18(3):286–7.
80. Conway W, Sugawa C, Ono H, Lucas C. Upper GI foreign body. Surg Endosc. 2007;21(3):455–60.
81. Eisen GM, Baron TH, Dominitz JA, et al. Guideline for the management of ingested foreign bodies. Gastrointest Endosc. 2002;55(7):802–6.
82. Zhang S, Cui Y, Gong X, Gu F, Chen M, Zhong B. Endoscopic management of foreign bodies in the upper gastrointestinal tract in south China: a retrospective study of 561 cases. Dig Dis Sci. 2010;55(5):1305–12.
83. Ferrucci JT Jr, Long JA Jr. Radiologic treatment of esophageal food impaction using intravenous glucagon 1. Radiology. 1977;125(1):25–8.
84. Sodeman TC, Harewood GC, Baron TH. Assessment of the predictors of response to glucagon in the setting of acute esophageal food bolus impaction. Dysphagia. 2004;19(1):18–21.
85. Tibbling L, Bjorkhoel A, Jansson E, Stenkvist M. Effect of spasmolytic drugs on esophageal foreign bodies. Dysphagia. 1995;10(2):126–7.
86. Trenkner S, Maglinte D, Lehman G, Chernish S, Miller R, Johnson C. Esophageal food impaction: treatment with glucagon. Radiology. 1983;149(2):401–3.
87. Vicari JJ, Johanson JF, Frakes JT. Outcomes of acute esophageal food impaction: success of the push technique. Gastrointest Endosc. 2001;53(2):178–81.
88. Saeed Z, Michaletz P, Feiner S, Woods K, Graham D. A new endoscopic method for managing food impaction in the esophagus. Endoscopy. 1990;22(5):226–8.
89. Rösch W, Classen M. Fiber endoscopic foreign body removal from the upper gastrointestinal tract. Endoscopy. 1972;4(04):193–7.
90. Kay M, Wyllie R. Pediatric foreign bodies and their management. Curr Gastroenterol Rep. 2005;7(3):212–8.
91. Chauvin A, Viala J, Marteau P, Hermann P, Dray X. Management and endoscopic techniques for digestive foreign body and food bolus impaction. Dig Liver Dis. 2012;45(7):529–42.
92. Pfau PR. Removal and management of esophageal foreign bodies. Tech Gastrointest Endosc. 2014;16(1):32–9.
93. Yong P, Teh C, Look M, et al. Removal of a dinner fork from the stomach by double-snare endoscopic extraction. Hong Kong Med J. 2000;6(3):319–21.
94. Little DC, Shah SR, St Peter SD, et al. Esophageal foreign bodies in the pediatric population: our first 500 cases. J Pediatr Surg. 2006;41(5):914–8.
95. Waltzman ML, Baskin M, Wypij D, Mooney D, Jones D, Fleisher G. A randomized clinical trial of the management of esophageal coins in children. Pediatrics. 2005;116(3):614–9.
96. Bennett DR, Baird CJ, Chan K-M, et al. Zinc toxicity following massive coin ingestion. Am J Forensic Med Pathol. 1997;18(2):148–53.
97. A-Kader HH. Foreign body ingestion: children like to put objects in their mouth. World J Pediatr. 2010;6(4):301–10.
98. Dhawan SS, Ryder KM, Pritchard E. Massive penny ingestion: the loot with local and systemic effects. J Emerg Med. 2008;35(1):33–7.
99. Liao Z, Gao R, Xu C, Li Z-S. Indications and detection, completion, and retention rates of small-bowel capsule endoscopy: a systematic review. Gastrointest Endosc. 2010;71(2):280–6.

100. Höög CM, Bark L-Å, Arkani J, Gorsetman J, Broström O, Sjöqvist U. Capsule retentions and incomplete capsule endoscopy examinations: an analysis of 2300 examinations. Gastroenterol Res Pract. 2011;2012:518718.
101. Ziachehabi A, Maieron A, Hoheisel U, Bachl A, Hagenauer R, Schöfl R. Capsule retention in a Zenker's diverticulum. Endoscopy. 2010;43:E387–E387.
102. Litovitz T, Whitaker N, Clark L, White NC, Marsolek M. Emerging battery-ingestion hazard: clinical implications. Pediatrics. 2010;125(6):1168–77.
103. Kulig K, Rumack CM, Rumack BH, Duffy JP. Disk battery ingestion: elevated urine mercury levels and enema removal of battery fragments. JAMA. 1983;249(18):2502–4.
104. Mant T, Lewis J, Mattoo T, et al. Mercury poisoning after disc-battery ingestion. Hum Exp Toxicol. 1987;6(2):179–81.
105. Sudhakar PJ, Al-Dossary J, Malik N. Spondylodiscitis complicated by the ingestion of a button battery: a case report. Korean J Radiol. 2008;9(6):555–8.
106. Votteler TP, Nash JC, Rutledge JC. The hazard of ingested alkaline disk batteries in children. JAMA. 1983;249(18):2504–6.
107. Commission UCPS. CPSC warns high-powered magnets and children make a deadly mix. 2011.
108. Control CFD, Prevention. Gastrointestinal injuries from magnet ingestion in children--United States, 2003-2006. MMWR Morb Mortal Wkly Rep. 2006;55(48):1296–300.
109. De Roo AC, Thompson MC, Chounthirath T, et al. Rare-earth magnet ingestion–related injuries among children, 2000–2012. Clin Pediatr. 2013;52(11):1006–13.
110. Abbas MI, Oliva-Hemker M, Choi J, et al. Magnet ingestions in children presenting to US emergency departments, 2002–2011. J Pediatr Gastroenterol Nutr. 2013;57(1):18–22.
111. Hwang J-B, Park MH, Choi S-O, Park W-H, Kim AS. How strong construction toy magnets are! A gastro-gastro-duodenal fistula formation. J Pediatr Gastroenterol Nutr. 2007;44(2):291–2.
112. Otjen JP, Rohrmann CA Jr, Iyer RS. Imaging pediatric magnet ingestion with surgical-pathological correlation. Pediatr Radiol. 2013;43(7):851–9.
113. Butterworth J, Feltis B. Toy magnet ingestion in children: revising the algorithm. J Pediatr Surg. 2007;42(12):e3–5.
114. Traub SJ, Hoffman RS, Nelson LS. Body packing — the internal concealment of illicit drugs. N Engl J Med. 2003;349(26):2519–26.
115. Mozes O, Guranda L, Portnoy O, Apter S, Konen E, Amitai M. Radiographic features of intracorporeally smuggled liquid cocaine. Forensic Sci Med Pathol. 2014;10(4):535–42.
116. Lancashire M, Legg P, Lowe M, Davidson SM, Ellis B. Surgical aspects of international drug smuggling. BMJ. 1988;296(6628):1035–7.
117. Beno S, Calello D, Baluffi A, Henretig FM. Pediatric body packing: drug smuggling reaches a new low. Pediatr Emerg Care. 2005;21(11):744–6.
118. Boehnert M, Lewander W, Gaudreault P, Lovejoy F Jr. Advances in clinical toxicology. Pediatr Clin N Am. 1985;32(1):193–211.
119. Booker RJ, Smith JE, Rodger MP. Packers, pushers and stuffers—managing patients with concealed drugs in UK emergency departments: a clinical and medicolegal review. Emerg Med J. 2009;26(5):316–20.
120. Farmer JW, Chan SB. Whole body irrigation for contraband body packers. J Clin Gastroenterol. 2003;37(2):147–50.
121. Hoffman RS, Smilkstein MJ, Goldfrank LR. Whole bowel irrigation and the cocaine body-packer: a new approach to a common problem. Am J Emerg Med. 1990;8(6):523–7.
122. June R, Aks SE, Keys N, Wahl M. Medical outcome of cocaine body stuffers. J Emerg Med. 2000;18(2):221–4.
123. Lyons M 2nd, Tsuchida A. Foreign bodies of the gastrointestinal tract. Med Clin North Am. 1993;77(5):1101–14.
124. Koornstra JJ, Weersma RK. Management of rectal foreign bodies: description of a new technique and clinical practice guidelines. World J Gastroenterol: WJG. 2008;14(27):4403.
125. Clarke DL, Buccimazza I, Anderson FA, Thomson SR. Colorectal foreign bodies. Color Dis. 2005;7(1):98–103.
126. Barone JE, Sohn N, Nealon TF Jr. Perforations and foreign bodies of the rectum: report of 28 cases. Ann Surg. 1976;184(5):601.
127. Wigle RL. Emergency department management of retained rectal foreign bodies. Am J Emerg Med. 1988;6(4):385–9.
128. Lake JP, Essani R, Petrone P, Kaiser AM, Asensio J, Beart RW Jr. Management of retained colorectal foreign bodies: predictors of operative intervention. Dis Colon Rectum. 2004;47(10):1694–8.
129. Eftaiha M, Hambrick E, Abcarian H. Principles of management of colorectal foreign bodies. Arch Surg. 1977;112(6):691–5.
130. Uyemura MC. Foreign body ingestion in children. Am Fam Physician. 2005;72(2):287–91.
131. Schwartz J, Graham DY. Toothpick perforation of the intestines. Ann Surg. 1977;185(1):64.
132. Matsubara M, Hirasaki S, Suzuki S. Gastric penetration by an ingested toothpick successfully managed with computed tomography and endoscopy. Intern Med. 2007;46(13):971–4.
133. Vesna D, Tatjana A, Slobodan S, Slobodan N. Cardiac tamponade caused by migration of a swallowed sewing needle. Forensic Sci Int. 2004;139(2):237–9.
134. Sharland MG, McCaughan BC. Perforation of the esophagus by a fish bone leading to cardiac tamponade. Ann Thorac Surg. 1993;56(4):969–71.
135. Başer M, Arslantürk H, Kisli E, et al. Primary aortoduodenal fistula due to a swallowed sewing needle: a rare cause of gastrointestinal bleeding. Ulus Travma Acil Cerrahi Derg Turkish J Trauma Emerg Surg TJTES. 2007;13(2):154.
136. D'Costa H, Bailey F, McGavigan B, George G, Todd B. Perforation of the oesophagus and aorta after eating fish: an unusual cause of chest pain. Emerg Med J. 2003;20(4):385–6.
137. Sica GS, Djapardy V, Westaby S, Maynard ND. Diagnosis and management of aortoesophageal fistula caused by a foreign body. Ann Thorac Surg. 2004;77(6):2217–8.

Newer and Evolving Endoscopic Therapies for Gastroesophageal Reflux Disease

4

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Introduction

Gastroesophageal reflux disease (GERD) is characterized by the reflux of gastric contents into the esophagus, resulting in symptoms of heartburn and regurgitation or visible inflammation such as erosive esophagitis. In North America, the prevalence of GERD, when defined as at least weekly heartburn and/or acid regurgitation, is as high as 18.1–27.8% [1]. GERD is the most common disorder of the esophagus, the most common reason for outpatient gastroenterology consultation, and the most common reason for elective esophagogastroduodenoscopy (EGD) [2].

The major pathophysiological causes of GERD include an incompetent lower esophageal sphincter (LES) as a result of hypotensive LES, increased intra-abdominal pressure which overwhelms a near-normal LES, inappropriate transient LES relaxations (TLESRs), the presence of anatomic defects such as sliding hiatal hernias, and decreased contractile response of the diaphragm [3]. These causes can be compounded by esophageal dysmotility, reduced gastric acid clearance, delayed gastric emptying, poor mucus and bicarbonate secretion, and hypersensitivity to acid or bile reflux. These mechanisms result in heartburn and regurgitation but may also result in extraesophageal symptoms such as chest pain, cough, voice hoarseness, and aspiration pneumonia. Prolonged GERD results in complications such as esophageal strictures, Barrett's esophagus, and esophageal adenocarcinoma [4].

Proton pump inhibitors (PPIs) and histamine receptor antagonists ("H2-blockers") have revolutionized the treatment of GERD and are able to yield symptomatic relief in the majority of compliant patients with a once or twice daily regimen. PPIs are some of the best-selling drugs on the market both domestically and internationally. In the United States, 18.7 million prescriptions were written for esomeprazole (Nexium, AstraZeneca, Wilmington, DE) from 2013 to 2014, generating $6.3 billion in sales during that period [5]. Its predecessor, omeprazole (Prilosec, AstraZeneca), was the first drug ever to generate more than $5 billion in annual sales. Overall sales will likely further increase given that multiple PPIs including lansoprazole, omeprazole, and esomeprazole are now available over the counter.

However, there remain significant challenges in the management of GERD. In addition to long-term safety concerns such as drug-drug interactions and associations with osteoporosis, hypergastrinemia, *Clostridium difficile* colitis, pneumonia, and bacterial overgrowth, lifelong PPI therapy can be expensive over time, and the prospect of taking any medication for an entire lifetime is unappealing for many patients [6]. Furthermore, despite lifestyle modifications and maximal medical management, 20–40% of patients with GERD will have incomplete or unsatisfactory responses to PPIs due to a number of factors, including hypersensitivity, volume or bile refluxate, and poor compliance [7, 8]. Finally, PPIs and H2 blockers do not address the underlying anatomic and neuromuscular deficits responsible for GERD and are thus unable to eliminate symptoms of regurgitation.

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Surgical Management and the Rationale for an Endoscopic Approach

Surgery for GERD is indicated when standard medical therapy fails or is no longer feasible due to cost, patient noncompliance, drug-drug interactions, or adverse effects/intolerance. Surgery is also indicated when there are sequelae of GERD such as strictures, refractory asthma, aspiration pneumonia, or esophageal bleeding. The current gold standard surgical treatment for GERD is laparoscopic Nissen fundoplication (LNF) with hiatal hernia repair, if needed. LNF was first introduced in 1991 and remains the most frequently utilized surgical operation for GERD [9]. The goal of LNF is to treat the underlying anatomical causes of GERD by reestablishing the competence of the LES. Specifically, the fundoplication increases LES pressure, increases the length of the intra-abdominal segment of the LES, decreases gastroesophageal (GE) junction compliance, decreases the frequency of TLESRs, and restores the angle of His [3].

LNF has been demonstrated to have excellent outcomes, with improved relief of GERD symptoms and reduced PPI use with good long-term cost efficacy. Surgical series have shown average GERD cure rates approaching 87.7% at 5 years and 72.9% at 10 years [10]. However, there have been limitations to LNF, partly due to inherent surgical and anesthetic risks and partly due to recurrent symptoms necessitating resumption of PPI therapy. The mortality from LNF is quite low; a large cohort analysis of 7531 patients from the National Surgical Quality Improvement Program (NSQIP) database from 2005 to 2009 showed that overall surgical mortality for LNF was <1% and <0.05% among patients younger than 70 years of age [11]. However, there are a number of side effects, including postoperative dysphagia (often transient but may affect over 70% of patients in some studies), bloating, inability to belch, and increased flatus [10].

Furthermore, a significant number of patients will either need repeat anti-reflux surgery or require continuation or resumption of PPI use for persistent or recurrent symptoms. Randomized trials have demonstrated the non-superiority of surgical fundoplication when compared to PPI therapy at 5-year follow-up with regard to remission of GERD symptoms [12]. Many patients also simply do not desire surgery due to various reasons including costs, potential adverse events, and its inherently invasive nature. The potential for still requiring lifelong PPI therapy despite surgery makes surgical management even less appealing. As a result, despite the high rates of clinical success of LNF, the volume of LNF has actually declined over time, and there has been continued demand and research for a less invasive alternative [12].

For these reasons, an endoscopic option continues to remain an attractive alternative to medical and surgical therapy for GERD. Endoscopic intervention is minimally invasive, typically an outpatient procedure, and may avoid adverse events commonly seen with LNF such as bloating and dysphagia. Endoscopic techniques also do not preclude future LNF if symptoms recur or persist. The main challenge of endoscopic GERD treatment is that there are already highly efficacious minimally invasive alternative options such as LNF, as well as well-tolerated and highly effective antisecretory therapies such as PPIs. The ultimate goal of endoscopic management of GERD is to address, in a minimally invasive way, the underlying mechanisms of GERD (similar to LNF) while eliminating the need for continued medical management.

Indications and Contraindications for Endoscopic Management

In general, endoscopic therapies for GERD fall into three major categories: implantation or injection of bulking agents, radiofrequency treatment, and endoscopic tissue apposition.

Indications

Endoscopic therapies for GERD are generally indicated for patients with documented symptomatic GERD, positive esophageal pH studies, and hiatal hernias <3 cm in length [3]. The ideal candidate for an endoscopic option is the patient who does not desire surgery, does not remember to take medications or does not wish to be on lifelong PPI therapy, is responsive to or was initially responsive to PPI therapy, and/or has a symptomatic small hiatal hernia.

Additionally, data from a prospective registry of patients undergoing transoral incisionless fundoplication (TIF), a type of endoscopic anti-reflux procedure, demonstrated that for patients with chronic GERD, persistent typical symptoms while on PPIs (GERD health-related quality-of-life [HRQL] score ≥15) and an objectively confirmed diagnosis of GERD were the best predictors of success, and therefore those parameters should also be considered when evaluating patients for endoscopic therapy [13].

Indications

- Documented symptomatic GERD.
- Positive esophageal pH studies.
- Hiatal hernias <3 cm in length.
- Responsive or initially responsive to PPI therapy.
- Patient does not desire surgery.
- Patient noncompliant with medications or does not wish to remain on long-term PPI.
- GERD HRQL ≥15 while on PPI therapy.

Contraindications

There are no absolute contraindications for endoscopic management of GERD. In general, patients with evidence of pulmonary disease, achalasia, dysphagia, Barrett's esophagus, large hiatal hernias (3 cm or greater), morbid obesity, severe medical comorbidities, collagen vascular disease, or esophageal dysmotility disorders were excluded from studies involving endoscopic anti-reflux technologies [3]. While they are not relative contraindications, they were excluded from the original studies for a variety of reasons; patients with Barrett's esophagus were initially excluded due to concern that thermal treatments would lead to progression of Barrett's esophagus, and patients with dysphagia were excluded due to concern for worsening of their swallowing difficulties.

Patients who are pregnant should also be excluded. Furthermore, endoscopic management of GERD should not be offered to patients who only periodically need medical therapy for GERD symptoms. Patients specifically being considered for radiofrequency treatment should be excluded if they have any implants near the LES which may conduct radiofrequency energy.

Relative Contraindications

- Severe cardiopulmonary disease or medical comorbidities
- Morbid obesity
- Achalasia
- Esophageal dysmotility disorders, such as scleroderma
- Dysphagia
- Barrett's esophagus
- Large hiatal hernia (3 cm or greater)
- Collagen vascular disease
- Pregnancy
- Patients who only periodically need PPIs for symptoms
- Implants near the LES which may conduct radiofrequency energy (RF treatment only)

Injectable or Implantable Bulking Agents

The theory of implantable and injectable bulking agents into the GE junction is to augment the natural mechanical barrier to reflux. The technique was first reported in 1984 by O'Conner and colleagues in an experimental canine model to control reflux using a bulking agent of either bovine dermal collagen or Teflon (polytetrafluoroethylene) resin into the distal esophagus of dogs with surgically induced GERD [14]. The procedure required multiple, sometimes large-volume injections but with modest efficacy and poor durability. Over the years, multiple further attempts were made to develop an injectable or implantable bulking agent; however, none of these treatments remain on the market at this time due to either lack of sustainable clinical efficacy or due to serious adverse events. For historical purposes, the four injectable bulking agents which are no longer available include Enteryx, Gatekeeper, Plexiglas microspheres, and Durasphere [6].

The Enteryx (Boston Scientific, Natick, MA) procedure involved injecting a solid-state biopolymer of ethylene vinyl alcohol intramurally into the distal esophagus. It was recalled in 2005 following reports of severe adverse events in which injection resulted in esophageal perforation, one death due to esophageal abscess, and one death due to aortic puncture with subsequent aortoenteric fistula formation [6]. The Gatekeeper (Medtronic Inc., Minneapolis, MN) system was an injectable hydrogel prosthesis that was voluntarily withdrawn by the manufacturer due to poor efficacy as well as various severe adverse events including severe chest pain, pleural effusion, and esophageal perforation [15]. Plexiglas microspheres (Arkema Inc., Bristol, PA) were injectable polymethylmethacrylate beads which had been used in one small study to treat GERD in human subjects [16]. The compound was approved by the US Food and Drug Administration (FDA) as biologically inert filler in cosmetic treatments; however, it was never approved as an endoluminal injection for GERD. Finally, Durasphere (Carbon Medical Technologies, St. Paul, MN) was comprised of injectable carbon-coated beads suspended in a water-based gel. A small study demonstrated improvement in DeMeester score and PPI dependence at 12 months of follow-up after injection of these beads [17]. The compound is FDA approved for treatment of urinary stress incontinence but also never received approval as an endoscopic treatment for GERD.

Radiofrequency (RF) Treatment

Radiofrequency treatment was approved in April 2000 for endoscopic management of GERD. The Stretta device (Mederi Therapeutics Inc., Norwalk, CT) uses a transoral flexible catheter with a balloon-basket assembly fitted with four titanium electrodes to deliver radiofrequency energy into the esophageal wall, the LES complex, and gastric cardia (Figs. 4.1 and 4.2) [18]. The therapeutic mechanisms are complex and not completely understood. Radiofrequency energy delivery to the LES was originally thought to involve tissue necrosis causing local inflammation, collagen deposition, tissue remodeling, and muscular thickening of

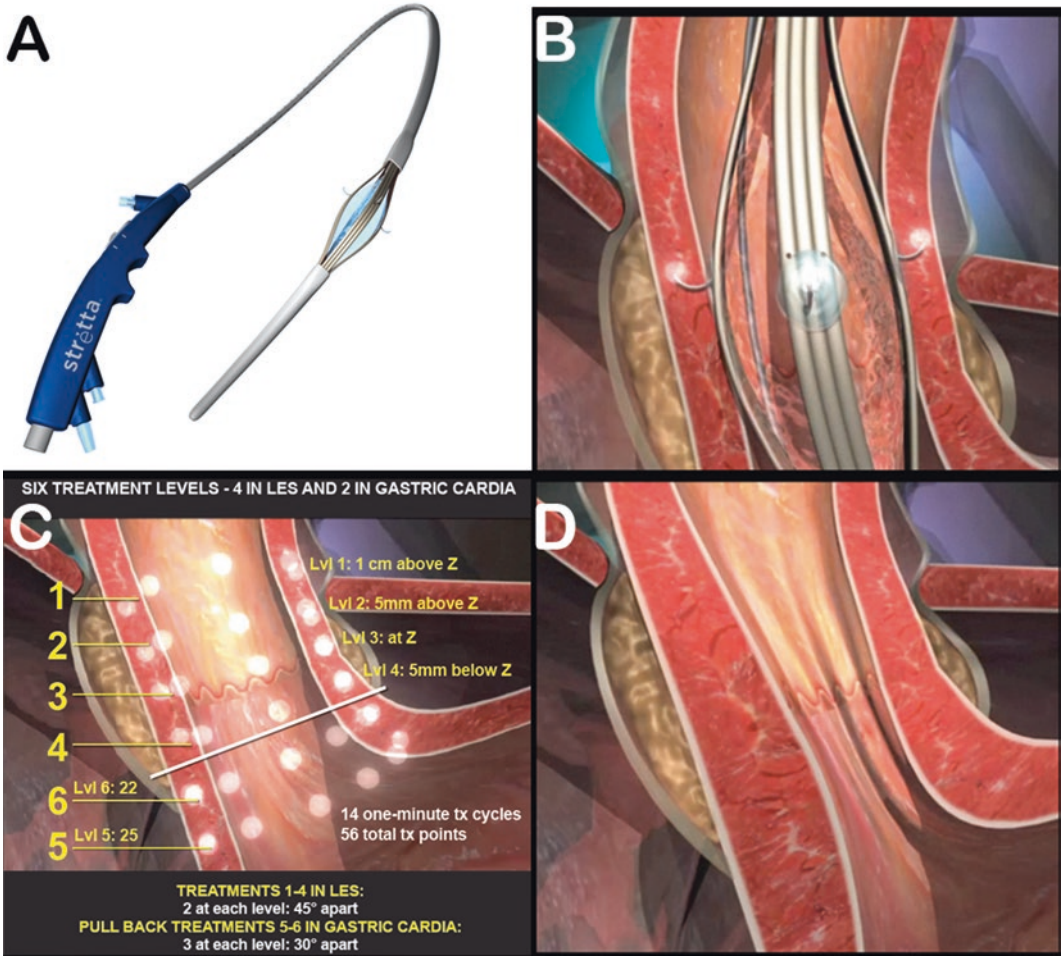

Fig. 4.1 Stretta RF procedure. (**a**) The Stretta catheter is a flexible soft-tip catheter similar to a 20-French Maloney bougie, measuring about 65 cm in length. (**b**) The catheter is passed transorally, positioned 1 cm above the Z-line, balloon inflated, needles delivered, followed by delivery of radiofrequency energy. (**c**) A total of four levels of treatment are performed, at 1 cm above the Z-line, 5 mm above the Z-line, at the Z-line, and 5 mm below the Z-line, with two treatments 45° apart at each level. The catheter is advanced into the stomach, balloon inflated and pulled back gently into the hiatus, followed by delivery of radiofrequency energy to complete two additional levels of treatment in the gastric cardia, with three treatments 30° apart at each level. (**d**) The RF procedure is postulated to improve GERD by increasing the LES thickness and decreasing TLESRs (Images courtesy of Mederi Therapeutics, Inc.)

the LES, resulting in reduced tissue compliance and tightening of the LES. Subsequent studies have demonstrated a decrease in the frequency of TLESRs, which is thought to represent the sequelae of thermal neurolysis or alteration of vagal efferent fibers, resulting in inhibition of the motor component of reflux episodes [19].

Stretta RF Therapy

The procedure is typically performed under anesthesia. A bite block is placed into the patient's mouth, and the patient is placed into the left lateral semirecumbent position. A pre-procedure EGD is performed to evaluate the patient's anatomy and determine their suitability for undergoing Stretta. Specifically, the gastroesophageal junction is carefully evaluated, and the distance from the incisors to the Z-line is measured.

Next, the Stretta system is introduced. The Stretta catheter is flexible with a soft tip similar to a 20-French Maloney bougie. The total length from the handle to the RF needles is 65 cm. A balloon-basket assembly at the distal end is expandable to a maximum 3 cm outer diameter. This is used to position and deploy four 5.5 mm nickel-titanium needle electrodes into the smooth muscle of the GE junction. The four-channel catheter incorporates eight temperature sensors which provide information to the RF generator control unit regarding tissue and mucosal temperature.

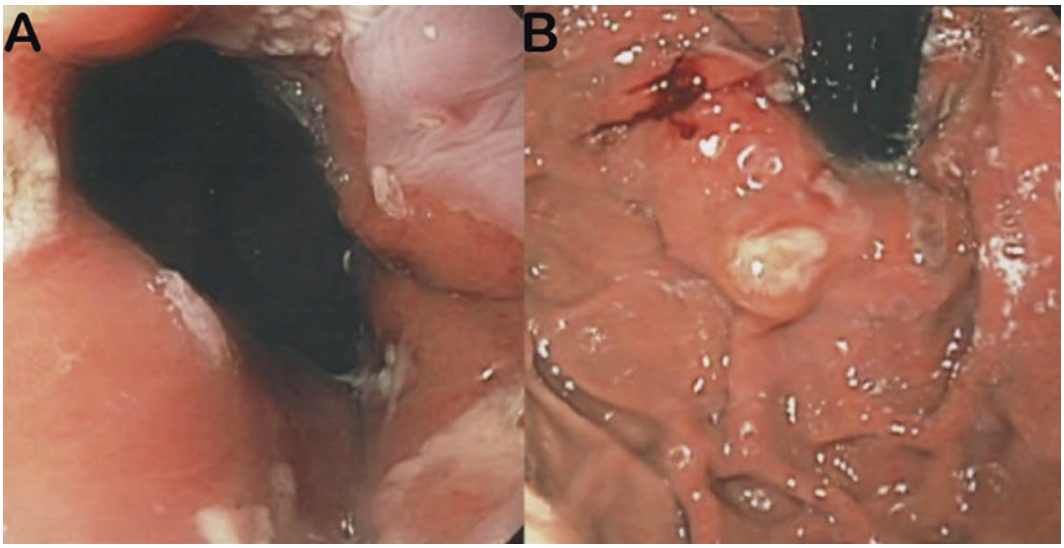

Fig. 4.2 Clinical images of Stretta RF procedure. (**a**) Anterograde view of the GE junction following Stretta treatment. (**b**) Retroflexed views of the gastric cardia and gastroesophageal junction following Stretta treatment (From Triadafilopoulos [57])

Once the needles from the Stretta catheter are properly deployed within the muscle of the GEJ, there is a distinctive reduction in impedance from >500 ohms to 100–300 ohms, which confirms muscle contact. A four-channel RF generator then delivers RF energy (465 kHz, 2–5 watts) to each needle electrode. The temperature is monitored at the tip of each needle, allowing modulation of power output to achieve a target tissue temperature of 85 °C for 60 s. Mucosal temperature is similarly monitored and maintained below 30 °C by delivering chilled plain water (30 mL/min) through the catheter tip, while suctioning via a separate channel to avoid fluid accumulation.

A total of four levels of treatment are performed, at 1 cm above the Z-line, at 5 mm above the Z-line, at the Z-line, and at 5 mm below the Z-line, with two treatments 45 degrees apart at each level. Subsequently, the catheter is advanced into the stomach, balloon inflated and pulled back gently into the hiatus, followed by delivery of radiofrequency energy to complete two additional levels of treatment in the gastric cardia, with three treatments 30° apart at each level. Overall, patients receive RF energy at 56 treatment sites over a period of 35 min. Following completion of the procedure, repeat endoscopy is performed to assess the treatment.

Patients should follow up with their gastroenterologist at regular intervals, initially at every 3 months for the first year, every 6 months for the second year, and annually thereafter. Initial follow-up focuses on adverse events related to the procedure, while later follow-up focuses on the degree of reflux symptoms.

Review of Existing Data

Stretta is the earliest FDA-approved endoscopic procedure for the management of GERD still available today and is currently the most widely studied and widely used of any minimally invasive treatment for GERD. As a result, it has benefitted from a large body of clinical investigation, including randomized controlled trials, long-term follow-up studies, and multiple reviews and meta-analyses.

A total of four randomized controlled trials have been published either comparing RF therapy (Stretta) versus PPI or Stretta versus sham procedure plus PPI, with anywhere from 6- to 12-month follow-up [20–23]. The majority of trials demonstrated that patients receiving Stretta experienced significant reduction in heartburn symptoms and quality-of-life (QOL) scores and greater reduction or discontinuation of PPI use when compared to patients receiving sham procedure. Subgroup analysis of the initial randomized trial by Corley and colleagues showed that responders who had >50% improvement in QOL scores also had significant decreases in 24-hour acid exposure in these patients compared to nonresponders [20]. However, a subsequent randomized trial by Coron and colleagues showed no difference in heartburn scores, QOL scores, mean daily dose of PPI at 6 or 12 months, or esophageal acid exposure between patients receiving either RF treatment or PPI alone [21].

The randomized trial by Aziz and colleagues studied the effects of a single treatment of Stretta, versus double treatment

Steps to the Stretta RF Therapy Procedure

Initial endoscopy	Record distance from incisors to Z-line
Passage of catheter over guidewire	After endoscopy and measurement of the distance from the bite block to the Z-line and diaphragm, a stiff coated guidewire with flexible tip is placed
	The endoscope is removed, and the Stretta catheter is passed over the guidewire
Initial radiofrequency delivery	The catheter is positioned 1 cm above the Z-line. Guidewire is removed
	Balloon inflated with low pressure (2.5 psi) to coapt the basket and mucosa
	Needles are deployed by advancing a thumb control on the catheter handle
	Radiofrequency energy delivered
	Target tissue temperature of 85 °C for 60 s. During delivery, mucosa is irrigated and cooled below 30 °C with chilled plain water at 30 mL/min. Suction provided via separate channel to avoid fluid accumulation
	Rotate catheter 45° and repeat treatment to create the first ring of eight lesions
Four anterograde treatments	First treatment ring (eight lesions) is 1 cm above the Z-line
	Balloon inflated and needles are deployed at 0.5 cm above Z-line
	Second treatment ring (eight lesions) is 0.5 cm above the Z-line
	Balloon inflated and needles are deployed at Z-line
	Third treatment ring (eight lesions) is at the Z-line
	Balloon inflated and needles are deployed at 0.5 cm below Z-line
	Fourth treatment ring (eight lesions) is 0.5 cm below the Z-line
Passage of catheter into stomach	After completing four anterograde rings of lesions, catheter is passed into the stomach
	Catheter is fully inflated to 25 cc air, pulled back into the hiatus until resistance is met
	Needles are deployed
	Radiofrequency energy delivered
	Rotate catheter 45° clockwise from original position and repeat treatment
	Rotate catheter 45° counterclockwise from original position and repeat treatment
Two retrograde treatments	First retrograde treatment ring (12 lesions)
	Second retrograde treatment ring by inflating balloon to 22 cc air and pulling back until resistance is met
	Balloon inflated and needles deployed. Treatment is delivered. Rotate 45° clockwise and 45° counterclockwise and repeat (12 lesions)
Final endoscopy	Remove device, assess RFA treatment effect. Total four anterograde treatments (8 lesions each), two retrograde treatments (12 lesions each). Total 56 lesions

Adverse Events and Follow-Up

Postoperative care	Pain medication as needed. GI cocktail: viscous lidocaine, Donnatal, antacids
	Continue PPIs for 2 weeks. Advance diet as tolerated
	Follow up every 3 months for 1 year, then every 6 months for 2nd year, then annually
Adverse events	Few early adverse events including esophageal perforation, <0.5% major adverse event after 2005
	Most common side effect is self-limited chest pain
	Several reports of delayed gastric emptying in randomized controlled trials

Practical Considerations

Preoperative medications	Antiemetics and anticholinergics
Anesthesia	Monitored anesthesia care
Position	Semirecumbent
Stretta catheter	The Stretta catheter is flexible with a soft tip much like a 20-French Maloney bougie.
	Total length from handle to needles is 65 cm.
Irrigation and suction	Mucosa is cooled with chilled irrigation fluid during treatment.
	Suction line evacuates collected fluid around the basket.
Stretta control module introduction	The Stretta control module is a four-channel RF generator which monitors the temperature of tissue and mucosa, as well as tissue impedance, during radiofrequency delivery
	If either target or mucosa temperatures exceed safe levels, the power output to that specific channel is automatically discontinued

Important technique tips	Check position if any abnormal impedance or temperatures
	If mucosal temperature is too high, reduce balloon pressure
	Rotate catheter at the shaft
	Minimize pullback pressure when applying retrograde treatments
	If pullback ≥2 cm, reposition or abandon pullback

of Stretta, versus sham treatment [22]. Follow-up at 12 months demonstrated significant improvement in GERD-related symptoms, LES pressure, and reduced esophageal acid exposure in both active treatment arms, but not the sham procedure. Only 16.6% of patients in the single-treatment group were completely off PPI, but 50% of patients in the double-treatment group were able to completely discontinue PPI use.

Several studies have now also reported the long-term outcomes of Stretta. Liang and colleagues published a prospective observational study reporting on 5-year follow-

Stretta RF Therapy Randomized Trials

Author (year)	Design	Duration (mo)	Results
Corley et al. [20] (2003)	RF (35 patients) vs sham (29 patients)	6	Primary outcomes:
			Decreased heartburn (61% vs 33%, $p = 0.05$)
			> 50% improvement in HRQL (61% vs 30%, $p = 0.03$)
			Secondary outcomes:
			No difference in medication use (55% vs 61%, $p = 0.67$)
			No difference in esophageal acid exposure
			No difference in LES pressure
			No difference in esophagitis
Coron et al. [21] (2008)	RF (23 patients) vs PPI (20 patients)	12	Primary outcome:
			More patients stopped/decreased PPI (78% vs 40%, $p = 0.01$)
			At 6 months
			More patients stopped/decreased PPI (56% vs 35%, $p = 0.10$)
			At 12 months
			Secondary outcomes:
			No difference in HRQL
			No difference in esophageal acid exposure
			No difference in mean daily dose of PPI
			No difference in esophagitis
Aziz et al. [22] (2010)	Single session RF vs double session RF vs sham (12 patients each)	12	Primary outcome:
			HRQL improved in both Stretta groups compared to sham ($p < 0.01$)
			More patients normalized HRQL in double RF vs single RF (58% vs 17%, $p = 0.035$)
			Secondary outcomes:
			Decreased PPI use in both Stretta groups ($p < 0.01$)
			Improved LES basal pressure ($p < 0.01$)
			Decreased esophageal acid exposure ($p < 0.01$)
Arts et al. [23] (2012)	RF vs sham (11 patients each)	6	Primary outcome: Decreased GE junction compliance ($p < 0.05$) Secondary outcomes: Improved symptom score ($p < 0.005$) No difference in esophageal acid exposure No difference in LES pressure No difference in medication use

up of 138 of 152 initially treated patients [24]. Symptom scores were reduced at 6 months and sustained to 5 years. At 6 months, 27.5% of patients were reported to be completely off PPIs, increasing to 42.8% at 5 years. Dughera and colleagues also published 8-year follow-up of 26 of 86 initially treated patients, of which 7 patients restarted daily PPIs and 5 of these patients ultimately underwent LNF [25]. Overall, there was a significant decrease in heartburn score and increased QOL scores that were still sustained at 8 year follow-up ($p = 0.003$), with 76.9% of patients remaining completely off PPI therapy at 8 years. None of the patients developed endoscopic esophagitis, but the median LES pressures showed no significant improvement at 8-year follow-up. Finally, Noar and colleagues published a prospective open-label study reporting on 10-year follow-up of 149 of 217 initial patients who underwent Stretta for refractory GERD [26]. They demonstrated that 72% of patients had normalization of health-related quality-of-life (HRQL) scores, 64% had >50% reduction in baseline PPI use, 41% achieved discontinuation of PPI use, and 34% had no endoscopic esophagitis at 10-year follow-up.

Two studies have compared Stretta against other minimally invasive procedures for GERD. When compared to LNF, both procedures demonstrated effective symptom relief and safety at 5-year follow-up, although LNF resulted in greater symptomatic improvement and rates of PPI independence [27]. When compared to endoscopic full-thickness plication, both procedures demonstrated effective symptom relief and PPI independence at 4-year follow-up, although plication resulted in greater reduction in regurgitation, while RF resulted in greater reduction in heartburn and cough [28].

However, large systematic reviews evaluating the efficacy of Stretta have been conflicted in their recommendations. A systematic review in 2012 by Perry and colleagues which included 1441 patients across 20 studies showed that RFA produced significant improvement in reflux symptoms, heartburn scores, DeMeester scores, and HRQL scores [29]. Stretta was found to improve but not normalize esophageal acid exposure but did not significantly increase LES pressure. In stark contrast, the most recent systematic review in 2014 by Lipka and colleagues included all four randomized trials but determined all of them to be of poor methodological quality [30]. Pooled outcomes showed no significant benefit of Stretta over sham therapy for improvement in HRQL, discontinuation of PPI therapy, mean change in LES pressure, or mean time for which pH was <4. Their meta-analysis concluded that there was no evidence for efficacy of RFA for treatment of GERD. While the methodology of these two reviews continues to be debated, the data appears to generally suggest that Stretta has an acceptable safety profile and may effectively reduce symptom burden and HQRL scores up to 8–10 years following intervention. However, sustained improvement in objective outcomes, especially when compared to surgical intervention, has not been routinely demonstrated, and Stretta has not been found to consistently result in pH normalization [29].

The Stretta procedure has generally maintained an excellent safety profile. In clinical studies, there were few early adverse events including esophageal perforation but a < 0.1% major adverse event rate after 2005 [31]. In more recent studies, the most common side effect is chest pain, often self-limited and not requiring intervention [32].

Tissue Apposition Systems

Endoscopic tissue apposition systems attempt to mimic LNF by mechanically bolstering the LES or improving the anti-reflux barrier by creating a plication of tissue at or just below the GEJ.

Initial technologies included the EndoCinch endoluminal gastroplication (C.R. Bard Inc., Murray Hill, NJ) and the NDO Plicator full-thickness plication (Ethicon Endo-Surgery, Cincinnati, OH) systems [3]. EndoCinch was FDA approved in 2000 for the treatment of GERD and allowed for placement of threaded sutures at the GE junction to cinch the junction and enhance the barrier to reflux. An early study had demonstrated safety and efficacy up to 2 years, with reduction in symptom scores, PPI dependence, and esophageal acid exposure [33]. However, a follow-up study showed that at 4-year follow-up, there was 80% PPI dependence and 64% treatment failure, mostly attributed to suture loss at 12–18 months [34]. The device is thus no longer available.

The NDO Plicator system was approved by the FDA in 2003 and allowed for transmural suturing at the GE junction to increase the anatomic barrier to reflux. However, the device was recalled following reports of device failure requiring surgical extraction. A revised version was reapproved in 2007, with studies showing reduction of reflux symptoms and PPI dependence at 5 years without long-term adverse events [35]. When compared against Stretta, plication resulted in greater improvement in regurgitation symptoms; however when compared against LNF, surgery had greater reduction in reflux and in symptom scores [36]. Production of the NDO Plicator was terminated in 2008 by the manufacturer.

Currently two systems exist for endoscopic tissue apposition: EsophyX (EndoGastric Solutions, San Mateo, CA) and MUSE (Medigus, Omer, Israel).

EsophyX TIF

The EsophyX procedure, termed transoral incisionless fundoplication (TIF), uses an endolumenal device to achieve an incisionless 270° anterior fundoplication. The treatment has been demonstrated to decrease distensibility

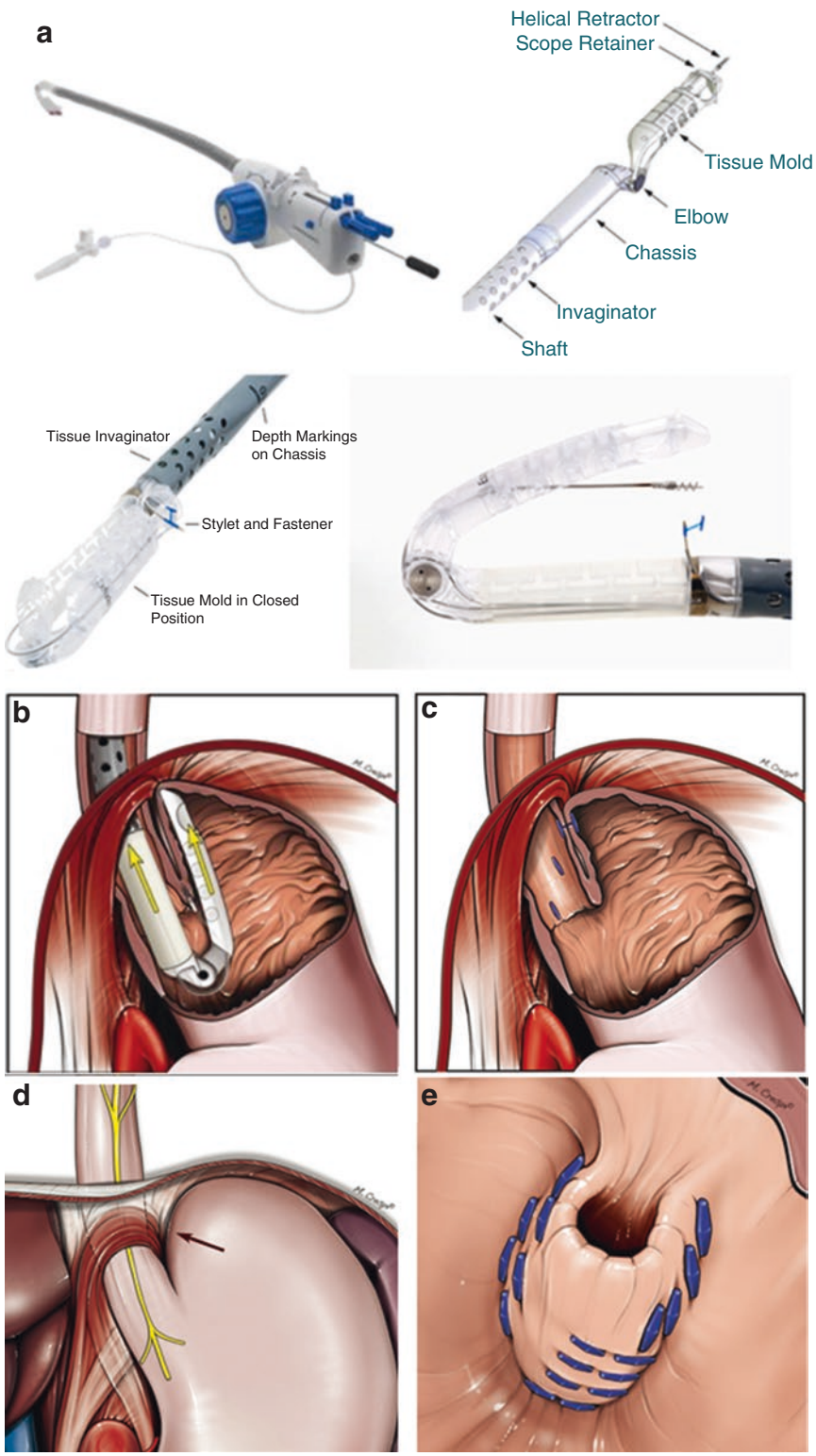

Fig. 4.3 EsophyX TIF 2.0 procedure. (**a**) General view of the device and of the working end of the device including the tissue invaginator, tissue mold, and helical retractor. (**b**) The tissue mold is secured to the gastric fundus. (**c**) The TIF 2.0 technique creates an esophagogastric fundoplication proximal to the Z-line. (**d**) During the procedure, caution is needed to avoid incorporating the diaphragm into the plication. (**e**) Postoperative view with positions of various plication sets (From Bell and Cadiere [58])

of the GE junction, enhance reflux symptom control, and reduce the number of TLESR episodes. The EsophyX system was approved in 2007 and employs a proprietary tissue manipulator and a minimum of 12 full-thickness polypropylene fasteners (Figs. 4.3 and 4.4) [37]. The procedure attempts to mimic LNF by elongating the intra-abdominal esophagus, reducing a small hiatal hernia if present, approximating and tightening the fundus around the distal esophagus, recreating the angle of His, and restoring the distal high pressure zone. The device claims

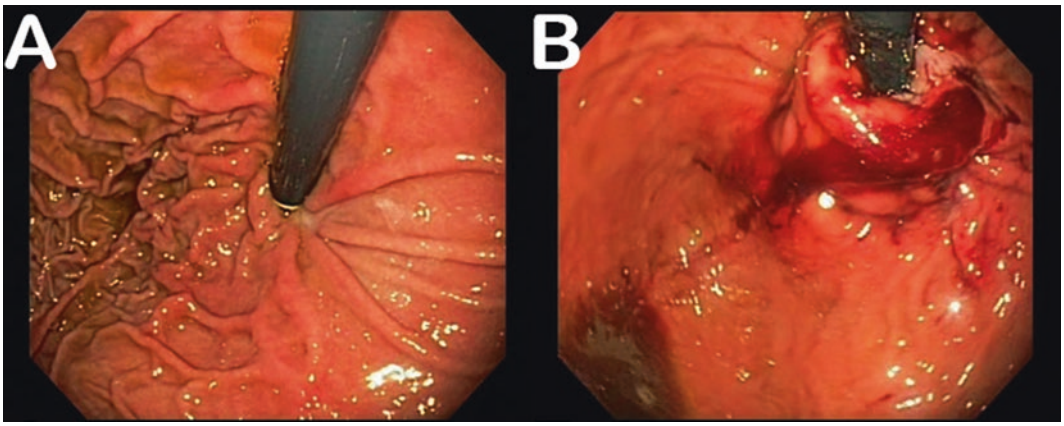

Fig. 4.4 Clinical images of EsophyX TIF 2.0 procedure. (**a**) Retroflexed views of the gastric cardia and gastroesophageal junction prior and (**b**) following TIF procedure (From Bell and Cadiere [58])

multiple potential advantages over LNF, including a more physiologic repair than a 360° wrap, decreased dysphagia and gas bloat, a better safety profile, and the ability for revision, if necessary. Additionally, there are also new hybrid approaches combining TIF with laparoscopic hiatal hernia repair [38].

The TIF procedure has undergone several iterations of development. The original procedure, known as endoluminal fundoplication (ELF), involved a gastrogastric plication with fastener placement below the Z-line. Subsequently, the procedure evolved into the first version of TIF, which utilized an esophagogastric plication with fastener placement 1 cm above the Z-line. The current procedure is known as TIF 2.0 and is an esophagogastric plication using a 240–270° wrap and fastener placement 1–3 cm above the Z-line (longer along the greater curvature of the stomach) [37]. According to the manufacturer, the goal of TIF is to repair the antireflux barrier, reduce the hiatal hernia (≤2 cm), restore the dynamics of the angle of His, and create a 2–4 cm-long antireflux valve, while achieving a 240–270° wrap similar to the Toupet, Hill, and Belsey fundoplication procedures.

The procedure is typically performed under general anesthesia. A bite block is placed into the patient's mouth, and the patient is placed into the left lateral semirecumbent position. A pre-procedure EGD is performed to evaluate the patient's anatomy and determine their suitability for undergoing TIF. Specifically, the gastroesophageal junction is carefully evaluated for the presence of any Barrett's esophagus or large hiatal hernias (defined as >2–3 cm in length) which would preclude successful TIF. The existing gastroesophageal valve is assessed and Hill classification assigned.

If the patient is deemed an acceptable candidate based on initial EGD, the TIF procedure may proceed. Periprocedural antibiotic prophylaxis, antiemetics, and anticholinergics are given. The EsophyX device, used with a flexible endoscope, is gently introduced into the stomach under constant visualization. If a hiatal hernia is present, it is reduced by returning the squamocolumnar junction to its natural position by using a supplementary vacuum suction system within the device. The endoscope and the device are then retroflexed in the stomach, and a helical retractor is engaged into the tissue slightly distal to the Z-line. The fundus of the stomach is folded up and around the distal esophagus utilizing the tissue mold and chassis of the device. After locking all the tissue manipulating elements, an integrated suction apparatus is activated to gently grasp the distal esophagus and position it in the abdominal cavity distal to the diaphragm. Subsequently, H-shaped polypropylene (SerosaFuse) fasteners, which have the strength equivalent of 3.0 sutures, are delivered through apposed layers of esophageal and fundus tissue in order to anchor the repair. The fasteners are deployed about 1–3 cm above the Z-line.

This process is repeated to create a full-thickness, partial circumference (approximately 240–270°), anterior gastroesophageal fundoplication. Approximately 12–20 fasteners are implanted during the procedure to create fusion of the esophageal and fundus tissues and form the valve. Following completion of TIF, the quality of the created valve is carefully documented endoscopically prior to withdrawal of the endoscope and termination of the procedure.

Patients should follow up with their gastroenterologist at regular intervals, initially at every 3 months for the first year, every 6 months for the second year, and annually thereafter. Initial follow-up focuses on adverse events related to the procedure, while later follow-up focuses on the degree of reflux symptoms.

Steps to the EsophyX TIF 2.0 Procedure

Initial endoscopy	Height hiatal hernia ≤2 cm, reduces fully, record distance from incisors to hiatus
	Transverse dimensions of hiatus <3 cm max
Device introduction	Tissue mold handle to left shoulder orients elbow of tissue mold to course of pharynx
Device retroflexion	Direct vision with endoscope retroflexed
CO2 insufflation	Through working channel, pressure 12–15 mmHg
Identify anatomic landmarks	Lesser curve (12 o'clock); greater curve (6 o'clock)
Initial helical screw deployment	12 o'clock insertion at Z-line/GE junction
Three anterior rotational plication sets	Roll tissue from 6 o'clock anteriorly toward 1 o'clock with tissue mold; tension on helical retractor; gastric desufflation
	Lock helical retractor and tissue mold; apply suction to tissue invaginator for 30 s
	Advance device to within 1 cm of distance corresponding to measured distance to hiatal landmark; rotate device out of corner to align tissue mold
	Advance stylet furthest from corner (posterior in this case) first, deploy fastener
	Complete first rotational plication set by advancing another stylet and deploy second fastener
	Create two additional anterior rotational plication sets at slightly different depths. This will create plications from 2 o'clock to 4 o'clock at depths up to 3 cm
Rotate tissue mold through lesser curve to posterior corner	Advance device with helical retractor cable slack, tissue mold partially closed, and rotate device counterclockwise
Three posterior rotational plication sets	Similar to the anterior plication sets, but rotation is now clockwise from 6 o'clock toward 11 o'clock, and the anterior stylet is advanced first. Three plication sets will be created from 7 o'clock to 10 o'clock at different depths up to 3 cm
Rotate tissue mold back through lesser curve back to anterior corner	
Two anterior longitudinal plication sets at 12:30–2 o'clock	Gentle longitudinal advanced caudally with the helical retractor and infolding of tissue with the tissue mold during gastric desufflation to create two anterior longitudinal plication sets of 1–2 cm depth
Reposition helical retractor to 4 o'clock	This is the second helical retractor placement and is done to aid in caudal retraction for the final longitudinal plication
One greater curve longitudinal plication set at 5 o'clock	This plication set must be performed carefully with attention to the location of the diaphragm
One additional plication set	As needed
Remove device	Release helical retractor and pull back into tissue mold
	Straighten tissue mold under direct visualization
	Remove device while observing esophagus with endoscope just inside device. Helical retractor should be pulled back; tissue mold knob externally to left shoulder
Final endoscopy	Assess plication; assess for bleeding or perforation

Adverse Events and Follow-Up

Postoperative care	Pain medication as needed. GI cocktail: viscous lidocaine, Donnatal, antacids
	Continue PPIs for 2 weeks. Clear to full liquid diet without carbonation. Consider water-soluble contrast study before discharge
Adverse events	<0.45% major adverse event
	Most common side effects are gas bloat and dysphagia
	Several reports of nausea, abdominal pain, chest pain in randomized controlled trials

Practical Considerations

Preoperative medications	Antiemetics, antibiotics, and anticholinergics
Anesthesia	General anesthesia
Position	Semirecumbent
Important technique tips	During procedure, caution needed to avoid incorporating the diaphragm into the plication

Review of Existing Data

Multiple retrospective and prospective studies have been published regarding safety and efficacy of TIF. However, due to multiple revisions to the TIF procedure, long-term data are lacking. Muls and colleagues published a 3-year follow-up of 66 out of 86 initial patients who underwent TIF and showed that 80% of patients continued to have significant improvement in HRQL scores at 3 years; discontinuation of daily PPI was maintained in 74% of patients. Esophagitis was reduced from 78% to 38% at 3 years, with complete resolution of esophagitis in over half of those patients [39]. However, 12 patients underwent repeat procedures (2 LNF and 10 TIF) for treatment failure. Testoni and colleagues published 6-year follow-up of 14 of 50 initial patients who underwent TIF, again with similar results with regard to discontinuation of PPIs and improvement in HRQL scores [40]. Long-term response appeared to be best predicted by initial response in the first 6–12 months, with the best candidates for TIF being patients with hiatal hernia <2 cm in length and Hill grade I–II valves.

The US TIF 2.0 registry is a prospective, open-label, multicenter study comprised of patients undergoing TIF 2.0, reported by Bell and colleagues [41]. Data analyzed at 6-month follow-up indicated 89% elimination of troublesome regurgitation, 72% elimination of heartburn, 65% complete elimination of symptoms, 80% independence from PPIs, and 54% normalized esophageal acid exposure. The improvement was sustained at 12-month follow-up, with 83% elimination of troublesome regurgitation, 78% elimination of heartburn, 64% complete elimination of symptoms, 74% independence from PPIs, and 52% normalized esophageal acid exposure. At 24-month follow-up, HRQL scores improved by >50% in 66% of patients, and the rate of daily PPI use decreased from 91% to 29%.

Recently, four randomized controlled trials have been published either comparing TIF versus PPI or TIF versus sham procedure plus PPI, with anywhere from 6- to 18-month follow-up [42–45]. All four trials demonstrated significant reduction in trouble regurgitation and GERD symptoms among patients receiving TIF; however, results have been largely mixed with regard to improvement in esophageal acid exposure, normalization of pH, healing of erosive esophagitis, and reduction in the number of reflux episodes. In general, the four recent randomized trials appear to suggest that TIF is more effective than PPI in the elimination of troublesome regurgitation and equivalent to PPI in normalizing distal esophageal acid exposure.

Some concern exists regarding the long-term durability of the procedure. The RESPECT trial used a cross-over design, which showed that at 18-month follow-up, 71% of the PPI/sham group had treatment failure and crossed over to TIF;

EsophyX TIF 2.0 Randomized Trials

Author (year)	Design	Duration (mo)	Results
Trad et al. [42] (TEMPO, 2015)	TIF off PPI (40 patients) vs PPI (23 patients)	6	Primary outcome: Greater elimination of regurgitation (97 vs 50%, $p = 0.006$)
			Secondary outcomes:
			No difference in esophageal acid exposure
			Greater complete cessation of PPI use 90 vs 13%, $p = 0.003$)
			Greater rate of complete healing of esophagitis
			(90 vs 38%, $p = 0.018$)
Hunter et al. [43] (RESPECT, 2015)	TIF + PPI (87 patients) vs sham + PPI (42 patients)	6	Primary outcome:
			Greater elimination of regurgitation (67 vs 45%, $p = 0.023$)
			Secondary outcomes:
			Decreased esophageal acid exposure ($p < 0.001$)
			No difference in reduction of GERD symptom scores
			At 18-month follow-up, 71% of sham + PPI group had crossed over to TIF, 28% of TIF group had resumed PPI
Witteman et al. [44] (2015)	TIF (40 patients) vs PPI (20 patients)	6	Primary outcome: >50% improvement in HRQL (55 vs 5%, $p < 0.001$)
			Secondary outcomes:
			No difference in esophageal acid exposure
			No difference in number of reflux episodes
			No difference in esophagitis
			Increased LES resting pressure ($p = 0.004$)
			Greater initial complete cessation of PPI use (74 vs 0%), but 61% resumed PPI at 12-month follow-up
			Hill grade I valves created in 90% at time of TIF, only 35% remaining at 12-month follow-up

Author (year)	Design	Duration (mo)	Results
Hakansson et al. [45] (2015)	TIF (44 patients) vs PPI (22 patients)	6	Primary outcome:
			Greater number of days in remission of GERD symptoms
			(197 vs 107 days, $p < 0.001$)
			Secondary outcomes:
			Greater reduction of GERD symptom scores ($p < 0.005$)
			Greater incidence of normalization of esophageal acid
			exposure (69 vs 20%, $p = 0.04$)
			Greater complete cessation of PPI use (59 vs 18%, $p = 0.01$)

however, 28% of the TIF group required resumption of PPI therapy [43]. A Dutch randomized trial additionally showed that while Hill grade I valves were created in 90% of patients at the time of TIF, only 35% of them remained at 12-month follow-up [44]. A multinational European randomized trial demonstrated that only 59% of patients with chronic GERD remained in clinical remission at 6 months [45].

Several studies have compared TIF against surgical fundoplication. Toomey and colleagues published a prospective cohort study of three cohorts of 20 patients undergoing TIF, LNF, or Toupet fundoplications [46]. All three cohorts of patients had similar reduction in symptom frequency and severity; however, patients undergoing TIF had significantly shorter operative times and length of hospital stay. However, a separate prospective study from Frazzoni and colleagues comparing two cohorts of ten patients undergoing TIF or LNF demonstrated greater efficacy of LNF in improving objective reflux parameters on pH and impedance testing [47].

No systematic review has yet to be published since the additional randomized trials were published in 2015. The most recent systematic review was published by Wendling and colleagues in 2013, evaluating 4 retrospective and 11 prospective studies [48]. Their meta-analysis demonstrated an overall cessation rate of PPI therapy of 67% at 8 months. Overall adverse events in 559 total patients included 6 cases of hemorrhage, 1 case of mediastinal abscess, 4 cases of esophageal perforation, 3 cases of dysphagia, and 7 cases of bloating. Approximately 7.2% of patients failed TIF and required Nissen fundoplication, with overall failure rate of 8.1% when including cases of re-do TIF.

The TIF procedure has generally maintained an excellent safety profile with minimal postoperative side effects such as gas bloat and dysphagia. The serious adverse event rate in more than 16,700 TIF procedures performed commercially worldwide is <0.45%. In clinical studies, serious adverse event rates are reported to be <3% and included all procedures performed during studies evaluating feasibility, safety, and initial learning curve.

Medigus MUSE

The MUSE system uses a surgical endostapler under ultrasound guidance and standard staples and was recently approved by the FDA in 2014. Initial 6-month follow-up data were encouraging; however, there were two early severe adverse events including esophageal leak and post-procedural upper gastrointestinal bleeding [49]. One long-term multicenter study evaluating outcomes at 4-year follow-up of 37 patients showed no new severe adverse events, 83.8% independence from PPIs at 6 months and 69.4% at 4 years post-procedure, overall decreased daily dosage of GERD medications, and improved HRQL scores at 6 months and 4 years post-procedure [50]. Significantly decreased esophageal acid exposure was seen at 6 months, with 44.9% reduction in the mean total time distal esophageal pH ≤ 4 among all patients undergoing the procedure. However, larger studies investigating the safety, effectiveness, and long-term durability of this technique are warranted.

Emerging Surgical Technologies and Future Directions

While the focus of this chapter has been on endoscopic techniques to treat GERD, several new surgical technologies have been developed for the minimally invasive treatment of GERD. These include Linx (Torax Medical, Shoreview, MN), an implantable ring of titanium magnetic core beads placed laparoscopically around the distal esophagus for sphincter augmentation, and EndoStim (EndoStim, St. Louis, MO), an implantable pulse generator and bipolar stimulator that delivers electrical energy to the LES in order to increase resting pressure. A few studies have been published regarding these technologies [51–53], but additional research will be needed to evaluate the safety and efficacy of these surgical therapies for GERD, to compare their risks and benefits relative to LNF, and to better define specific patient subgroups for which these therapies may be beneficial.

Conclusions

The main endoscopic technologies available today, Stretta and EsophyX TIF, are viable clinical alternatives to LNF for management of GERD. However, the available data still shows mixed results, and neither of these procedures have been proven to be superior to the current gold standard LNF. Current guidelines published by the American Society for Gastrointestinal Endoscopy (ASGE) state that "endoscopic antireflux therapy [may] be considered for selected patients with uncomplicated GERD after careful discussion with the patient regarding potential adverse effects, benefits, and other available therapeutic options" [4].

A large body of evidence has demonstrated the safety, efficacy, durability, and repeatability of Stretta RF treatment. The major benefit of Stretta is that it does not preclude subsequent surgical or RFA treatments [6]. Furthermore, Stretta may provide potential treatment for patients who have failed LNF. The current guidelines from the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) strongly recommend Stretta for adult patients with GERD who have been partially or completely responsive to antisecretory pharmacologic therapy and who have declined laparoscopic fundoplication, based on a high quality of evidence [54].

Similarly, increasing evidence demonstrates the safety and efficacy of the EsophyX TIF procedure. TIF may be most effective for selected patients with hiatal hernia <2 cm in length and Hill grade I–II valves, although the ideal patient population has yet to be fully elucidated due to lack of long-term follow-up data [3]. Present SAGES guidelines suggest that EsophyX may be effective in patients with a hiatal hernia <2 cm with typical and atypical GERD but that further studies are required to define optimal techniques, patient selection criteria, and device and technique safety [54].

Although the results from Stretta and EsophyX seem promising, there remains no evidence to demonstrate the superiority of either approach over LNF. Studies of endoscopic management are hampered by the inability to demonstrate normalization of esophageal acid exposure [6]. Instead, studies continue to suggest that patients may require repeat procedures, resume PPI therapy, or ultimately require LNF due to recurrent or refractory GERD symptoms [55]. One study demonstrated that a third of patients undergoing TIF required surgical revision (i.e., LNF) after 3 years [56]. Prospective studies comparing TIF to LNF have demonstrated greater efficacy of LNF in improving objective reflux parameters on pH and impedance testing [47].

In summary, minimally invasive endoscopic therapies for the management of GERD continue to evolve, and many technologies have come and gone over the last 30 years. Physicians currently have a variety of tools ranging from highly effective medications to surgical and endoscopic procedures for which to treat GERD. LNF remains the gold standard for invasive therapy for GERD, and despite numerous advances, no endoscopic treatment has yet to demonstrate superiority over LNF. Despite studies demonstrating the safety and efficacy of the two currently available endoscopic therapies, Stretta and EsophyX TIF, none of these therapies have successfully normalized esophageal acid exposure, and they remain second-line interventional therapies behind LNF. Appropriate patient selection, as well as institutional and practitioner expertise, should be carefully considered prior to pursuing endoscopic alternatives to established first-line medical and surgical therapies.

Final Words

- Endoscopic therapies continue to evolve; many technologies have come and gone.
- LNF remains the gold standard for invasive therapy for GERD.
- Despite advances, no endoscopic treatment has yet to demonstrate superiority over LNF.
- Major current available therapies include Stretta RF treatment and EsophyX TIF.
- The ideal patient for endoscopic therapy has symptomatic GERD with positive esophageal pH studies; responsive or initially responsive to PPI therapy; decreased quality of life, with small hiatal hernia; and who does not desire to undergo surgery and does not wish to remain on long-term PPI therapy.
- Appropriate patient selection and institutional and practitioner expertise should be considered prior to pursuing endoscopic therapies for GERD.

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References

1. El-Serag HB, Sweet S, Winchester CC, et al. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2014;63:871–80.
2. Peery AF, Dellon ES, Lund J, et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology. 2012;143:1179–87 e1–3.
3. Hummel K, Richards W. Endoscopic treatment of gastroesophageal reflux disease. Surg Clin North Am. 2015;95:653–67.
4. ASGE Standards of Practice Committee. The role of endoscopy in the management of GERD. Gastrointest Endosc. 2015;81:1305–10.
5. Top 100 Most Prescribed, Top-Selling Drugs. Medscape. Aug 01, 2014. http://www.medscape.com/viewarticle/829246. Accessed 10 Oct 2014.
6. Lo WK, Mashimo H. Critical Assessment of Endoscopic Techniques for Gastroesophageal Reflux Disease. J Clin Gastroenterol. 2015;49:720–4.

7. Fass R. Proton-pump inhibitor therapy in patients with gastro-oesophageal reflux disease: putative mechanisms of failure. Drugs. 2007;67:1521–30.
8. Subramanian CR, Triadafilopoulos G. Refractory gastroesophageal reflux disease. Gastroenterol Rep (Oxf). 2015;3:41–53.
9. Broeders JA, Rijnhart-de Jong HG, Draaisma WA, et al. Ten-year outcome of laparoscopic and conventional nissen fundoplication: randomized clinical trial. Ann Surg. 2009;250:698–706.
10. Kellokumpu I, Voutilainen M, Haglund C, et al. Quality of life following laparoscopic Nissen fundoplication: assessing short-term and long-term outcomes. World J Gastroenterol. 2013;19:3810–8.
11. Niebisch S, Fleming FJ, Galey KM, et al. Perioperative risk of laparoscopic fundoplication: safer than previously reported-analysis of the American College of Surgeons National Surgical Quality Improvement Program 2005 to 2009. J Am Coll Surg. 2012;215:61–8. discussion 68-9
12. Galmiche JP, Hatlebakk J, Attwood S, et al. Laparoscopic antireflux surgery vs esomeprazole treatment for chronic GERD: the LOTUS randomized clinical trial. JAMA. 2011;305:1969–77.
13. Bell RC, Fox MA, Barnes WE, et al. Univariate and multivariate analyses of preoperative factors influencing symptomatic outcomes of transoral fundoplication. Surg Endosc. 2014;28:2949–58.
14. O'Connor KW, Madison SA, Smith DJ, et al. An experimental endoscopic technique for reversing gastroesophageal reflux in dogs by injecting inert material in the distal esophagus. Gastrointest Endosc. 1984;30:275–80.
15. Fockens P, Bruno MJ, Gabbrielli A, et al. Endoscopic augmentation of the lower esophageal sphincter for the treatment of gastroesophageal reflux disease: multicenter study of the Gatekeeper Reflux Repair System. Endoscopy. 2004;36:682–9.
16. Feretis C, Benakis P, Dimopoulos C, et al. Endoscopic implantation of Plexiglas (PMMA) microspheres for the treatment of GERD. Gastrointest Endosc. 2001;53:423–6.
17. Ganz RA, Fallon E, Wittchow T, et al. A new injectable agent for the treatment of GERD: results of the Durasphere pilot trial. Gastrointest Endosc. 2009;69:318–23.
18. Triadafilopoulos G, Dibaise JK, Nostrant TT, et al. Radiofrequency energy delivery to the gastroesophageal junction for the treatment of GERD. Gastrointest Endosc. 2001;53:407–15.
19. Tam WC, Schoeman MN, Zhang Q, et al. Delivery of radiofrequency energy to the lower oesophageal sphincter and gastric cardia inhibits transient lower oesophageal sphincter relaxations and gastro-oesophageal reflux in patients with reflux disease. Gut. 2003;52:479–85.
20. Corley DA, Katz P, Wo JM, et al. Improvement of gastroesophageal reflux symptoms after radiofrequency energy: a randomized, sham-controlled trial. Gastroenterology. 2003;125:668–76.
21. Coron E, Sebille V, Cadiot G, et al. Clinical trial: radiofrequency energy delivery in proton pump inhibitor-dependent gastro-oesophageal reflux disease patients. Aliment Pharmacol Ther. 2008;28:1147–58.
22. Aziz AM, El-Khayat HR, Sadek A, et al. A prospective randomized trial of sham, single-dose Stretta, and double-dose Stretta for the treatment of gastroesophageal reflux disease. Surg Endosc. 2010;24:818–25.
23. Arts J, Bisschops R, Blondeau K, et al. A double-blind sham-controlled study of the effect of radiofrequency energy on symptoms and distensibility of the gastro-esophageal junction in GERD. Am J Gastroenterol. 2012;107:222–30.
24. Liang WT, Wu JM, Wang F, et al. Stretta radiofrequency for gastroesophageal reflux disease-related respiratory symptoms: a prospective 5-year study. Minerva Chir. 2014;69:293–9.
25. Dughera L, Rotondano G, De Cento M, et al. Durability of stretta radiofrequency treatment for GERD: results of an 8-year follow-up. Gastroenterol Res Pract. 2014;2014:531907.
26. Noar M, Squires P, Noar E, et al. Long-term maintenance effect of radiofrequency energy delivery for refractory GERD: a decade later. Surg Endosc. 2014;28:2323–33.
27. Liang WT, Wu JN, Wang F, et al. Five-year follow-up of a prospective study comparing laparoscopic Nissen fundoplication with Stretta radiofrequency for gastroesophageal reflux disease. Minerva Chir. 2014;69:217–23.
28. Jeansonne LO, White BC, Nguyen V, et al. Endoluminal full-thickness plication and radiofrequency treatments for GERD: an outcomes comparison. Arch Surg. 2009;144:19–24. discussion 24
29. Perry KA, Banerjee A, Melvin WS. Radiofrequency energy delivery to the lower esophageal sphincter reduces esophageal acid exposure and improves GERD symptoms: a systematic review and meta-analysis. Surg Laparosc Endosc Percutan Tech. 2012;22:283–8.
30. Lipka S, Kumar A, Richter JE. No evidence for efficacy of radiofrequency ablation for treatment of gastroesophageal reflux disease: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2015;13:1058–67. e1
31. Franciosa M, Triadafilopoulos G, Mashimo H. Stretta radiofrequency treatment for GERD: a safe and effective modality. Gastroenterol Res Pract. 2013;2013:783815.
32. Triadafilopoulos G, DiBaise JK, Nostrant TT, et al. The Stretta procedure for the treatment of GERD: 6 and 12 month follow-up of the U.S. open label trial. Gastrointest Endosc. 2002;55:149–56.
33. Chen YK, Raijman I, Ben-Menachem T, et al. Long-term outcomes of endoluminal gastroplication: a U.S. multicenter trial. Gastrointest Endosc. 2005;61:659–67.
34. Schiefke I, Zabel-Langhennig A, Neumann S, et al. Long term failure of endoscopic gastroplication (EndoCinch). Gut. 2005;54:752–8.
35. Pleskow D, Rothstein R, Kozarek R, et al. Endoscopic full-thickness plication for the treatment of GERD: Five-year long-term multicenter results. Surg Endosc. 2008;22:326–32.
36. Kaindlstorfer A, Koch OO, Antoniou SA, et al. A randomized trial on endoscopic full-thickness gastroplication versus laparoscopic antireflux surgery in GERD patients without hiatal hernias. Surg Laparosc Endosc Percutan Tech. 2013;23:212–22.
37. Bell RC, Cadiere GB. Transoral rotational esophagogastric fundoplication: technical, anatomical, and safety considerations. Surg Endosc. 2011;25:2387–99.
38. Ihde GM, Besancon K, Deljkich E. Short-term safety and symptomatic outcomes of transoral incisionless fundoplication with or without hiatal hernia repair in patients with chronic gastroesophageal reflux disease. Am J Surg. 2011;202:740–6;discussion 746-7
39. Muls V, Eckardt AJ, Marchese M, et al. Three-year results of a multicenter prospective study of transoral incisionless fundoplication. Surg Innov. 2013;20:321–30.
40. Testoni PA, Testoni S, Mazzoleni G, et al. Long-term efficacy of transoral incisionless fundoplication with Esophyx (Tif 2.0) and factors affecting outcomes in GERD patients followed for up to 6 years: a prospective single-center study. Surg Endosc. 2015;29:2770–80.
41. Bell RC, Barnes WE, Carter BJ, et al. Transoral incisionless fundoplication: 2-year results from the prospective multicenter U.S. study. Am Surg. 2014;80:1093–105.
42. Trad KS, Barnes WE, Simoni G, et al. Transoral incisionless fundoplication effective in eliminating GERD symptoms in partial responders to proton pump inhibitor therapy at 6 months: the TEMPO Randomized Clinical Trial. Surg Innov. 2015;22:26–40.
43. Hunter JG, Kahrilas PJ, Bell RC, et al. Efficacy of transoral fundoplication vs omeprazole for treatment of regurgitation in a randomized controlled trial. Gastroenterology. 2015;148:324–33. e5
44. Witteman BP, Conchillo JM, Rinsma NF, et al. Randomized controlled trial of transoral incisionless fundoplication vs. proton pump inhibitors for treatment of gastroesophageal reflux disease. Am J Gastroenterol. 2015;110:531–42.
45. Hakansson B, Montgomery M, Cadiere GB, et al. Randomised clinical trial: transoral incisionless fundoplication vs. sham intervention to control chronic GERD. Aliment Pharmacol Ther. 2015;42:1261–70.

46. Toomey P, Teta A, Patel K, et al. Transoral incisionless fundoplication: is it as safe and efficacious as a Nissen or Toupet fundoplication? Am Surg. 2014;80:860–7.
47. Frazzoni M, Conigliaro R, Manta R, et al. Reflux parameters as modified by EsophyX or laparoscopic fundoplication in refractory GERD. Aliment Pharmacol Ther. 2011;34:67–75.
48. Wendling MR, Melvin WS, Perry KA. Impact of transoral incisionless fundoplication (TIF) on subjective and objective GERD indices: a systematic review of the published literature. Surg Endosc. 2013;27:3754–61.
49. Zacherl J, Roy-Shapira A, Bonavina L, et al. Endoscopic anterior fundoplication with the Medigus Ultrasonic Surgical Endostapler (MUSE) for gastroesophageal reflux disease: 6-month results from a multi-center prospective trial. Surg Endosc. 2015;29:220–9.
50. Kim HJ, Kwon CI, Kessler WR, et al. Long-term follow-up results of endoscopic treatment of gastroesophageal reflux disease with the MUSE endoscopic stapling device. Surg Endosc. 2015;29:220–9.
51. Ganz RA, Peters JH, Horgan S, et al. Esophageal sphincter device for gastroesophageal reflux disease. N Engl J Med. 2013;368:719–27.
52. Ganz RA, Edmundowicz SA, Taiganides PA, et al. Long-term outcomes of patients receiving a magnetic sphincter augmentation device for gastroesophageal reflux. Clin Gastroenterol Hepatol. 2015;14:671–7.
53. Rodriguez L, Rodriguez P, Gomez B, et al. Long-term results of electrical stimulation of the lower esophageal sphincter for the treatment of gastroesophageal reflux disease. Endoscopy. 2013;45:595–604.
54. Auyang ED, Carter P, Rauth T, et al. SAGES clinical spotlight review: endoluminal treatments for gastroesophageal reflux disease (GERD). Surg Endosc. 2013;27:2658–72.
55. Wilson EB, Barnes WE, Mavrelis PG, et al. The effects of transoral incisionless fundoplication on chronic GERD patients: 12-month prospective multicenter experience. Surg Laparosc Endosc Percutan Tech. 2014;24:36–46.
56. Witteman BP, Kessing BF, Snijders G, et al. Revisional laparoscopic antireflux surgery after unsuccessful endoscopic fundoplication. Surg Endosc. 2013;27:2231–6.
57. Triadafilopoulos G. Stretta: a valuable endoscopic treatment modality for gastroesophageal reflux disease. World J Gastroenterol. 2014;20(24):7730.
58. Bell RC, Cadiere RB. Transoral rotational esophagogastric fundoplication: technical, anatomical, and safety considerations. Surg Endosc. 2011;25(7):2390.

Recent Advances in Imaging of Barrett's Esophagus

5

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Introduction

Barrett's esophagus (BE) is a premalignant metaplastic process resulting from chronic inflammation in the lower esophagus. Its importance arises from the 10- to 20-fold increase in the risk of developing esophageal adenocarcinoma (EAC) (RR, 11.2; 95% confidence interval 8.8–14.4) over time due to subsequent dysplastic change [1]. The prevalence of BE is increasing and ranges from 0.4% to 20% depending on the population studied [2, 3]. Studies have shown improvement in patient outcomes with early detection of dysplasia in patients who are on an endoscopic surveillance program [4, 5]. Surveillance endoscopy however has poor compliance rates [6]. Some studies have also shown miss rates of up to 57% [7]. Concerns about the imitations of the current standard have fueled the quest to "see better, earlier" [8, 9].

The annual rate of incidence for malignant disease in patients with BE ranges from 0.2% to 2.0% [8–10]. The "Seattle protocol" is presently recommended as the ideal surveillance guide [11–19]. This involves obtaining random four-quadrant biopsies in every 2 cm BE segment. BE evolves gradually in sequence of histologically recognizable stages from intestinal metaplasia to dysplasia (low to high grade) to intramucosal and invasive carcinoma [12]. This offers a window of opportunity for early detection and curative therapy. A thorough and systematic inspection of the mucosa is important. Quite often the mucosa itself is obscured by saliva, reflux from gastric contents, or even blood from biopsies. Adequate lavage (with water or 1% acetylcysteine) along with proper insufflation is required for a thorough inspection of the entire mucosa to identify any early mucosal change. Recognition of dysplasia in BE is subjective and can be difficult even for skilled endoscopists.

Rationale for Advanced Endoscopic Imaging

To be able to replace the Seattle protocol, any targeted biopsy technique has to be able to demonstrate, at the very minimum, non-inferiority in sensitivity and specificity, if not some degree of superiority. The Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) initiative by the American Society for Gastrointestinal Endoscopy (ASGE) has proposed a per-patient sensitivity of greater than 90% and a negative predictive value (NPV) of above 98% for detecting HGD or early EAC [13]. Additionally, the ASGE has also suggested that any new technology should have a specificity that is sufficiently high (80%) to allow a reduction in the number of biopsies (compared with random biopsies). Available (and under evaluation) techniques for advanced endoscopic imaging can be grouped into two main groups: (1) wide-field detection techniques and (2) point measurement techniques (Table 5.1).

Wide-Field Detection Techniques

High-Definition White Light Endoscopy

High-resolution high-definition endoscopes (HD-WLE) have improved optics including a high-density charge-coupled device (CCD) chips which display images with resolution of 800,000 pixels or more (compared to 300,000 pixel image in standard scopes) on a compatible high-definition monitor

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Table 5.1 Advanced endoscopic imaging techniques for BE

	Brief description	Improvement over standard imaging
Wide-field detection techniques		
High-definition white light endoscopy (HD-WLE)	Use of a high-definition optical system and compatible monitor	Higher resolution of displayed image; resolution and magnification (up to x115) improve identification of mucosal abnormalities
Narrowband imaging (NBI)	Filter with blue/green light	Higher contrast and easier recognition of abnormal mucosa due to visualized vascular pattern
Autofluorescence imaging (AFI)	Enhanced imaging utilizing autofluorescence properties of endogenous fluorophores	Altered autofluorescence from dysplastic tissue renders it magenta
Chromoendoscopy (CE)	Utilizes dyes (organic and inorganic) to highlight abnormal tissue	Acetic acid topical spray (1–3% solution) – accentuates dysplastic mucosa Methylene blue topical spray – highlights intestinal metaplasia
Post-processing digital chromoendoscopy (PPDC)	Post-processing of image to enhance output	Improved visualization of mucosal and vascular patterns
Optical coherence tomography (OCT)	Cross-sectional imaging of esophageal mucosa	Similar to ultrasonography; but uses coherent broadband light
Biomarker labeling	Visually tagged probe molecules binding to neoplastic cells	Similar to immunohistochemistry in histology but "live"; highlights suspicious areas with improved contrast
Point measurement techniques		
Confocal laser endomicroscopy (CLE)	Analysis in situ using laser and intravenous contrast agent	High magnification (up to 1250 fold) allows real-time histological analysis
Elastic scattering spectroscopy (ESS)	Analysis of interaction of light with mucosal surface on the principle of elastic scattering	Abnormal tissue detected by noting characteristics like nuclear size, crowding, etc.
Raman spectroscopy	Analysis of interaction of light with mucosal surface on the principle of inelastic scattering	Subtle changes in molecular composition of neoplastic tissue are used to identify suspicious areas

(Figs. 5.1, 5.2, and 5.3). Magnification (up to 115 times) can improve characterization of any mucosal abnormality. Longer inspection time with HD-WLE was associated with significant increase in number of lesions detected in a study of 112 patients (34% with HGD or EAC) [14]. In this study, an average inspection time of greater than 1 min per centimeter of BE enabled a higher lesion detection rate (54.2% vs. 13.3%; $p = 0.04$), with a trend toward a higher detection rate of HGD/EAC (40.2% vs. 6.7%; $p = 0.06$). As with all technological advances, this technology will inherently make its way into most endoscopy units as the new standard of care.

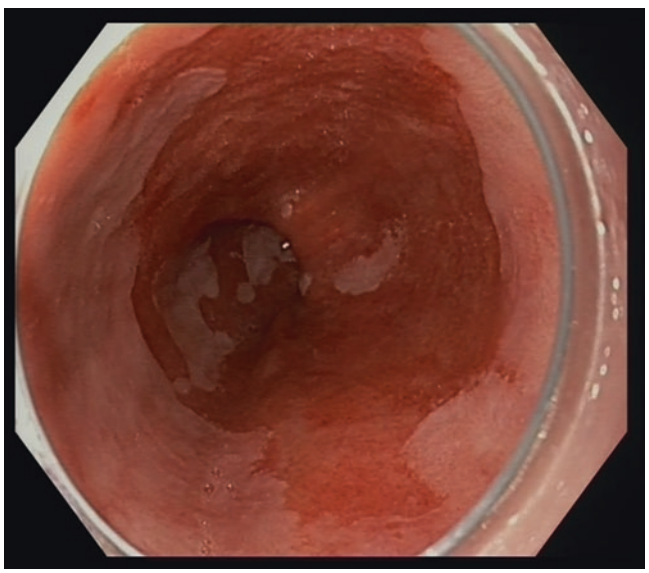

Fig. 5.1 Overview of a long segment of Barrett's esophagus (BE) on high-definition white light endoscopy (HD-WLE)

Chromoendoscopy

Chromoendoscopy (CE) involves using a dye spray onto the mucosa to highlight and improve detection of mucosal abnormalities and aids in characterization of lesions. The dyes most commonly used for CE in BE are methylene blue and acetic acid.

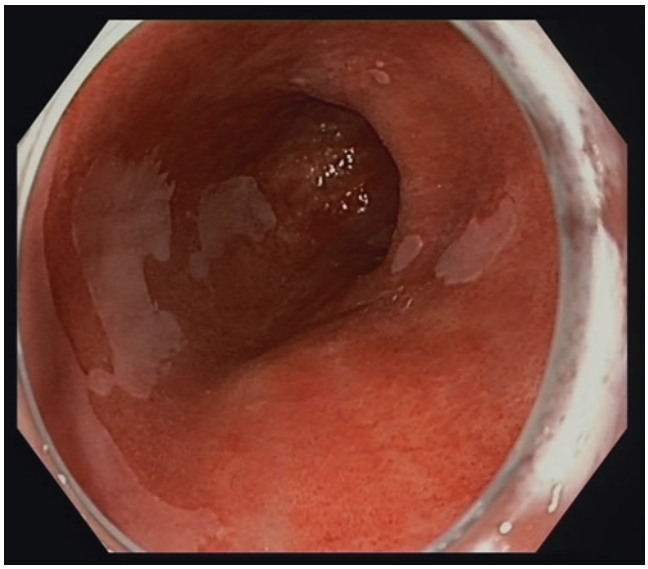

Fig. 5.2 Mid-segment of BE on HD-WLE

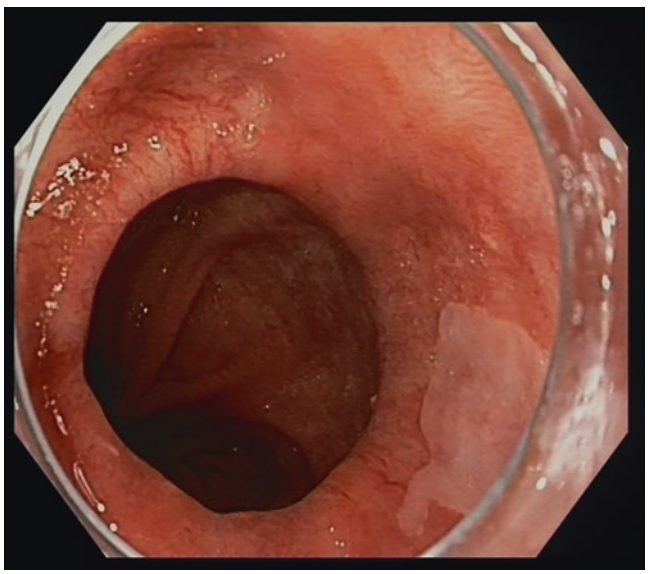

Fig. 5.3 Lower segment BE on HD-WLE

Methylene Blue Chromoendoscopy

Methylene blue (MB) is a vital dye that is actively taken up by absorbent intestinal-type epithelium in BE and dysplastic cells but not by squamous or gastric mucosa or gastric-type metaplasia within the distal esophagus [15]. During MB CE, specialized intestinal metaplasia typically stains blue, whereas a lighter intensity and increased heterogeneity in the staining pattern predict HGD and/or EAC.

MB CE in BE has been around for almost a decade now with numerous studies showing variable results (sensitivity 53–98%; specificities 32–97%) [16–22]. A meta-analysis of nine studies including 450 patients comparing detection rates of neoplasia in BE with MB staining showed comparable results to random four-quadrant biopsies with no clear advantage in terms of number of biopsies obtained [23]. There is a theoretical risk of carcinogenesis with MB staining (due to DNA damage by absorbed MB), but no permanent or clinically significant risks have been established [24].

Acetic Acid Chromoendoscopy

Low concentration (1–3%) spray of acetic acid (AA) eliminates the superficial mucus layer by breaking down glycoprotein disulfide bonds and subsequently causes transient reversible deacetylation of cellular proteins. The transient disruption of the single-layered columnar mucosal barrier occurs in a few minutes, leading to whitening of the tissue with vascular congestion lasting for 2–3 min. This leads to marked accentuation of the villi and mucosal pit pattern when AA reaches the capillaries in the stroma. The whitening effect is lost in dysplastic areas earlier than in the surrounding mucosa [25–28].

Studies have shown excellent correlation between the lesions predicted to be neoplastic by AA and those diagnosed by histologic analysis ($r = 0.99$) A 2.5 fold increase in detection of visible abnormalities during endoscopy was seen with AA compared with standard white light endoscopy (WLE) alone [29–31]. In a study spanning 5 years, Bhandari et al. noted a significant false-positive rate of 25% although there was a twofold increase in the detection rate of neoplasia when compared with WLE (96% vs. 48%; $p = 0.001$) [32].

The main drawbacks of CE are the increased procedure time, lack of reproducibility, and concerns with false-positive results. In addition, the carcinogenic effects due to DNA damage by MB remains an issue.

Narrowband Imaging

Narrowband imaging (NBI) was first described by Gono et al. in 2004 (Olympus Corporation, Tokyo, Japan) [33]. An additional filter, activated by pushing a button on the endoscope, alters the image contrast by increasing the contribution of short wavelength blue (440–460 nm) and green (540–560 nm) lights. These narrowbands of light display superficial capillary network (hemoglobin absorbs blue light better) and subepithelial vessels (deeper penetration of longer wavelength green light helps visualization of deeper vessels) (Figs. 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, and 5.10). Post-processing combination produces a high-definition image of the mucosa with visualization of subtle irregularities and altered vascular patterns [34]. Sharma et al. described relatively high sensitivity and specificity with NBI and described the various morphological patterns which were identified with this technology including ridge, villous,

circular or irregular mucosal, and/or vascular patterns [35]. In a small prospective study of 28 patients by Kara et al., additional areas of HGD were detected with NBI compared to WLE (four additional lesions in three patients); however this did not translate into increases in the number of cases diagnosed with HGD/EAC [36]. An international randomized controlled trial [37] comparing NBI with HD-WLE revealed that NBI required fewer biopsies per patient (3.6 vs. 7.6; $p < 0.0001$) and detected a higher proportion of areas with dysplasia (30% vs. 21%; $p = 0.01$). The conclusion of this study was that while all areas of HGD and cancer had an irregular mucosal or vascular pattern when examined with NBI, importantly, no areas of regular mucosal/vascular pattern harbored HGD or cancer, suggesting that biopsies of these areas can be avoided. This trial showed that NBI-targeted biopsies appear to be more efficient than random four-quadrant biopsies.

A systematic review of NBI found a good sensitivity ranging from 77% to 100%; high specificity (79–94%) and accuracy of 88–96% in differentiating gastric from intestinal mucosa in BE [38]. While identifying mucosal and vascular patterns during NBI is the most important factor in diagnosing areas harboring HGD/EAC, two studies have shown that NBI does not improve interobserver agreement or accuracy over HD-WLE [39, 40]. The overall yield for correctly identifying images of early neoplasia was 81% for HD-WLE, 72% for NBI, and 83% for HD-WLE with NBI, with no significant difference between experts and non-experts (interobserver agreement range 0.40–0.56). This study highlights the pitfalls of NBI in term of reproducibility of results in the community and need for formal training to realize its incremental benefit over HD-WLE.

The main advantages of NBI are the ability to evaluate both mucosal and vascular patterns at the same time, wide availability, and ease of use with no additional risk to the patient. The main disadvantages relate to the cost of equipment and need for trained manpower to interpret the images in real time.

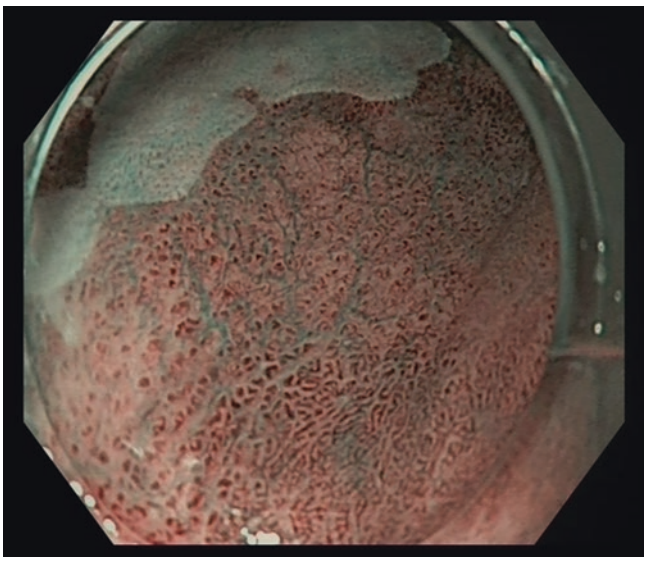

Fig. 5.4 Upper segment BE on narrowband imaging (NBI)

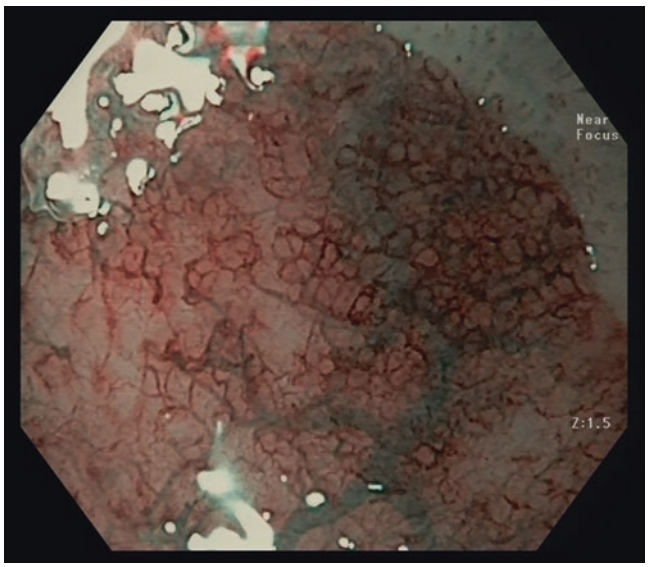

Fig. 5.5 Upper segment of BE with low magnification: note increased vascularity but no change in caliber of vessels

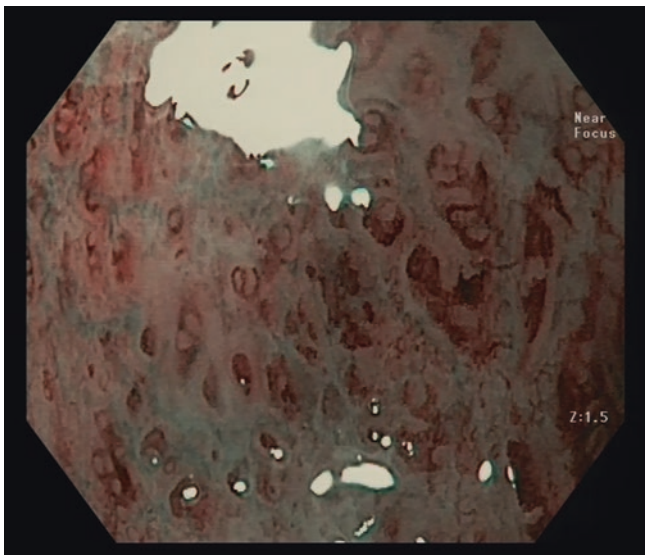

Fig. 5.6 Area seen on image 5 with high magnification: increased vascularity and some change in caliber of vessels

Autofluorescence Imaging

Certain tissues like collagen, elastin, aromatic amino acids, porphyrins and flavins exhibit a natural tendency of autofluorescence (shorter wavelength light is absorbed and a

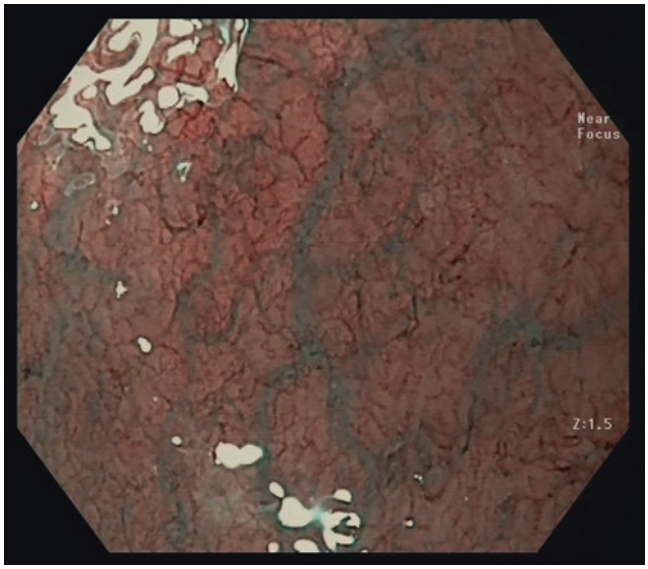

Fig. 5.7 Another area which demonstrates regular vascular in keeping with a non-dysplastic segment

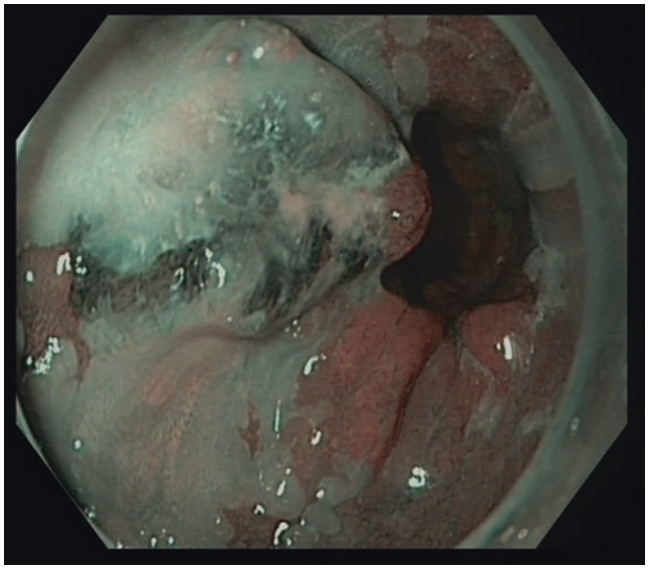

Fig. 5.9 View on narrowband imaging (NBI)

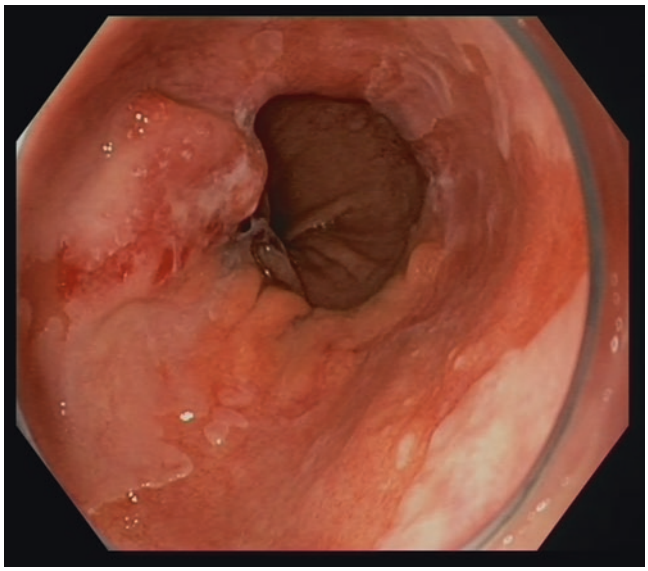

Fig. 5.8 Nodular area within Barrett's overlying squamous epithelization

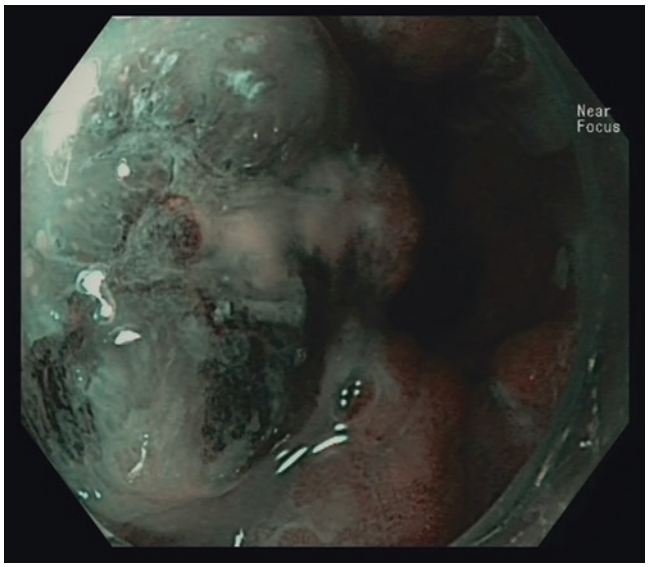

Fig. 5.10 Distorted pit pattern and vasculature on NBI and high magnification

longer wavelength light emitted). Autofluorescence imaging (AFI) utilizes this property to produce real-time pseudocolor images. Differences in AFI characteristics enable differentiation between normal and neoplastic tissue [41–43]. Post-processing of images captured during AFI renders normal tissue as green, blood vessels as dark green, and dysplastic/neoplastic areas as magenta. Change in nuclear-cytoplasmic ratio, loss of collagen, and neovascularization in dysplastic tissue create a difference in color from the surrounding mucosa (AFI-positive lesion) and aid identification of areas suspicious for malignancy [43]. In BE, the change is believed to result primarily from collagen in the stroma along with reabsorption by hemoglobin.

Kara et al. compared AFI with WLE in 22 patients with HGD and noted a sensitivity of 91% but with a low specificity (43%), mainly due to high false-positive rates [44]. They subsequently combined NBI with AFI and noted a reduction in the false-positive rates (10% from 40%) [45]. Combined use of WLE, NBI, and AFI (endoscopic trimodal imaging [ETMI]) was compared to WLE in 87 patients with suspected HGD/EAC. There was no statistically significant difference in overall detection rate for neoplasia (84% vs. 72%; $p > 0.05$) [46].

The major limitations of AFI are a high false-positive rate and no statistically significant difference in identifying dysplastic or neoplastic tissue (thought mainly due to low intensity signal changes in AFI from dysplastic or neoplastic tissue). Current literature and recommendations from various societies do not support AFI in BE imaging.

Post-processing Digital Chromoendoscopy (PPDC)

Concerns about adverse effects of locally applied or injected stains led to development of proprietary algorithms in post-processing of digital images to achieve effects similar to CE. The main advantage of this is the ease of use, involving an on-demand activation of an algorithm by pressing a button on the endoscope. Currently two systems for PPDC are available both of which combine post-processing with HD-WLE to improve visualization (*flexible spectral imaging color enhancement* (FICE) and blue laser imaging (BLI) by Fuji Corporation, Saitama, Japan, and *I-Scan* from Pentax Medical, Tokyo, Japan).

Pohl et al. conducted a randomized crossover study comparing FICE with AA CE and found a comparable sensitivity of 87% [47]. Others have noted improved sensitivity of FICE and AA CE compared to HD-WLE in detecting HGD (100% vs. 14%), with 100% specificity [48]. I-Scan consists of three different algorithms: surface enhancement (SE), contrast enhancement (ConE), and tone enhancement (TE) [49]. SE and ConE enhancement functions work in real time without impairing the original color; TE algorithm analyzes red, blue, and green images individually and produces a combined new image post-processing. This image is designed to enhance minute mucosal structures and subtle changes in color. In patients with gastroesophageal reflux disease, combination of WLE and I-Scan may significantly improve detection of early reflux change.

Optical Coherence Tomography (OCT)

This technique of endoscopic imaging may resemble endoscopic ultrasound. However it relies on near-infrared light (not acoustic waves) scattering to generate very high-quality cross-sectional images of epithelial and subepithelial tissue layers. OCT is performed using specialized probes that are passed down the instrument channels of endoscopes. However, since light waves are used in acquiring the signals, no tissue contact or exogenous contrast is required.

Studies looking at assessing the role of OCT in BE are limited and have small sample sizes. Evans et al. evaluated 55 patients with BE and showed sensitivity and specificity of 83% and 75%, respectively, in differentiating HGD from EAC [59]. Of note, this study looked at differentiating HGD from EAC, not at surveillance of BE for dysplastic changes. Another pioneering prospective study on OCT noted a sensitivity of 97% and specificity of 92% in detecting intestinal metaplasia in BE [50]. In a study of 33 patients looking at identifying dysplastic changes in BE, Isenberg and colleagues reported an accuracy rate of 78% albeit with high interobserver variability (56–98%) [51].

Inherent to the cross-sectional imaging nature of this technique, the future may hold a role for staging modality in EAC rather than in surveillance for dysplastic mucosa. More extensive clinical evaluation is required to define the role of OCT in either BE or EAC. The current limitations of OCT include high cost of equipment, problems with image acquisition, extensive training required in interpreting them, and high interobserver variability.

Biomarker Labeling

Dysplasia or neoplasia induces a change in the nature of expressed cell-surface markers. Molecular biomarkers, as measurable parameters, have different levels of expression which may help differentiating neoplastic and normal mucosa. These markers can be selectively targeted by specific antibodies, which are in turn labeled for visual (or fluorescence) visualization. In a paper published by Bird-Lieberman, alterations in cell-surface glycans in adenocarcinoma have been identified which can then specifically target changes in lecithin-binding properties [52]. Endoscopic application of wheat germ agglutinin (containing lecithin) allowed visualization of areas of HGD that were not detected by traditional methods. Lu and colleagues identified a cell-surface peptide specific to adenocarcinoma. This was labeled with a topical application of fluorescein tagged antibody and visualized with a fluorescence endoscope after a wash to remove any unbound antibody [53].

While advances in target identification, probe development, and optical instrumentation are creating new opportunities for early identification of dysplasia and neoplasia by molecular imaging; at the moment, biomarker labeling remains a technique under the realms of research.

Point Measurement Techniques

Confocal Laser Endomicroscopy

Confocal laser endomicroscopy (CLE) allows for real-time in vivo histological evaluation of areas of suspected neoplasia.

CLE uses a low-power laser light focused on a single point in a microscopic field of view. The light emanating from this point is focused through a pinhole to a detector. It allows for a high spatial resolution magnified image with magnifications up to 1250 times. The beam-focused spot traverses in horizontal and vertical directions to cover the area of interest, and the signal is processed to give a high-resolution two-

dimensional gray-scale image [54, 55]. CLE has been evaluated in BE and noted to have accuracy of up to 97.4% for detection of dysplasia [56]. Not only has this accuracy been difficult to duplicate [57], there has been criticism for CLE as it is expensive and has a long learning curve as interpretation of histopathology needs to be "relearned."

Elastic Scattering Spectroscopy

The principle behind elastic scattering spectroscopy (ESS) is a phenomenon of elastic scattering of white light by mucosa and submucosal tissues. This scattering is dependent on phenotypical characteristics like size and shape of cell nuclei and degree of cell crowding. This scattering (spectral signals) can be captured with special fiber optic probes passed down an endoscope to be processed into a digital image. This capture and processing takes place over a very short span of time; enabling imaging in "real time" compared to relatively long acquisition time required in most of the more recent imaging modalities.

Dysplastic and neoplastic tissue can be differentiated on the basis of their ESS "signature" which reflects the difference in cellular architecture. Since the scattering happens to a lesser extent, from deeper tissues as well, there is an element of interference in ESS that limits the accuracy to 85% [58]. In an interesting study of 81 patients by Lovat et al., ESS not only had a sensitivity and specificity of 92% and 60%, respectively, in identification of HGD but also sensitivity and specificity of 79% to differentiate HGD from inflammation [59].

Raman Spectroscopy

Raman spectroscopy (RS) is similar to ESS in that it relies on scattering of white light, but in the case of RS, it is the inelastic scattering that is used to generate a biochemical profile of the esophageal mucosa. Subtle changes in the molecular composition in neoplastic tissue can be detected and aid identification as such [60, 61]. A major drawback of RS is that the signal is typically very weak, and the differences may be too subtle to be appreciated.

Endoscopic Polarized Scanning Spectroscopy

This is relatively the newest of modalities described in endoscopic imaging techniques. It combines polarized light scattering spectroscopy with diffuse reflectance spectroscopy within the same instrument. Unlike other modalities of spectroscopy, it can image the entire esophagus and has shown great promise in detection of dysplasia in BE [62].

Conclusion

Surveillance in Barrett's esophagus is aimed at detecting progression to dysplasia and esophageal adenocarcinoma at an early stage. The current gold standard for screening remains HD-WLE with careful inspection of the entire

Practical Considerations

- Early detection of dysplastic change in BE can improve patient outcomes.
- There have been numerous promising advances in endoscopic imaging. These can be grouped either as wide-field (detection) or point measurement technologies.
- Chromoendoscopy (CE): Methylene blue or acetic acid is used to stain and highlight mucosal characteristics as an aid to enhance abnormal mucosal features. Although available, these dyes are deemed to be too cumbersome to use.
- NBI relies on difference in depth of penetration (and hence the visualization) of narrowed wavelength blue and green lights. Recent studies have shown benefit in reducing biopsies and increasing the yield of dysplasia.
- AFI relies on inherent properties of autofluorescence by different tissues and their unique characteristics. Normal tissue appears green and dysplastic or neoplastic tissue appears magenta. This technology has unfortunately fallen by the wayside due to the poorer resolution of images and high false-positive rates.
- Post-processing digital chromoendoscopy including FICE and I-Scan is based on an on-demand activation of a processing algorithm to generate images similar to CE. More studies are awaited.
- OCT creates high-quality cross-sectional images using near-infrared light. More studies are awaited.
- Point measurement techniques including confocal laser endomicroscopy, elastic scattering spectroscopy, Raman spectroscopy, and endoscopic polarized scanning spectroscopy are all novel developments and rarely available outside of the context of tertiary research academic centers.
- The current gold standard remains high-definition white light endoscopy which involves careful inspection of the entire area at risk, with ample of time spent with suction and insufflation, adequate lavage, and a methodical and thorough inspection including taking targeted biopsies from abnormal areas followed by sampling other normal areas according to the Seattle protocol.

area at risk, targeting abnormal areas for sampling followed by the Seattle protocol. A number of new techniques have been developed to aid the endoscopist in early detection of dysplastic changes. These techniques are classified into either wide-field detection techniques (e.g., NBI, AFI, CE, etc.) or point measurement techniques (e.g., CLE, ESS, etc.). There is however a need for more extensive studies to assess the role of these techniques in clinical practice and comparison to the current standard. The main disadvantages include the prohibitive costs of equipment and software as well as the steep learning curve. It cannot be emphasized enough that these techniques are meant to aid a skilled experienced endoscopist in the diagnosis and are not meant as a replacement for the time required to carefully inspect the entire area at risk.

References

1. Hvid-Jensen F, Pedersen L, Drewes AM, Sorensen HT, Funch-Jensen P. Incidence of adenocarcinoma among patients with Barrett's esophagus. N Engl J Med. 2011;365:1375–83.
2. Pohl H, Welch G. The role of over diagnosis and reclassification in the marked increase of esophageal adenocarcinoma incidence. J Natl Cancer Inst. 2005;97:142–6.
3. Rahman AA, Singh R, Sharma P. Management of Barrett's esophagus. Minerva Gastroenterol Dietol. 2013;59:13–23.
4. Evans JA, Early DS, Fukami N, et al. The role of endoscopy in Barrett's esophagus and other premalignant conditions of the esophagus. Gastrointest Endosc. 2012;76:1087–94.
5. Almond LM, Barr H. Advanced endoscopic imaging in Barrett's oesophagus. Int J Surg. 2012;10:236–41.
6. Falk GW, Ours TM, Richter JE. Practice patterns for surveillance of Barrett's esophagus in the United States. Gastrointest Endosc. 2000;52:197–203.
7. Vieth M, Ell C, Gossner L, et al. Histological analysis of endoscopic resection specimens from 326 patients with Barrett's esophagus and early neoplasia. Endoscopy. 2004;36:776–81.
8. Eckardt VF, Kanzler G, Bernhard G. Life expectancy and cancer risk in patients with Barrett's esophagus: a prospective controlled investigation. Am J Med. 2001;111:33–7.
9. Bhat S, Coleman HG, Yousef F, et al. Risk of malignant progression in Barrett's esophagus patients: results from a large population- based study. J Natl Cancer Inst. 2011;103:1049–57.
10. Hvid-Jensen F, Pedersen L, Drewes AM, et al. Incidence of adenocarcinoma among patients with Barrett's esophagus. N Engl J Med. 2011;365:1375–83.
11. Curvers WL, van Vilsteren FG, Baak LC, et al. Endoscopic trimodal imaging versus standard video endoscopy for detection of early Barrett's neoplasia: a multicenter, randomized, crossover study in general practice. Gastrointest Endosc. 2011;73:195–203.
12. Boerwinkle D, Swager AF, Curvers WL, Bergman JJGHM. The clinical consequences of advanced imaging techniques in Barrett's esophagus. Gastroenterology. 2014;146:622–9.
13. Sharma P, Savides TJ, Canto MI, et al. The American Society for Gastrointestinal Endoscopy PIVI (preservation and incorporation of valuable endoscopic innovations) on imaging in Barrett's esophagus. Gastrointest Endosc. 2012;76:252–4.
14. Gupta N, Gaddam S, Wani SB, et al. Longer inspection time is associated with increased detection of high-grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus. Gastrointest Endosc. 2012;76:531–8.
15. Trivedi PJ, Braden B. Indications, stains and techniques in chromoendoscopy. QJM. 2013;106(2):117–31.
16. Canto MI, Setrakian S, Willis JE, et al. Methylene blue staining of dysplastic and non-dysplastic Barrett's esophagus: an in vivo and ex vivo study. Endoscopy. 2001;33:391–400.
17. Canto MI, Setrakian S, Petras RE, et al. Methylene blue selectively stains intestinal metaplasia in Barrett's esophagus. Gastrointest Endosc. 1996;44:1–7.
18. Kiesslich R, Hahn M, Herrmann G, et al. Screening for specialized columnar epithelium with methylene blue: chromoendoscopy in patients with Barrett's esophagus and a normal control group. Gastrointest Endosc. 2001;53:47–52.
19. Kouklakis GS, Kountouras J, Dokas SM, et al. Methylene blue chromoendoscopy for the detection of Barrett's esophagus in a Greek cohort. Endoscopy. 2003;35:383–7.
20. Sharma P, Topalovski M, Mayo MS, et al. Methylene blue chromoendoscopy for detection of short-segment Barrett's esophagus. Gastrointest Endosc. 2001;54:289–93.
21. Dave U, Shousha S, Westaby D. Methylene blue staining: is it really useful in Barrett's esophagus? Gastrointest Endosc. 2001;53:333–5.
22. Gangarosa LM, Halter S, Mertz H. Methylene blue staining and endoscopic ultrasound evaluation of Barrett's esophagus with low-grade dysplasia. Dig Dis Sci. 2000;45:225–9.
23. Ngamruengphong S, Sharma VK, Das A. Diagnostic yield of methylene blue chromoendoscopy for detecting specialized intestinal metaplasia and dysplasia in Barrett's esophagus: a meta-analysis. Gastrointest Endosc. 2009;69:1021–8.
24. Olliver JR, Wild CP, Sahay P, et al. Chromoendoscopy with methylene blue and associated DNA damage in Barrett's oesophagus. Lancet. 2003;362:373–4.
25. Canto MI. Acetic-acid chromoendoscopy for Barrett's esophagus: the "pros". Gastrointest Endosc. 2006;64:13–6.
26. Lambert R, Rey JF, Sankaranarayanan R. Magnification and chromoscopy with the acetic acid test. Endoscopy. 2003;35:437–45.
27. Rey JF, Inoue H, Guelrud M. Magnification endoscopy with acetic acid for Barrett's esophagus. Endoscopy. 2005;37:583–6.
28. Costello S, Singh R. Endoscopic imaging in Barrett's oesophagus: applications in routine clinical practice and future outlook. Clin Endosc. 2011;44:87–92.
29. Fortun PJ, Anagnostopoulos GK, Kaye P, et al. Acetic acid-enhanced magnification endoscopy in the diagnosis of specialized intestinal metaplasia, dysplasia and early cancer in Barrett's oesophagus. Aliment Pharmacol Ther. 2006;23:735–42.
30. Bhandari P, Kandaswamy P, Cowlishaw D, et al. Acetic acid-enhanced chromoendoscopy is more cost-effective than protocol-guided biopsies in a high- risk Barrett's population. Dis Esophagus. 2012;25:386–92.
31. Longcroft-Wheaton G, Duku M, Mead R, et al. Acetic acid spray is an effective tool for the endoscopic detection of neoplasia in patients with Barrett's esophagus. Clin Gastroenterol Hepatol. 2010;8:843–7.
32. Bhandari P, Kandaswamy P, Cowlishaw D, et al. Acetic acid-enhanced chromoendoscopy is more cost-effective than protocol-guided biopsies in a high- risk Barrett's population. Dis Esophagus. 2012;25:386–92.
33. Gono K, Obi T, Yamaguchi M, et al. Appearance of enhanced tissue features in narrow-band endoscopic imaging. J Biomed Opt. 2004;9:568–77.
34. Sharma P, Bansal A, Mathur S, et al. The utility of a novel narrow band imaging endoscopy system in patients with Barrett's esophagus. Gastrointest Endosc. 2006;64:167–75.
35. Sharma P, Bansal A, Mathur S, et al. The utility of a novel narrow band imaging endoscopy system in patients with Barrett's esophagus. Gastrointest Endosc. 2006;64:167–75.

36. Kara MA, Peters FP, Rosmolen WD, et al. High-resolution endoscopy plus chromoendoscopy or narrow-band imaging in Barrett's esophagus: a prospective randomized crossover study. Endoscopy. 2005;37:929–36.
37. Sharma P, Hawes RH, Bansal A, et al. Standard endoscopy with random biopsies versus narrow band imaging targeted biopsies in Barrett's oesophagus: a prospective, international, randomized controlled trial. Gut. 2013;62:15–21.
38. Curvers WL, van den Broek FJ, Reitsma JB, et al. Systematic review of narrow-band imaging for the detection and differentiation of abnormalities in the esophagus and stomach. Gastrointest Endosc. 2009;69:307–17.
39. Curvers WL, Bohmer CJ, Mallant-Hent RC, et al. Mucosal morphology in Barrett's esophagus: inter-observer agreement and role of narrow band imaging. Endoscopy. 2008;40:799–805.
40. Herrero LA, Curvers WL, Bansal A, et al. Zooming in on Barrett oesophagus using narrow-band imaging: an international observer agreement study. Eur J Gastroenterol Hepatol. 2009;21:1068–75.
41. Almond LM, Barr H. Advanced endoscopic imaging in Barrett's oesophagus. Int J Surg. 2012;10:236–41.
42. Lee MH, Buterbaugh K, Richards-Kortum R, et al. Advanced endoscopic imaging for Barrett's esophagus: current options and future directions. Curr Gastroenterol Rep. 2012;14:216–25.
43. Filip M, Iordache S, Saftoiu A, et al. Autofluorescence imaging and magnification endoscopy. World J Gastroenterol. 2011;17:9–14.
44. Kara MA, Peters FP, Ten Kate FJ, et al. Endoscopic video autofluorescence imaging may improve the detection of early neoplasia in patients with Barrett's esophagus. Gastrointest Endosc. 2005;61:679–85.
45. Kara MA, Peters FP, Fockens P, et al. Endoscopic video autofluorescence imaging followed by narrow band imaging for detecting early neoplasia in Barrett's esophagus. Gastrointest Endosc. 2006;64:176–85.
46. Curvers WL, Herrero LA, Wallace MB, et al. Endoscopic tri-modal imaging is more effective than standard endoscopy in identifying early-stage neoplasia in Barrett's esophagus. Gastroenterology. 2010;139:1106–14.
47. Pohl J, May A, Rabenstein T, et al. Comparison of computed virtual chromoendoscopy and conventional chromoendoscopy with acetic acid for detection of neoplasia in Barrett's esophagus. Endoscopy. 2007;39:594–8.
48. Camus M, Coriat R, Leblanc S, et al. Helpfulness of the combination of acetic acid and FICE in the detection of Barrett's epithelium and Barrett's associated neoplasias. World J Gastroenterol. 2012;18:1921–5.
49. Saxena P, Canto MI. Red flag imaging techniques in Barrett's esophagus. Gastrointest Endosc Clin N Am. 2013;23:535–47.
50. Evans JA, Bouma BE, Bressner J, et al. Identifying intestinal metaplasia at the squamocolumnar junction by using optical coherence tomography. Gastrointest Endosc. 2007;65:50–6.
51. Isenberg G, Sivak MV Jr, Chak A, Wong RC, Willis JE, Wolf B, et al. Accuracy of endoscopic optical coherence tomography in the detection of dysplasia in Barrett's esophagus: a prospective, double-blinded study. Gastrointest Endosc. 2005;62:825–31.
52. Bird-Lieberman EL, Neves AA, Lao-Sirieix P, O'Donovan M, Novelli M, Lovat LB, et al. Molecular imaging using fluorescent lectins permits rapid endoscopic identification of dysplasia in Barrett's esophagus. Nat Med. 2012;18:315–21.
53. Lu S, Wang TD. In vivo cancer biomarkers of esophageal neoplasia. Cancer Biomark. 2008;4:341–50.
54. Polglase AL, McLaren WJ, Skinner SA, Kiesslich R, Neurath MF, Delaney PM. A fluorescence confocal endomicroscope for in vivo microscopy of the upper- and the lower-GI tract. Gastrointest Endosc. 2005;62:686–95.
55. Almadi MA, Neuman H. Probe based confocal laser endomicroscopy of the pancreatobiliary system. World J Gastroenterol. 2015;21(44):12696–708.
56. Goetz M, Kiesslich R. Confocal endomicroscopy: in vivo diagnosis of neoplastic lesions of the gastrointestinal tract. Anticancer Res. 2008;28:353–60.
57. Pohl H, Rosch T, Vieth M, Koch M, Becker V, Anders M, et al. Miniprobe confocal laser microscopy for the detection of invisible neoplasia in patients with Barrett's oesophagus. Gut. 2008;57:1648–53.
58. Haidry R, Butt MA, Lovat LB. Advances in endoscopy. Medicine. 2011;39:279–83.
59. Lovat LB, Johnson K, Mackenzie GD, Clark BR, Novelli MR, Davies S, et al. Elastic scattering spectroscopy accurately detects high grade dysplasia and cancer in Barrett's oesophagus. Gut. 2006;55:1078–83.
60. Bergholt MS, Zheng W, Lin K, Ho KY, Teh M, Yeoh KG, et al. In vivo diagnosis of esophageal cancer using image-guided Raman endoscopy and biomolecular modeling. Technol Cancer Res Treat. 2011;10:103–12.
61. Bergholt MS, Zheng W, Lin K, Ho KY, Teh M, Yeoh KG, et al. Characterizing variability in in-vivo Raman spectra of different anatomical locations in the upper gastrointestinal tract toward cancer detection. J Biomed Opt. 2011;16(3):037003.
62. Qiu L, Pleskow DK, Chuttani R, et al. Multispectral scanning during endoscopy guides biopsy of dysplasia in Barrett's esophagus. Nat Med. 2010;16:603–6.

Endoscopic Management of Barrett's Esophagus

6

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Introduction

Barrett's esophagus (BE) is a premalignant condition, which can lead to development of esophageal adenocarcinoma (EAC). The traditional definition of BE has been the presence of intestinal metaplasia (IM) in the columnar-lined epithelium replacing the normal squamous epithelium in the distal esophagus [1–2]. The well-established risk factors associated with development of BE include long-standing gastroesophageal reflux disease (GERD), male gender, age over 50 years, smoking, and central adiposity [3–5]. The role of endoscopic screening and surveillance is to identify changes (dysplasia), which can lead to development of EAC. The incidence of EAC in the USA has been rising in the past few decades [6, 7].

Role of Endoscopy in Diagnosis and Surveillance of Barrett's Esophagus

Endoscopy plays an integral role in diagnosis and management of Barrett's esophagus.

Diagnosis of Barrett's Esophagus

The endoscopic appearance of BE has been described as a salmon-colored or pink-colored appearance of mucosa in the esophagus. A standardized system called the "Prague classification" [8] has been devised in order to uniformly describe findings suggestive of BE. This includes the length of the circumferential (C) involvement of the esophagus and the maximal extent of the tongue of BE (M). For example, a circumferential involvement of 2 cm and longest tongue of BE segment is 4 cm, then the grading according to the Prague classification would be Barrett's C2M4.

More recent guidelines [9] recommend that the minimum length of the esophageal columnar mucosa/tongue before an endoscopic diagnosis of BE can be made is 1 cm. Biopsies of the esophageal columnar mucosa are required once the endoscopic diagnosis has been made. It is important to note that biopsies of the cardia, segments <1 cm, or the irregular z-line should be avoided, as this probably does not represent BE and might have implications on future surveillance and management.

Histological grading-based diagnosis includes non-dysplastic BE, indefinite for dysplasia, low-grade dysplasia, high-grade dysplasia, intramucosal carcinoma, and invasive carcinoma. Any diagnosis of dysplasia from the local institution pathologist requires further workup including the need for interpretation by an expert gastrointestinal pathologist. If there is evidence of inflammation endoscopically, the patient should be treated aggressively with high-dose proton pump inhibitor therapy for 8–12 weeks followed by repeat endoscopy with biopsy.

White light endoscopy has a high sensitivity for picking up BE and in most instances can be as high as 80–90% [10, 11]. Other adjuncts to endoscopy that have been evaluated include narrow band imaging [12–15], chromoendoscopy, and wide area transepithelial sampling (WATS).

Practical Considerations

- Risk factors associated with development of BE include long-standing GERD, male gender, age over 50 years, smoking, and central adiposity.
- The minimum length of the esophageal columnar mucosa/tongue before an endoscopic diagnosis of BE can be made is 1 cm.

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Surveillance of Barrett's Esophagus

Most contemporary studies report a low incidence of cancer development in patients with non-dysplastic BE (less than 0.5% annually). In a recent meta-analysis, wherein pooled data from 57 studies was included, the annual incidence of EAC was 0.33% and was lower for those with shorter segments of BE (<3 cm) at 0.19% [16]. Based on the low rate of progression of non-dysplastic BE to EAC, a surveillance interval of 3–5 years is recommended as per recent guidelines [1].

For low-grade dysplasia, the rates of progression to cancer have varied from 0.4% to 8% annually. This wide variability in progression rates can be attributed to the study cohort, duration of follow-up, number of pathologists confirming the diagnosis, and the end point (i.e., cancer development vs. high-grade dysplasia and/or cancer development). In a meta-analysis, the annual incidence of EAC in LGD (low-grade dysplasia) was reported as 0.5% and for the combined end point of high-grade dysplasia and EAC together at 1.7% [17]. Given the high interobserver variability in the diagnosis of LGD, it is recommended to seek opinion from an experienced gastrointestinal pathologist [18]. If surveillance is pursued in these patients, endoscopic biopsies should be in accordance with the Seattle protocol, with targeted biopsies of visible abnormalities followed by 4 quadrant biopsies ever 1 cm throughout the length [19–21].

Practical Considerations

- The annual incidence of EAC with shorter segments of BE (<3 cm) is around 0.19%.
- The annual incidence of EAC in low-grade dysplasia (LGD) is around 0.5%.

Role of Advanced Imaging Techniques in Barrett's Esophagus

In recent years there has been a great deal of interest in advanced imaging techniques in order to identify dysplasia and EAC, and if detected in real time, treatment can potentially be offered during the same endoscopy session. The imaging techniques can be divided into two broad categories: (1) wide field and (2) cross-sectional (Table 6.1) [22].

Table 6.1 Imaging techniques in Barrett's esophagus

Wide field imaging	Cross-sectional imaging
Standard white light endoscopy	Optical coherence tomography (OCT)
High-definition white light endoscopy (HD-WLE)	Optical frequency domain imaging (OFDI)
Chromoendoscopy Electronic chromoendoscopy	Confocal laser endomicroscopy (CLE)
NBI, IScan, FICE Autofluorescence imaging (AFI)	

High-Definition White Light/High-Resolution Endoscopy

Recent advances in endoscopic technology have led to improvement in the resolution of images. High-definition white light endoscopy (HD-WLE) gives >10 [6] pixel resolution [23]. Uses of several HD-WLE endoscopes allow for high-magnification images and are traditionally used with a cap fitted onto the distal end of the endoscopy. The use of HD-WLE is recommended for use for surveillance of BE and has been shown to be superior to conventional WLE [1, 24]. It has also been recommended to conduct a careful, slow examination of the BE segment (approximately 1 min/cm of BE length) and pay special attention to the right hemisphere between 12 o'clock and 6 o'clock position, as it might harbor HGD/EAC more frequently [25].

Chromoendoscopy

This employs the use of different stains to enhance the mucosal surface characteristics. Chromoendoscopy is combined with HD-WLE to improve the yield for detection of dysplasia and EAC. The different types of stains used can be categorized as absorptive (vital), contrast, and reactive stains. The stains mostly studied for use in BE include vital stains (acetic acid, Lugol's solution, methylene blue, and toluidine blue) and contrast stains (e.g., indigo carmine). The vital stains are absorbed by the mucosa and enhance the surface features. Contrast stains highlight the mucosa by accumulating in the pits and grooves of the tissue. For the application of stains, usually a spray catheter is employed, and pan staining is done while moving the endoscope back and forth. A recent meta-analysis of 14 studies that included a total of 843 patients showed that the use of chromoendoscopy increased the dysplasia detection by 34% (95% CI, 20–56%; $P < 0.0001$) [26].

Electronic Chromoendoscopy

NBI has been the most widely evaluated technique in this group and employs the wavelength that corresponds to peak wavelength absorbed hemoglobin (400–650 nm). The optical filters produce blue (440–460 nm) and green light (540–560 nm). This wavelength enhances visualization of tissue capillary, subepithelial vasculature, and surface topography [13]. A recent meta-analysis reported a sensitivity of 95% and specificity of 91% for the detection of HGD and a sensitivity of 91% and specificity of 85% for BE diagnosis [27]. Most recently ASGE assessed the role of advanced imaging technologies including NBI for

surveillance in patients with Barrett's esophagus. This included 15 studies with 1620 patients where sufficient data were present to calculate a per patient negative predictive value (NPV). The overall mean NPV for NBI was 97%. The per patient sensitivity and specificity of other new imaging techniques ranged from 33% to 100% and 56% to 100%, respectively [28].

Autofluorescence Imaging (AFI)

This modality uses blue light with wavelength of 395–475 nm, to excite endogenous fluorophores, such as elastin and collagen, and collects fluorescence in the visible spectrum (490–625 nm). Dysplastic mucosa appears green, and neoplasia appears magenta in color during AFI examination of the BE mucosa. There has been technological improvement in AFI (generation II) and has resulted in increased detection of HGD and EAC by 44% [29]. However, the false-positive rate is quite high, and at this time it is not recommended for routine use.

Confocal Laser Endomicroscopy (CLE)

Confocal imaging uses blue laser light (488 nm) to agitate or excite intravenously injected fluorescein and collects real time cross-sectional microscopic images. A magnification of beyond 1000 x can be achieved to view cellular structures. There are two main types of CLE: probe CLE (pCLE) and endoscope based (eCLE).

pCLE is a catheter that is passed through the working channel of the gastroscope, whereas in eCLE the optics are integrated into the tip of the endoscope.

The imaging interpretation is based on the appearance of the capillary structures and the cellular architecture. In a multicenter prospective study that included 100 patients with suspected BE, the addition of pCLE examination to WLE and NBI helped increase the detection rates of HGD/EAC patients. The overall sensitivity and specificity rates were 90.4% (95% CI, 76–97) and 89.9% (95% CI, 84–94), respectively [28].

Optical Coherence Tomography (OCT) and Optical Frequency Domain Imaging (OFDI)

Both these imaging technologies employ low coherence of laser to measure the time delay between the backscattering of light from the tissue surface and the reference beam. The concept of ultrasound is employed in OCT, but instead light is used as the source and a high axial resolution (1–10 μm) is achieved but the depth is only 1–2 mm [30]. The scanning technology used for OFDI is more advanced and collects the images based on OCT but at much higher speeds and can also produce three-dimensional images. Preliminary studies with the volumetric laser endomicroscopy probe have shown it to be a safe and effective technique in BE patients [31].

Practical Considerations

- The use of HD-WLE is recommended for use for surveillance of BE (superior to conventional WLE).
- The stains mostly studied for use (chromoendoscopy) in BE include vital stains (acetic acid, Lugol's solution, methylene blue, and toluidine blue) and contrast stains (e.g., indigo carmine).
- NBI is a widely evaluated technique in BE. It employs the wavelength that corresponds to peak wavelength absorbed hemoglobin (400–650 nm).
- In CLE the imaging interpretation is based on the appearance of the capillary structures and the cellular architecture.
- OCT and OFDI imaging technologies employ low coherence of laser to measure the time delay between the backscattering of light from the tissue surface and the reference beam.

Role of Endoscopic Ultrasound (EUS)

For local staging, EUS has been compared to computed tomography (CT), and the accuracy of diagnosing the correct depth of invasion is 85–90% compared to 50–80% with CT scan, and regional nodal staging accuracy is 70–80% with EUS compared to 50–70% for CT scan [32, 33]. Some experts advocate the use of EUS especially if there is a suspicious lesion or nodular area present within the BE segment but that EUS should not preclude from performing a diagnostic endoscopic mucosal resection, given that there can be under-staging and over-staging present with the use of EUS [1, 20]. EUS is, however, advocated in patients who have T1b lesions or higher (invasion to submucosa) in sampling locoregional lymph nodes as metastasis can be present and can alter management [1].

Role of Diagnostic Endoscopic Mucosal Resection (EMR)

For achieving successful treatment of BE (HGD or EAC), an accurate diagnosis is the key. At this time, it is recommended that if there is a visible lesion present on endoscopy, the patient should undergo a diagnostic EMR for initial diagnosis and also for treatment. Diagnostic EMR has helped in the accurate staging of these lesions and has resulted in change in diagnosis in up to 44% of the patients. In some studies upgrading of histology from HGD to EAC has been noted in 18.5% of patients and to invasive EAC in 40% [34, 35].

Role of Therapeutic Endoscopic Mucosal Resection (EMR) and Endoscopic Submucosal Dissection (ESD)

For visible early cancerous lesions in the esophagus, resection can be achieved either by piecemeal EMR or en bloc for larger lesions using ESD. For T1a cancers, the local spread to lymph nodes is low [36–38]; therefore, endoscopic resection through EMR or ESD can be curative. The use of resection is usually combined with ablation of the entire BE segment as data suggest high recurrence and progression to neoplasia if the entire BE is not eradicated [39]. T1a cancers can be successfully treated in 91–98% of cases with EMR [40–43], provided good patient selection and also no local lymph node involvement is present. Endoscopic submucosal dissection (ESD) can be utilized for lesions more than 2 cm in size or in selected T1b lesions, although usually surgery is recommended for T1b lesions; the risk for locoregional spread of EAC to lymph nodes is high (12–37%) [36–38, 44] although resection therapy has been successfully performed in T1b patients with low-risk features. The low-risk features include invasion of the upper 1/3 of the submucosal (sm1), absence of lymph vessel/vein infiltration, histological grade (G1/G2), and macroscopic type I/II [45].

The efficacy of EMR and ESD in patients with neoplastic Barrett's esophagus was compared in a recent randomized study [46]. Patients with high-grade intraepithelial neoplasia (HGIN) or early EAC </= 3 cm were randomized. R0 resection was achieved more frequently with ESD (10/17 vs. 2/17, $p = 0.01$), but there was no difference in complete remission from neoplasia at 3 months. During the follow-up period (23.1 ± 6.4 months), only one patient in the ESD group had recurrent EAC. In addition, the time required for ESD and complication rates is much higher than EMR.

Practical Considerations

- For local staging EUS has the accuracy of diagnosing the correct depth of invasion that is 85–90% compared to 50–80% with CT scan.
- If there is a visible lesion present on endoscopy, the patient should undergo a diagnostic EMR for initial diagnosis and also for treatment.
- T1a cancers can be successfully treated in 91–98% of cases with EMR.
- T1b can be successfully treated by ESD in selected patients.

Ablative Therapies

Photodynamic Therapy (PDT)

This was one of the initial mucosal ablation techniques studied in a RCT but now is of historical importance. In a large, multicenter RCT, PDT was shown to reduce the incidence of adenocarcinoma (28% in the control arm vs. 13% PDT). The initial study was reported at 2-year [47] follow-up, and then the results were again confirmed at 5 years of follow-up, showing long-term durability of treatment results [48].

Radiofrequency Ablation (RFA)

As the term suggests, this technology applies radiofrequency energy to the BE segment. RFA can be achieved by using either the circumferential balloon-based system or focal devices. The balloon-based system includes a high-power energy generator, a sizing balloon catheter, and then several sizes of balloon ablation catheters that are equipped with electrodes that encircle the delivery balloon catheter. The new-generation balloon does not require the sizing step thereby improving the efficiency of the procedure. The treatment with the balloon goes from proximal to distal with minimal overlap and is repeated till the entire BE segment is ablated. After the initial balloon treatment at follow-up, either it can be repeated or if there are small areas of residual columnar mucosa, they can be treated with the focal RFA device [49, 50].

RFA was evaluated in a multicenter sham-controlled RCT [51], and the primary outcome was eradication of BE at 12 months. In the intention to treat analysis, for the LGD group, there was 90.5% eradication vs. 22.7% ($P < 0.001$) in the control group, and in HGD patients, there was 81% eradication compared to 19% ($P < 0.001$) in the controls. In another prospective multicenter trial (uncontrolled), where stepwise circumferential and focal ablation patients were followed for 2.5 years, complete remission of intestinal metaplasia was achieved in 98% of the patients [52]. In a US multicenter study using EMR plus RFA, after 24 months of complete eradication of BE, the incidence of recurrence was 33%; 22% of all the recurrences were dysplastic BE [53]. In another study where 246 patients with either HGD or intramucosal cancer (IMC) were included, the recurrence rates of dysplasia after complete eradication of BE were similar in both groups (HGD 8% vs. IMC, 9.5%; p = 0.44; RR, 1.2; 95% CI 0.5–3.0) and remained similar after 5 years of follow-up (HGD 13.5% vs. IMC, 11.4%; $p = 0.53$; RR 0.85, 95% CI 0.3–2.7) [54]. Therefore, ongoing surveillance is recommended after complete eradication-IM is achieved.

Cryotherapy

Cryotherapy or cryoablation is a noncontact method of causing tissue injury and can be achieved by using either liquid nitrogen or CO2. Cryospray ablation (CSA Medical, Baltimore, MD, USA) uses low-pressure (2–3 psi) liquid nitrogen at – 196 °C, whereas Polar Wand (GI Supply, Camp Hill, PA, USA) uses CO_2 stored in a small-pressurized container (450–750 psi) and the gas is delivered through a catheter which can be passed through the channel of the endoscope. A more recently tested device uses a balloon catheter to deliver cryoablation (C2 therapeutics, CA).

Retrospective data evaluating safety and efficacy shows that with the use of cryotherapy, eradication of HGD can be achieved in 97% of the treated patients with complete eradication of intestinal metaplasia in 57% [55]. In a more recent study of safety and efficacy in 96 patients using the National Cryospray Registry [56], complete eradication of HGD was achieved in 81%, LGD eradication in 91%, and intestinal metaplasia eradication in 77% of the treated patients.

Argon Plasma Coagulation (APC) and Hybrid APC

APC employs a noncontact thermal method of coagulation of tissue through the use of an inert gas, argon. This gas flows through a flexible catheter that has a tungsten electrode at the distal tip. As the gas passes over the electrode, it becomes ionized and passes electricity through an arc of ionized argon gas (plasma), which causes tissue coagulation. The depth of coagulation is dependent on the gas flow rate and the power setting of the power generator.

The RCT by Manner et al. included patients that underwent treatment of Barrett's neoplasia (high-grade intraepithelial neoplasia (HGIN) or mucosal cancer) initially with endoscopic resection. A total of 64 patients were randomized to APC of residual segment vs. surveillance. Disease-free survival was the primary outcome being measured. The number of lesions seen in APC group was 1 (3%) and surveillance group was 11 (36.7%), leading to a higher recurrence-free survival in APC group ($P = 0.005$) [57]. The second RCT by Sie C et al. compared APC vs. surveillance in a total of 129 patients with NDBE or LGD BE. HGD developed in one patient in APC group and three in surveillance group, whereas LGD developed in one patient in APC group and six in the surveillance group. This study also showed that APC reduced the extent of BE [58].

A relatively newer approach using APC has been termed as "hybrid APC." This involves submucosal injection of saline prior the thermal ablative therapy with APC. In a series of 50 patients that underwent hybrid APC, complete eradication of BE was seen in 78% of the patients. Strictures were noted in only 2% of the patients. This pilot series showed this hybrid approach is safe and effective for BE ablation with a low complication rate [59].

Practical Considerations

- With regard to balloon ablation, the new-generation devices do not require the sizing step of balloon thereby improving the efficiency of the procedure.
- Cryotherapy or cryoablation is a noncontact method of causing tissue injury and can be achieved by using either liquid nitrogen or CO2.
- APC employs a noncontact thermal method of coagulation of tissue through the use of an inert gas, argon.
- "Hybrid APC" involves submucosal injection of saline prior the thermal ablative therapy with APC.

Challenges with Endoscopic Therapy

Complications

The complications related with endoscopic management of BE can be divided into major and minor complications. Major complications include significant bleeding requiring hospitalization, transfusion or intervention, pneumomediastinum, pneumothorax, perforation, stricture formation, ulcerations, cardiac arrhythmias, and in rare instances death. Minor complications include transient dysphagia, odynophagia, chest pain, heartburn, fevers, and sore throat.

For EMR, in a large study of 681 patients undergoing 2513 EMRs, significant bleeding (requiring intervention, transfusion, or hospitalization) was 1.2% [60]. The reported perforation rate for experienced physicians with EMR is 0.5% [60–62] and, however, can be as high as 5% [63]. Esophageal stenosis rates vary from 6% to 88% in various studies. They are more common if larger lesions or areas are resected [63–65].

A recent publication evaluated 37 studies (comprising of 9200 patients) for complications related to RFA therapy. The overall complication rate was 8.8% (95% CI, 6.5–11.9%) with strictures accounting 5.6% (95% CI, 4.2–7.4%) of complications [66].

With conventional APC, the reported complication rate can range up to 24% including perforation, pneumomediastinum, subcutaneous emphysema, transmural burn syndrome, ulceration, and stricture formation [67–70]. On the other hand, hybrid APC is associated with low rate of esophageal stenosis (2%) [59] though it's a novel approach, although further data are awaited.

Recurrences After Endoscopic Therapy

The above-described ablative therapies for BE are highly effective, but there is still an important role of surveillance after ablation. Recurrence of disease has been reported in virtually every long-term study; studies with RFA have shown up to 30–35% recurrence rates at 2–3 years of follow-up. Similarly in patients undergoing widespread EMR, although complete eradication of neoplasia was achieved in 90% of the patients, during a mean follow-up of 64.8 months, recurrence rate of 6.2% neoplasia and 39.5% non-dysplastic BE were seen [71]. Risk factors for recurrence included older age, non-Caucasian race, and increasing length of BE length [72].

Endoscopic Quality, Case Volume, and Expertise

The majority of the efficacy trials have been performed at centers of expertise and the equipment available to handle the complications related to the different modalities used. The ultimate goal of endoscopic treatment is to improve patient outcomes and also to minimize complications. In order to achieve this, it is recommended that treatment should be done at centers of high volume where >15 cases of HGD are treated yearly [73]. The British Society of Gastroenterology also recommended certain case volume for training (30 supervised EMR and 30 mucosal ablations) and to maintain skills (15 EMRs/year) [9]. Also, to minimize variability in reporting and misinterpretation, standard reporting of quality measures is needed [74]. Patient selection also plays a very important role in determination of complications (more comorbid conditions will have higher risk for complications). Anticoagulation status and antiplatelet status also need to be addressed with the patient prior to therapy as these procedures are considered high-risk endoscopic procedures [75].

Conclusions Endoscopic approach to diagnosis of BE should be standardized, and clear identification of anatomical landmarks during endoscopy is critical.

- Advances in diagnostic imaging technics can help with the diagnosis and management of dysplastic BE.
- The diagnosis of dysplasia in BE should be confirmed by an outside expert GI pathologist.
- Resection followed by ablation is the hybrid approach utilized for the majority of the patients undergoing endoscopic eradication therapy.
- The role of EMR is expanding in this patient population.

References

1. Shaheen NJ, Falk GW, Iyer PG, et al. ACG clinical guideline: diagnosis and management of Barrett's esophagus. Am J Gastroenterol. 2015;111(1):30–50.
2. Jung KW, Talley NJ, Romero Y, et al. Epidemiology and natural history of intestinal metaplasia of the gastroesophageal junction and Barrett's esophagus: a population-based study. Am J Gastroenterol. 2011;106:1447–55. quiz 1456.
3. Rubenstein JH, Mattek N, Eisen G. Age- and sex-specific yield of Barrett's esophagus by endoscopy indication. Gastrointest Endosc. 2010;71:21–7.
4. Singh S, Sharma AN, Murad MH, et al. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11:1399–1412 e7.
5. Rubenstein JH, Morgenstern H, Appelman H, et al. Prediction of Barrett's esophagus among men. Am J Gastroenterol. 2013;108:353–62.
6. Brown LM, Devesa SS. Epidemiologic trends in esophageal and gastric cancer in the United States. Surg Oncol Clin N Am. 2002;11:235–56.
7. Hur C, Miller M, Kong CY, et al. Trends in esophageal adenocarcinoma incidence and mortality. Cancer. 2013;119:1149–58.
8. Sharma P, Dent J, Armstrong D, et al. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. Gastroenterology. 2006;131:1392–9.
9. Fitzgerald RC, di Pietro M, Ragunath K, et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. Gut. 2014;63:7–42.
10. Eloubeidi MA, Provenzale D. Does this patient have Barrett's esophagus? The utility of predicting Barrett's esophagus at the index endoscopy. Am J Gastroenterol. 1999;94:937–43.
11. Kim SL, Waring JP, Spechler SJ, et al. Diagnostic inconsistencies in Barrett's esophagus Department of Veterans Affairs Gastroesophageal Reflux Study Group. Gastroenterology. 1994;107:945–9.
12. Sharma P. Narrow band imaging in Barrett's esophagus. Clin Gastroenterol Hepatol. 2005;3:S21–2.
13. Kuznetsov K, Lambert R, Rey JF. Narrow-band imaging: potential and limitations. Endoscopy. 2006;38:76–81.
14. Kara MA, Ennahachi M, Fockens P, et al. Detection and classification of the mucosal and vascular patterns (mucosal morphology) in Barrett's esophagus by using narrow band imaging. Gastrointest Endosc. 2006;64:155–66.
15. Reddymasu SC, Sharma P. Advances in endoscopic imaging of the esophagus. Gastroenterol Clin N Am. 2008;37:763–74. vii.
16. Desai TK, Krishnan K, Samala N, et al. The incidence of oesophageal adenocarcinoma in non-dysplastic Barrett's oesophagus: a meta-analysis. Gut. 2012;61:970–6.
17. Singh S, Manickam P, Amin AV, et al. Incidence of esophageal adenocarcinoma in Barrett's esophagus with low-grade dysplasia: a systematic review and meta-analysis. Gastrointest Endosc. 2014;79:897–909 e4. quiz 983 e1, 983 e3.
18. Montgomery E, Bronner MP, Goldblum JR, et al. Reproducibility of the diagnosis of dysplasia in Barrett esophagus: a reaffirmation. Hum Pathol. 2001;32:368–78.
19. Wani S, Falk GW, Post J, et al. Risk factors for progression of low-grade dysplasia in patients with Barrett's esophagus. Gastroenterology. 2011;141:1179–1186 e1.
20. Committee ASoP, Evans JA, Early DS, et al. The role of endoscopy in Barrett's esophagus and other premalignant conditions of the esophagus. Gastrointest Endosc. 2012;76:1087–94.

21. De Looze D. Endoscopic follow-up of Barrett's esophagus: protocol and implications. Acta Gastroenterol Belg. 2000;63:29–35.
22. Sturm MB, Wang TD. Emerging optical methods for surveillance of Barrett's oesophagus. Gut. 2015;64:1816–23.
23. Committee AT, Kwon RS, Adler DG, et al. High-resolution and high-magnification endoscopes. Gastrointest Endosc. 2009;69:399–407.
24. Corley DA, Mehtani K, Quesenberry C, et al. Impact of endoscopic surveillance on mortality from Barrett's esophagus-associated esophageal adenocarcinomas. Gastroenterology. 2013;145:312–9 e1.
25. Enestvedt BK, Lugo R, Guarner-Argente C, et al. Location, location, location: does early cancer in Barrett's esophagus have a preference? Gastrointest Endosc. 2013;78:462–7.
26. Qumseya BJ, Wang H, Badie N, et al. Advanced imaging technologies increase detection of dysplasia and neoplasia in patients with Barrett's esophagus: a meta-analysis and systematic review. Clin Gastroenterol Hepatol. 2013;11:1562–70 e1-2.
27. Song J, Zhang J, Wang J, et al. Meta-analysis of the effects of endoscopy with narrow band imaging in detecting dysplasia in Barrett's esophagus. Dis Esophagus. 2015;28:560–6.
28. Committee AT, Thosani N, Abu Dayyeh BK, et al. ASGE Technology Committee systematic review and meta-analysis assessing the ASGE preservation and incorporation of valuable endoscopic innovations thresholds for adopting real-time imaging-assisted endoscopic targeted biopsy during endoscopic surveillance of Barrett's esophagus. Gastrointest Endosc. 2016;83:684–698 e7.
29. Boerwinkel DF, Holz JA, Aalders MC, et al. Third-generation autofluorescence endoscopy for the detection of early neoplasia in Barrett's esophagus: a pilot study. Dis Esophagus. 2014;27:276–84.
30. Cobb MJ, Hwang JH, Upton MP, et al. Imaging of subsquamous Barrett's epithelium with ultrahigh-resolution optical coherence tomography: a histologic correlation study. Gastrointest Endosc. 2010;71:223–30.
31. Wolfsen HC, Sharma P, Wallace MB, et al. Safety and feasibility of volumetric laser endomicroscopy in patients with Barrett's esophagus (with videos). Gastrointest Endosc. 2015;82:631–40.
32. Schmassmann A. Esophageal carcinoma: accurate staging thanks to modern diagnostic methods open up new therapeutic strategies. Schweiz Med Wochenschr. 1999;129:1207–10.
33. Ziegler K, Sanft C, Zeitz M, et al. Evaluation of endosonography in TN staging of oesophageal cancer. Gut. 1991;32:16–20.
34. Nijhawan PK, Wang KK. Endoscopic mucosal resection for lesions with endoscopic features suggestive of malignancy and high-grade dysplasia within Barrett's esophagus. Gastrointest Endosc. 2000;52:328–32.
35. Larghi A, Lightdale CJ, Memeo L, et al. EUS followed by EMR for staging of high-grade dysplasia and early cancer in Barrett's esophagus. Gastrointest Endosc. 2005;62:16–23.
36. Griffin SM, Burt AD, Jennings NA. Lymph node metastasis in early esophageal adenocarcinoma. Ann Surg. 2011;254:731–6. discussion 736–7.
37. Pennathur A, Farkas A, Krasinskas AM, et al. Esophagectomy for T1 esophageal cancer: outcomes in 100 patients and implications for endoscopic therapy. Ann Thorac Surg. 2009;87:1048–54. discussion 1054–5.
38. Leers JM, DeMeester SR, Oezcelik A, et al. The prevalence of lymph node metastases in patients with T1 esophageal adenocarcinoma a retrospective review of esophagectomy specimens. Ann Surg. 2011;253:271–8.
39. Pech O, Behrens A, May A, et al. Long-term results and risk factor analysis for recurrence after curative endoscopic therapy in 349 patients with high-grade intraepithelial neoplasia and mucosal adenocarcinoma in Barrett's oesophagus. Gut. 2008;57:1200–6.
40. Stahl M, Budach W, Meyer HJ, et al. Esophageal cancer: clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2010;21(Suppl 5):v46–9.
41. May A, Ell C. Diagnosis and treatment of early esophageal cancer. Curr Opin Gastroenterol. 2006;22:433–6.
42. Ciocirlan M, Lapalus MG, Hervieu V, et al. Endoscopic mucosal resection for squamous premalignant and early malignant lesions of the esophagus. Endoscopy. 2007;39:24–9.
43. Ell C, May A, Pech O, et al. Curative endoscopic resection of early esophageal adenocarcinomas (Barrett's cancer). Gastrointest Endosc. 2007;65:3–10.
44. Sepesi B, Watson TJ, Zhou D, et al. Are endoscopic therapies appropriate for superficial submucosal esophageal adenocarcinoma? An analysis of esophagectomy specimens. J Am Coll Surg. 2010;210:418–27.
45. Manner H, May A, Pech O, et al. Early Barrett's carcinoma with "low-risk" submucosal invasion: long-term results of endoscopic resection with a curative intent. Am J Gastroenterol. 2008;103:2589–97.
46. Terheggen G, Horn EM, Vieth M, et al. A randomised trial of endoscopic submucosal dissection versus endoscopic mucosal resection for early Barrett's neoplasia. Gut. 2016;66(5):783–93.
47. Overholt BF, Lightdale CJ, Wang KK, et al. Photodynamic therapy with porfimer sodium for ablation of high-grade dysplasia in Barrett's esophagus: international, partially blinded, randomized phase III trial. Gastrointest Endosc. 2005;62:488–98.
48. Overholt BF, Wang KK, Burdick JS, et al. Five-year efficacy and safety of photodynamic therapy with Photofrin in Barrett's high-grade dysplasia. Gastrointest Endosc. 2007;66:460–8.
49. Ganz RA, Utley DS, Stern RA, et al. Complete ablation of esophageal epithelium with a balloon-based bipolar electrode: a phased evaluation in the porcine and in the human esophagus. Gastrointest Endosc. 2004;60:1002–10.
50. Smith CD, Bejarano PA, Melvin WS, et al. Endoscopic ablation of intestinal metaplasia containing high-grade dysplasia in esophagectomy patients using a balloon-based ablation system. Surg Endosc. 2007;21:560–9.
51. Shaheen NJ, Sharma P, Overholt BF, et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. N Engl J Med. 2009;360:2277–88.
52. Fleischer DE, Overholt BF, Sharma VK, et al. Endoscopic ablation of Barrett's esophagus: a multicenter study with 2.5-year follow-up. Gastrointest Endosc. 2008;68:867–76.
53. Gupta M, Iyer PG, Lutzke L, et al. Recurrence of esophageal intestinal metaplasia after endoscopic mucosal resection and radiofrequency ablation of Barrett's esophagus: results from a US Multicenter Consortium. Gastroenterology. 2013;145:79–86. e1.
54. Small AJ, Sutherland SE, Hightower JS, et al. Comparative risk of recurrence of dysplasia and carcinoma after endoluminal eradication therapy of high-grade dysplasia versus intramucosal carcinoma in Barrett's esophagus. Gastrointest Endosc. 2015;81:1158–66 e1-4.
55. Shaheen NJ, Greenwald BD, Peery AF, et al. Safety and efficacy of endoscopic spray cryotherapy for Barrett's esophagus with high-grade dysplasia. Gastrointest Endosc. 2010;71:680–5.
56. Ghorbani S, Tsai FC, Greenwald BD, et al. Safety and efficacy of endoscopic spray cryotherapy for Barrett's dysplasia: results of the National Cryospray Registry. Dis Esophagus. 2015;29(3):241–7.
57. Manner H, Rabenstein T, Pech O, et al. Ablation of residual Barrett's epithelium after endoscopic resection: a randomized long-term follow-up study of argon plasma coagulation vs. surveillance (APE study). Endoscopy. 2014;46:6–12.
58. Sie C, Bright T, Schoeman M, et al. Argon plasma coagulation ablation versus endoscopic surveillance of Barrett's esophagus: late outcomes from two randomized trials. Endoscopy. 2013;45:859–65.
59. Manner H, May A, Kouti I, et al. Efficacy and safety of hybrid-APC for the ablation of Barrett's esophagus. Surg Endosc. 2016;30:1364–70.

60. Tomizawa Y, Iyer PG, Wong Kee Song LM, et al. Safety of endoscopic mucosal resection for Barrett's esophagus. Am J Gastroenterol. 2013;108:1440–7. quiz 1448.
61. Fujishiro M, Kodashima S, Goto O, et al. Endoscopic submucosal dissection for esophageal squamous cell neoplasms. Dig Endosc. 2009;21:109–15.
62. Inoue H. Endoscopic mucosal resection for esophageal and gastric mucosal cancers. Can J Gastroenterol. 1998;12:355–9.
63. van Vilsteren FG, Pouw RE, Seewald S, et al. Stepwise radical endoscopic resection versus radiofrequency ablation for Barrett's oesophagus with high-grade dysplasia or early cancer: a multicentre randomised trial. Gut. 2011;60:765–73.
64. Seewald S, Akaraviputh T, Seitz U, et al. Circumferential EMR and complete removal of Barrett's epithelium: a new approach to management of Barrett's esophagus containing high-grade intraepithelial neoplasia and intramucosal carcinoma. Gastrointest Endosc. 2003;57:854–9.
65. Qumseya B, Panossian AM, Rizk C, et al. Predictors of esophageal stricture formation post endoscopic mucosal resection. Clin Endosc. 2014;47:155–61.
66. Qumseya BJ, Wani S, Desai M, et al. Adverse events after radiofrequency ablation in patients with Barrett's esophagus: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2016;14(8):1086–1095.e6.
67. Grade AJ, Shah IA, Medlin SM, et al. The efficacy and safety of argon plasma coagulation therapy in Barrett's esophagus. Gastrointest Endosc. 1999;50:18–22.
68. Ackroyd R, Tam W, Schoeman M, et al. Prospective randomized controlled trial of argon plasma coagulation ablation vs. endoscopic surveillance of patients with Barrett's esophagus after antireflux surgery. Gastrointest Endosc. 2004;59:1–7.
69. Van Laethem JL, Jagodzinski R, Peny MO, et al. Argon plasma coagulation in the treatment of Barrett's high-grade dysplasia and in situ adenocarcinoma. Endoscopy. 2001;33:257–61.
70. American Society for Gastrointestinal Endoscopy Technology C. Mucosal ablation devices. Gastrointest Endosc. 2008;68:1031–42.
71. Anders M, Bahr C, El-Masry MA, et al. Long-term recurrence of neoplasia and Barrett's epithelium after complete endoscopic resection. Gut. 2014;63:1535–43.
72. Pasricha S, Bulsiewicz WJ, Hathorn KE, et al. Durability and predictors of successful radiofrequency ablation for Barrett's esophagus. Clin Gastroenterol Hepatol. 2014;12:1840–7 e1.
73. Chadwick G, Groene O, Taylor A, et al. Management of Barrett's high-grade dysplasia: initial results from a population-based national audit. Gastrointest Endosc. 2016;83:736–742 e1.
74. Parasa S, Sharma P. Measuring quality of endoscopic eradication therapy in Barrett's esophagus. Gastrointest Endosc. 2016;83:743–5.
75. Committee ASoP, Acosta RD, Abraham NS, et al. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc. 2016;83:3–16.

Endoscopic Tissue Sampling: A Pathologist's Perspective (Good Endoscopists Think Ahead)

7

Robert H. Riddell

Introduction

Few endoscopists think further than the immediate question when taking biopsies, so thinking ahead is not usually part of endoscopic training. Further, it is very difficult to acquire this skill unless there is regular contact with a pathologist interested in GI pathology, such as might occur with regular biopsy rounds. Some diagnoses require clinical/endoscopic input particularly regarding either endoscopic appearances or medications the patient is taking; in the absence of which, the pathologists' response is likely to be descriptive and that "clinical correlation is required." In some instances this is inevitable if the histological diagnosis is unexpected, but usually it can be anticipated. When the pathologist has this information, then they may be in the best position to make the correlation, but in its absence it is easily shifted back to the clinician – a responsibility that pathologists are very willing to abrogate. This chapter will look at situations in which the endoscopist can anticipate the potential issue(s) the pathologist is likely to consider when a specific question is asked, the assumption being that the pathologist is able to take this responsibility and that criteria are available to answer the question. At the end of the day, the objective is to make an accurate diagnosis and ensure the most appropriate therapy for the patient while keeping everyone out of trouble from a diagnostic and management viewpoint.

Every time a scope is inserted, the endoscopist should mentally have a synoptic checklist which should include at least the following, much of which will find its way into the endoscopy report. Clearly some procedures are entirely therapeutic which may or may not generate material for pathological evaluation. Nevertheless (see Box 7.1).

Box 7.1 Endoscopic considerations regarding information for the pathologist

- Reason it is being done?
- What was found?
- Pictures to document (make them available) ideally with the pathology requisition.
- Which questions came up?
- Can pathology help?
- Is the pathologist able to answer the question?
- If so, which (set of) biopsies or endoscopic resections do I need to answer the question?
- Can I anticipate the next question that will come back at me from the pathologists (should such events occur)?
- Take appropriate biopsies.
- Give the pathologist the information and ask the question(s).

Reason it is being done.
What was found?
Pictures to document (make them available) ideally with the pathology requisition.
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Can I anticipate the next question that will come back at me from the pathologists (should such events occur)?
Take appropriate biopsies.
Give the pathologist the information and ask the question(s).

As an aside, a good proportion of the consultation cases we receive would not have been necessary had the original pathologist had access to the endoscopy report and relevant clinical information, especially including major diseases and

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a medication history. When the pathologist adds "clinical correlation is required" at the end of a report, it is usually a substitute for "you did not provide the information I needed to answer the question." Pathologists try to provide a good and accurate service with a short turnaround time. This is facilitated if they have access to these data. Relying on the pathologist to find and look up the endoscopy report assumes that they know where to find it and that if necessary it has been typed/submitted and is available, but when dealing with a large number of biopsies on a daily basis, they rarely have the time to do this. Unfortunately, pathologists also have a tendency to provide descriptions (e.g., chronic active colitis) without an interpretation (the real diagnosis). This leaves the interpretation to the clinician, who is often not the best person to make this call. Let us then look at some potential clinical circumstances where thinking ahead and sticking to well-defined guidelines may well pay dividends.

Eosinophilic Esophagitis (Box 7.2)

- Don't shortcut the biopsy protocol – take biopsies from both distal + mid-esophagus, and put each site in separate containers.
- Consider biopsying the stomach and duodenum – especially if typical appearances of EoE are present.

Box 7.2 Eosinophilic esophagitis (EoE)

- Don't shortcut the biopsy protocol – take biopsies from both distal + mid-esophagus and put each site in separate containers.
- Consider biopsying the stomach and duodenum – especially if typical appearances of EoE are present.

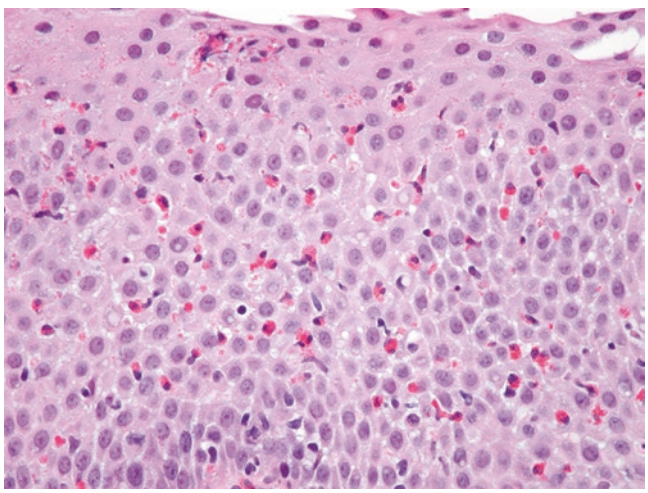

Fig. 7.1 Esophageal biopsy showing squamous mucosa with numerous eosinophils, sufficient for a diagnosis of "eosinophilic esophagitis"

There are well-defined guidelines for confirming or excluding this diagnosis [1, 2]. As a result, most endoscopists take biopsies from both the mid- and distal esophagus, but some try and bypass this so that biopsies are only taken from one site (mid- or lower esophagus – Fig. 7.1). While there may be some truth to the fact that eosinophils in the mid-esophagus are likely to represent EoE, the gradation of eosinophil numbers from distal to proximal makes it easier for the pathologist to make the diagnosis, especially when gastroesophageal reflux disease comes into the differential diagnosis. The fact that some patients with EoE respond to PPIs take some of the heat out of this, but when treating with steroids, it makes sense to ensure that the diagnosis is correct. Using the usual criterion of 15 eosinophils/hpf, a diagnostic sensitivity of 84%, 97%, and 100% for obtaining two,

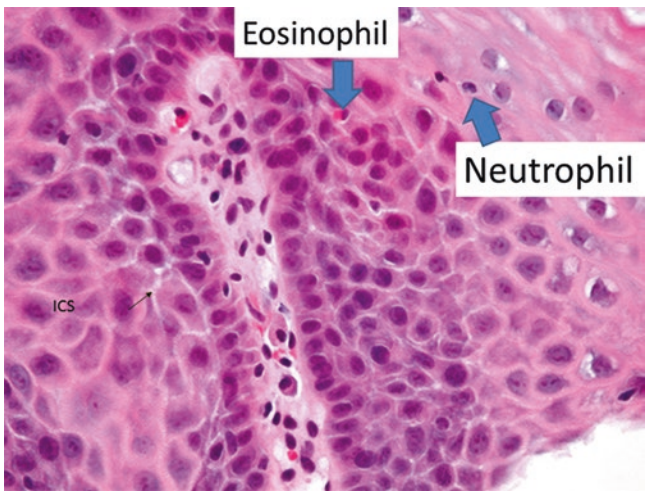

Fig. 7.2 Random biopsy from the GE junction. The thickened basal layer is interpreted as within physiological limits but the presence of occasional eosinophils and neutrophils (either) is better evidence of GERD

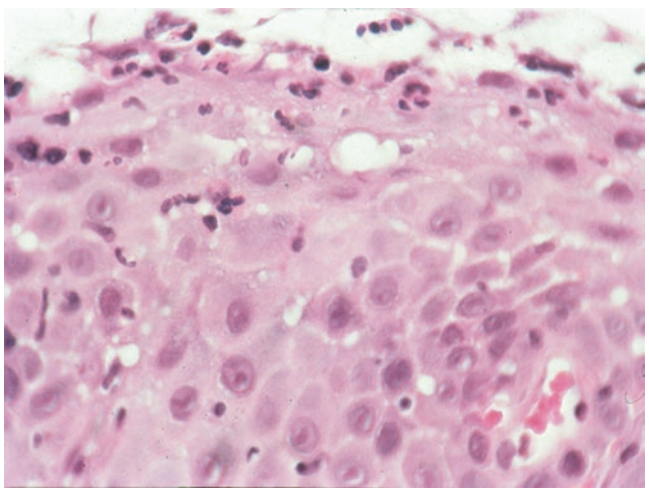

Fig. 7.3 Esophageal biopsy from the lower esophagus with superficial neutrophils. In this location, this suggests GERD but Candidiasis always needs to be excluded using a stain such as PAS-D or Grocott methenamine silver

three, and six biopsy specimens, respectively [3]. So two biopsies each from lower and mid-esophagus in separate containers are ideal (Figs. 7.2 and 7.3).

Thinking ahead in EoE is that, as in some patients it represents an allergic diatheses, especially to food, the possibility that there is also an eosinophilic infiltration in other parts of the gastrointestinal (GI) tract, and especially stomach and duodenum should be considered. Biopsying the stomach (antrum and body) and also duodenum anticipates this potential. While there are no guidelines, analogous to celiac disease, the bulb and second part seem reasonable biopsy sites. There is a considerable variation with how interested endoscopists deal with this issue in practice [4].

Gastroesophageal Reflux Disease (GERD) (Box 7.3)

1. Biopsies of the squamous mucosa immediately above the GE junction can be useful in confirming the diagnosis.
2. The diagnosis of Barrett's esophagus requires an appropriate endoscopic appearance.
3. Biopsying the normal cardia – don't do it.
4. Dysplasia in Barrett's esophagus – ablating low-grade dysplasia.
5. Is an "expert" pathology opinion really required?

Box 7.3 Gastroesophageal reflux disease (GERD)

- Biopsies of the squamous mucosa immediately above the GE junction can be useful in confirming the diagnosis.
- The diagnosis of Barrett's esophagus requires the endoscopic appearance.
- Biopsying the normal cardia – don't do it.

Biopsies of the squamous mucosa immediately above the GE junction can be useful in confirming the diagnosis. For decades, the fact that the lower 3 cm of squamous mucosa could show basal cell hyperplasia and papillary elongation was translated into "the lower esophagus should not be biopsied for GERD." This ignores the fact that neutrophils, eosinophils, and even healing erosions can be found on biopsy and, especially in the squamous mucosa close to the cardia, strongly suggest GERD (Figs. 7.2, 7.3). It is appreciated that endoscopy is usually not carried out for straightforward GERD, as response to PPIs usually provides as simple diagnostic test.

The diagnosis of Barrett's esophagus requires the endoscopic appearance. The diagnosis of Barrett's esophagus depends on a combination of a typical endoscopic appearance of Barrett's esophagus and an accompanying biopsy that shows intestinal metaplasia (IM) [5]. The implication of this is that a biopsy cannot just be taken with "?Barrett's" or "?BE" as the question, without including the endoscopic data. Without it, even the presence of intestinal metaplasia can only be reported as "intestinal metaplasia" present. If an interpretation is attempted, it can only be along the lines of "intestinal metaplasia present". If the biopsies were from cardia, this represents intestinal metaplasia at the cardia, but if the endoscopic appearances are appropriate, this represents Barrett's esophagus." Few pathologists have the time to be any more than descriptive, although some might go as far as "clinical correlation is required for interpretation." If you can't be bothered to tell us the endoscopic appearance, you are on your own.

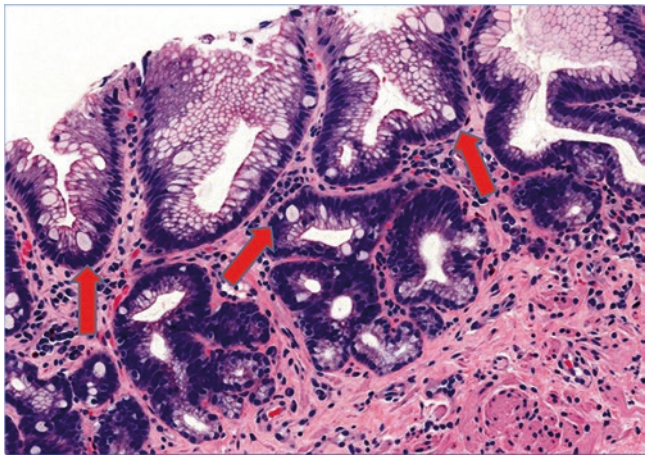

Fig. 7.4 Biopsy "from GE junction – R/O Barrett's". There is intestinal metaplasia (goblet cells, some of which are arrowed). However, without the endoscopic appearances (e.g. endoscopic tongue suggesting Barrett's), the pathologist can only be descriptive, with tthe likely exhortation that "clinical correlation is required" (= you did not give me the information needed for me to make the diagnosis)

Biopsying the normal cardia – don't do it! This brings us to whether one should biopsy the cardia. In some series, the prevalence of intestinal metaplasia has been found to be between 15% and 35% [6, 7]; biopsying a normal-appearing cardia may result in an additional question of how to manage IM at the cardia (Fig. 7.4). While it is apparent that IM at the cardia is the precursor of intestinal-type carcinomas at the cardia, following this population would overwhelm resources for what is likely very little return. However, it should also be remembered that antral mucosa and cardia mucosa are similar, and one is often reflected in the other. Patients with intestinal metaplasia in the antrum may therefore also have intestinal metaplasia at the cardia, and *Helicobacter* in the antrum may also be reflected at the cardia. The recommendation is therefore that the cardia is better left unbiopsied unless there is a lesion present [8].

Dysplasia in Barrett's esophagus – ablating low-grade dysplasia. Guidelines for intervention for dysplasia in Barrett's esophagus are changing, so that interventional therapy (EMR/ablation) may well be appropriate therapy for low-grade as well as high-grade dysplasia [5, 9]. From a pathologist's viewpoint, this brings us to a major issue.

Is an "expert" pathology opinion really required? The critical decision histologically is increasingly to separate indefinite for dysplasia (IND) from low-grade dysplasia (LGD), a decision that has low interobserver (kappa) values. In a Dutch study, of 293 patients with low-grade dysplasia (LGD) reviewed by an "expert" panel, 73% were downstaged to non-dysplastic Barrett's esophagus or IND. In only 27% was the initial diagnosis of LGD confirmed. Follow-up of all groups confirmed that this was meaningful: endoscopic follow-up in 264 patients of these patients (median follow-up of 39 months) found that for confirmed LGD, the risk of high-grade dysplasia (HGD) or invasive adenocarcinoma was 9.1% per patient-year. However, patients that had been downstaged to non-dysplastic Barrett's esophagus or IND had a progression risk of 0.6% and 0.9% per patient-year, respectively [10]. Fortunately, both endoscopic mucosal ablation (EMR) and ablation therapy have virtually no mortality and low morbidity, especially when compared with esophageal resection. Nevertheless EMR and ablation take time and resources and are not cheap and so need to be carried out only on appropriate patients.

This now raises the whole issue of whether all biopsies with a diagnosis of dysplasia in Barrett's esophagus should be reviewed by an expert/experienced GI pathologist, which in turn begs the question of who falls into this category. Experience does not necessarily equate with being an expert, although it is usually a prerequisite, and stating that a pathologist is "experienced" (which can have boundaries such as being at least x years post boards and signing out predominantly GI pathology) is likely less controversial than being an expert, which is hugely subjective. Having access to a sound opinion, for many endoscopists basically comes down to trust in the opinion of a specific pathologist, given that there are few data on which to base any decision for a specific pathologist. If one is fortunate enough to have a local "expert" who does seem to get it right consistently, then second opinions may not be necessary. The main problem is twofold:

(a) We tend to think of dysplasia in BE as a single spectrum, whereas in practice dysplasia can occur in numerous different types of mucosae found in BE. This therefore includes mucosae with both complete (goblet and absorptive cells, occasionally with Paneth cells as typically seen in small or large bowel) and incomplete intestinal metaplasia (an admixture of goblet cells with gastric-type mucous-producing cells as shown in Fig. 7.4) and also native gastric mucosa of all three subtypes – superficial foveolar, deep pyloric glands, and oxyntic (acid producing) mucosa [11]. Further, these can occur in combinations. Fortunately most are of intestinal type, but the gastric subtypes are much more difficult to grade, and gastric foveolar (originally called type II dysplasia) in particular can be seen admixed with intestinal-type dysplasias.

(b) Some biopsies of low-grade dysplasia, especially in biopsies with intestinal metaplasia, are very straightforward, but others can be extremely difficult, and even in a group setting, deciding what is truth may come down to a majority vote. Some variants, such as dysplasia limited to the crypt region (crypt dysplasia), non-intestinal dysplasias, and those on the spectrum somewhere between IFD and LGD, can be hugely subjective.

Gastric Biopsies (Box 7.4)

Box 7.4 Gastric biopsies

- Biopsying for *Helicobacter*: taking two antral and two oxyntic biopsies for *Helicobacter* or other diseases is an uncommon skill – get it right.
- Atrophic gastritis is often missed by endoscopists and pathologists alike.
- When gastric polyps are present, the "money" is usually in the background mucosa, so biopsy it as *Helicobacter* (2 + 2).

1. Biopsying for *Helicobacter*: taking two antral and two oxyntic biopsies for *Helicobacter* or other diseases is an uncommon skill – get it right.
2. Atrophic gastritis is often missed by endoscopists and pathologists alike.
3. When gastric polyps are present, the "money" is usually in the background mucosa, so biopsy it as *Helicobacter* (2 + 2).

Biopsying for Helicobacter It should be easy for trained endoscopists to take two antral and two oxyntic mucosal biopsies. However, most pathologists are aware that this is achieved relatively infrequently. Some endoscopists appear to think that the organisms are always present in the antrum, so only take biopsies from that site; many seem to know that both antral and body (oxyntic) biopsies are required (as in the AGA and ACG recommendations), while the fact that adding a biopsy from the incisura as in the updated Sydney system appears virtually unknown in North America. In a study from a major teaching hospital with a GI training program, a review of over 10,000 patients biopsied for *Helicobacter* showed

that only one region was actually sampled in 60% of patients (antrum 47%, body 13%). In those purported to have included both antral and body biopsies, both regions were actually sampled in 57%, the reminder being either both antrum or both body. When present, *Helicobacter* was actually found only in the antrum in 15%, only in the body in 21%, and at both sites in 65% [12]. Taking biopsies from only one site can therefore markedly underestimate the presence of *Helicobacter* (result in a false-negative result). It should be recalled that initially *Helicobacter* tends to be antral but shifts proximally with age/length of disease, possibly being enhanced in those with small parietal cell masses, those with aggressive organisms (toxins on the pathogenicity island), or those on long-term proton pump inhibitors (PPIs). The latter is physiologically interesting as the organisms' urease produces a cloud of ammonium ions around each organism that requires acid to prevent the ambient pH remaining below 8, as *Helicobacter* cannot survive at a higher pH. Usually ambient acid is sufficient, but in patients with severe atrophic gastritis or on high-dose PPIs, the organisms migrate proximally in search of acid and can even migrate into the canaliculi of parietal cells. It is relatively uncommon to find antral *Helicobacter* in patients taking daily PPIs. In addition *Helicobacter* is never found in areas of intestinal metaplasia as they require gastric mucin in which to grow. As intestinal metaplasia, especially *Helicobacter* related, tends to be antral, body biopsies are usually required to find the organism. Further, atrophy tends to progress proximally in a sleevelike manner so, relatively speaking, progressing faster up the lesser than greater curve; the biopsy from upper greater curve may therefore be the critical site in which to find *Helicobacter* in patients with atrophy and extensive metaplasia.

What then is the ideal combination of sites to biopsy? First, the prepyloric antrum and incisura are the areas in which *Helicobacter* usually thrive up so they are the best sites to biopsy. While the incisura is a recommended fifth site in the updated Sydney system, little heed is paid to that in North America. The prepyloric antrum in particular is the part of the antral mucosa containing gastrin-producing cells; as these can be easily identified on H and E sections, it is easy for pathologists to confirm that the antrum was indeed biopsied, so it is ideal. The targeting of the oxyntic mucosa needs to take into account that atrophy tends to go higher up the lesser curve, so while this is a good site for *Helicobacter*, it is also the best place to detect intestinal metaplasia and atrophic gastritis, in which *Helicobacter* are rarely found. If atrophy is recognized endoscopically, then the lesser curve is best avoided for *Helicobacter* detection but ideal to confirm atrophic gastritis (hence the wisdom of using the incisura as a fifth biopsy site in the updated Sydney system). The upper greater curve is the essential biopsy site under both of these circumstances. Interestingly, for some reason the surface mucosa of oxyntic mucosa strips off easily when biopsies are taken, so this needs to be a good biopsy. It may not matter much whether this is anterior, posterior, or upper greater curve as long as it is well into the oxyntic mucosa.

The best combination of sites that avoids the potential 15–21% miss rate when only one site is biopsied is therefore:

Two antral biopsies – prepyloric, opposing walls.
Two body (oxyntic) mucosa, e.g., ant- and post-wall or either of these plus upper greater curve.
An incisura biopsy is good for both *Helicobacter* and detecting atrophic gastritis.

Atrophic gastritis is often missed by endoscopists and pathologists alike. Atrophic gastritis is most frequently *Helicobacter* related and may also have an autoimmune component but only occasionally does one see pure autoimmune gastritis without *Helicobacter*. In 1969, Kimura and Takemoto provided an endoscopic classification system for atrophic gastritis and identified the "atrophic border," which started at the level of the proximal antrum (incisura on the lesser curve) and over time extended proximally in a uniform sleevelike manner at the same speed circumferentially [13]. By the time it reached the upper lesser curve, it was only halfway up the greater curve. At that time this was thought to be an aging change but is now recognized as a *Helicobacter*-related change in which atrophy creeps proximally destroying oxyntic mucosa and leaving simple pyloric-type glands with or without intestinal metaplasia. This has led to the term multifocal atrophic gastritis, which is a misnomer as it is largely the intestinal metaplasia that is multifocal but on a background of diffuse atrophic gastritis, although sometimes the intestinal metaplasia can completely replace the entire stomach. While the atrophic process is usually diffuse, sometimes small islands of inflamed oxyntic mucosa remain. Although it is usually stated that the antrum is normal, there is invariably mild chronic inflammation or reactive changes, or both, even in autoimmune gastritis; the rationale is likely that parietal cells still find their way down into the antrum so can invoke an immune reaction.

To take this one step further, atrophy can be subdivided endoscopically into closed, which is restricted to the lesser curve but extends for increasing distances proximally, and open which extends up the greater curve for increasing distances also. The carcinogenic risk increases with the degree of atrophy [14, 15].

However, as the oxyntic mucosa is lost, so is acid production, resulting in gradual and increasing hypergastrinemia. This results in changes in parietal cells in the residual oxyntic mucosa more commonly seen in patents on PPIs (which produces a similar hypergastrinemia) but also results in endocrine cell proliferation in the pyloric metaplasia, as these are gastrin sensitive. Recognizing the atrophic border seems problematic, and some are also unaware of its existence although, once explained, realize that they have been

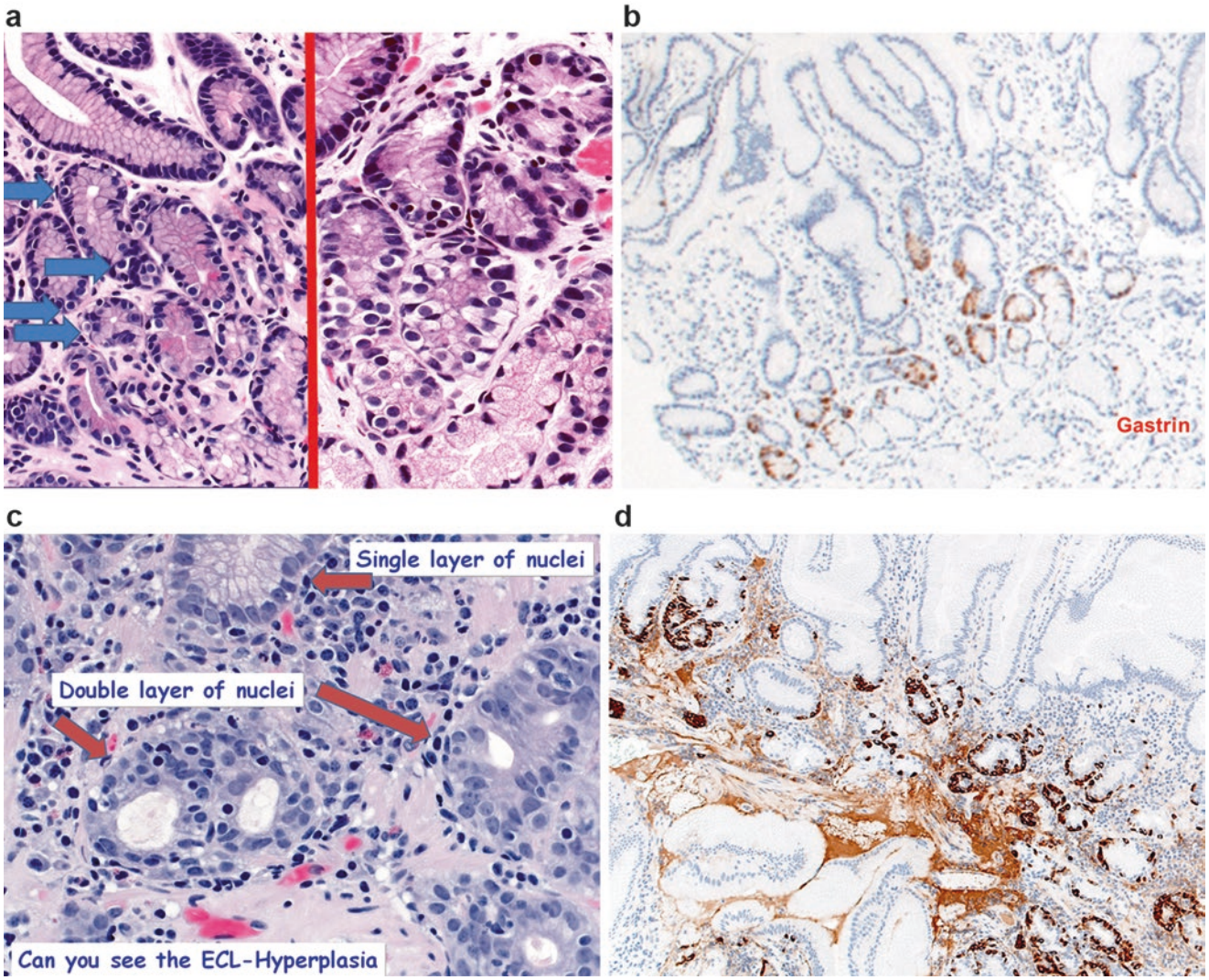

Fig. 7.5 Stomach in atrophic gastritis **a**) Antral mucosa with G-cell hyperplasia (the numerous fried eggs cells) indicative of hypergastrinemia). **b**) gastrin stain showing the normal distribution of G-cells in a band in the mid-zone **c**) atrophic gastritis in which the endocrine cell hyperplasia is visible as a double layer **d**) endocrine cells stain (synaptophysin) showing the rings of endocrine cells, which are the external layer of cells seen in c

seeing it. Biopsies of this type of mucosa may therefore be inadvertent and usually show a mixture of simple mucous-producing glands with or without intestinal metaplasia. From a pathologist's viewpoint, antral-type glands and metaplastic pyloric glands can initially appear identical, so it is only the location of the endocrine cells that allows theory distinction. In the antrum G cells are mid-zone, but in endocrine cell, hyperplasia are around the base of the crypts where they may be visible as a double cell layer that can often be seen if searched for but be difficult or impossible to recognize without endocrine cell stains (synaptophysin and chromogranin) as well as gastrin stain to show that the mucosa is not (Fig. 7.5).

The issue with atrophic gastritis is that while the endocrine cell hyperplasia can be diffuse, producing numerous small polyps, this is usually without clinical significance. However, the accompanying intestinal metaplasia has an increased risk of dysplasia and carcinoma which, in patients with severe disease and potentially pernicious anemia in addition, is likely an increased risk of about ×7 which still only amounts to a risk of <1% p.a [16]. However, if present, this is sufficient to justify follow-up, and although there are no evidence-based data for frequency of follow-up, once it is apparent that there are no dysplastic or invasive lesions are present (diagnostic endoscopies) and that serology (antibodies to intrinsic factor, parietal cells, *Helicobacter*, and serum B12 and gastrin levels) has been carried out, it is likely that endoscopy every 2 or 3 years should be sufficient [17]. If *Helicobacter*, or antibodies to it, are found, then it seems wise to eradicate residual

Helicobacter, although data that this has any effect on the natural history of the disease is lacking [18]. Some may reflect that they rarely or never see this disease, which may be a true statement and may mean they, or their pathologist, are missing it but may also mean that patients found to have B12-deficient megaloblastic anemia are more likely to find their way to a hematologist, who will document and treat the disease, but may not think of investigating the underlying gastric pathology.

When gastric polyps are present, the "money" is usually in the background mucosa, so biopsy it as Helicobacter (2 + 2). While it is self-evident that gastric polyps of unknown etiology need to be biopsied or removed, virtually all gastric polyps arise on a background (soil) of underlying disease of varying etiologies, many of which can be detected by biopsying the background mucosa at the time – a typical example of thinking ahead if it is done. Most adenomas develop on a background of intestinal metaplasia, which itself develops on a background of *Helicobacter* or atrophic gastritis.

Hyperplastic polyps and inflammatory polyps can be seen in stomachs with *Helicobacter* gastritis. Hyperplastic polyps, and adenomas of all types, including pyloric gland adenomas and multiple ECL (enterochromaffin-like) carcinoids/neuroendocrine tumors can be seen on a background of atrophic and autoimmune gastritis.

In all of these, the obvious follow-up is to go back and see what sort of mucosa these are arising on, so the 2 + 2 as described for *Helicobacter* (or 2 + 2 + 1 including the incisura) is required. So why not do it at the time the polyp is found? The only possible exception is in patients on long-term PPIs, e.g., for Barrett's esophagus in which fundic gland polyps subsequently develop but can be ascribed to the PPIs and subsequent hypergastrinemia.

However, a small proportion of polyps need a history, so polyps developing on a background of any of the polyposis syndromes (adenomatous polyposis including GAPPS syndrome, Lynch syndrome, Peutz-Jegher, juvenile polyposis, and PTEN/Cowden's syndrome [19]) need a clinical history mutational analysis to put it all together.

Duodenal Biopsies (Box 7.5)

1. Biopsy both the duodenal bulb as well as the second part to diagnose/exclude celiac disease.
2. Be aware that medications, especially olmesartan, can produce both the symptoms and a histological appearance identical to celiac disease (as well as gastritis and microscopic colitis).

Duodenal Biopsies for Celiac Disease: D2 and Bulb

For decades, we were taught to avoid biopsies from the duodenal bulb when taking biopsies for celiac disease as villi were small; there was a high incidence of confounding "peptic duodenitis" and sometimes large Brunner's glands compressing villi, all of which could confuse the morphologic picture. It has become apparent that celiac disease is a disease characterized by the presence of intraepithelial lymphocytes (IELs), i.e., no IELs and no celiac disease (unless treated). As the prevalence of *Helicobacter* diminished, its confounding effects on the duodenal bulb also declined, and in *Helicobacter* naïve patients obviously play no role. However, *Helicobacter* is associated with an increase in IELs in D2 albeit with normal villi [20], so it is in the differential diagnosis of a Marsh 1 lesion (IELs with normal villi in celiac disease). As *Helicobacter* decreases, because it had long been known that celiac disease was primarily a proximal duodenal disease, it was found that especially in children, biopsies from the duodenal bulb could sometimes show flat mucosa when more distal biopsies showed minimal changes [21]. Because an intraepithelial lymphocytosis in the second part of the duodenum can also be seen with *Helicobacter* gastritis, patients taking NSAIDs in all of their guises, patients with bacterial overgrowth and immune deficits such as those seen in CVID, the presence of a flat bulb biopsy leaves a differential that is celiac disease until proven otherwise [22] (Fig. 7.6). The exception is in patients taking olmesartan – see next section Moral – biopsy both sites.

Box 7.5 Duodenal biopsies

- Biopsy both the duodenal bulb and the second part to diagnose/exclude celiac disease.
- Be aware that medications, especially olmesartan, can produce both the symptoms and a histological appearance identical to celiac disease (as well as gastritis and microscopic colitis).

Olmesartan can produce both the symptoms and a histological appearance identical to that seen in celiac disease. Since the classic paper in 2012, most have become aware that occasional patients taking olmesartan can have both symptoms and a duodenal biopsy that can mimic celiac disease [23]. Symptoms can be severe and even accompanied by lymphocytic gastritis and both lymphocytic and collagenous colitis. While patients are usually

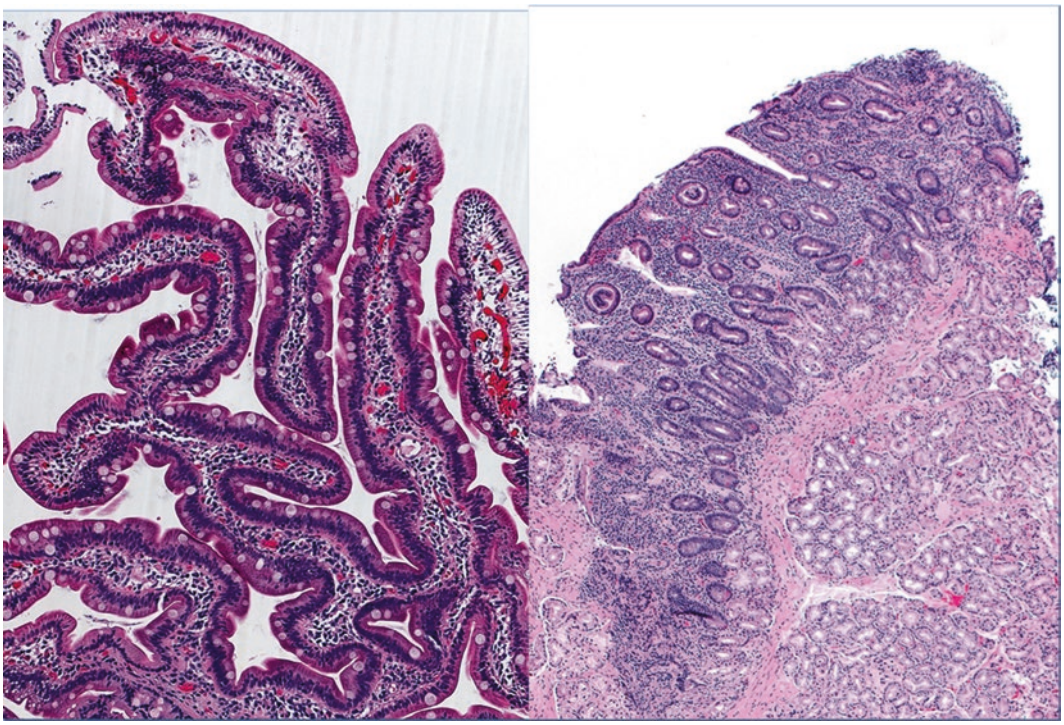

Fig. 7.6 Celiac disease D2 and bulb in a F28. The D2 biopsy (left) has well formed villi with scant intraepithelial lymphcytes. The biopsy from the duodenal bulb (right) is completely flat

also HLA – DQ2 or DQ8 – serological markers of celiac disease are negative. The obvious treatment is to recognize the cause and change therapy [24].

Terminal Ileal Biopsies (Box 7.6)

- Crohn's disease vs medication injury (NSAIDs/ASA) – what is the patient taking? Take the time to find out.

Ileal inflammation is occasionally encountered, usually in the form of erythema, erosions, or small ulcers; given the frequency of ingestion of NSAIDs and ASA in the population, medication-associated injury is always a consideration. However in a proportion of patients, these changes appear to be incidental with no known cause (including herbals and other OTC products). Although NSAIDs are well known as a cause of ulcers throughout the GI tract, chronic low-dose aspirin can cause a plethora of lesions in the ileum including erosions, round, serpiginous, or punched-out ulcers and, rarely, even large ulcers and strictures; some studies also suggest that enteric-coated aspirin, rather than buffered aspirin, may cause more damage to the small bowel mucosa [25]. In practice erosions are more likely to be associated with low-dose aspirin and ulcers with NSAIDs [26] (Fig. 7.7).

The most important differential diagnosis is that of medication-associated injury (NSAIDs/ASA) from Crohn's disease. It is usually impossible for pathologists to confirm either unless granulomas are present as they are not seen in medication-associated injury; otherwise the pathology in biopsies can be virtually identical as both tend to have chronic active ileitis with erosions or ulcers and features of chronic injury (architectural distortion, pyloric metaplasia, duplication of muscularis mucosae). Occasionally other diseases such as Behçet's disease or tuberculosis rear their heads, but Behçet's disease needs other clinical features of the disease, while TB needs a high index of suspicion. If TB is a serious consideration and if the organism cannot be identified in granulomas, some have found that laparoscopic examination of the ileum useful, as any possible tubercles can be both biopsied and sent for culture.

Box 7.6 Terminal ileal biopsies

- Crohn's disease vs medication injury (NSAIDs/ASA).
- What is the patient taking?
- Take the time to find out.

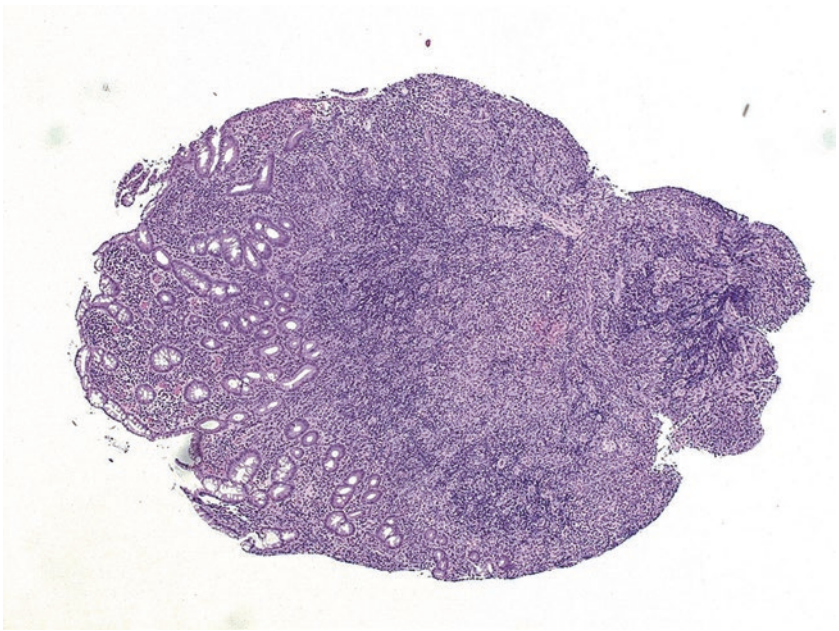

Fig. 7.7 Ileal biopsy from an "ulcer." Note the lack of villi, erosion and possibly an ulcer on the right (no epithelium) and a heavy inflammatory infiltrate. In the absence of granulomas this can be medications, especially NSAIDs or low dose ASA, or Crohn's. The endosopic appearances and medication history are critical in sorting this out

The real issue in practice is how often "incidental" ulcers herald subsequent Crohn's disease. The current best study excluded patients with colorectal symptoms or colorectal resection, a history of NSAID use (low-dose aspirin is not specifically mentioned), oral or genital ulcerations, and coincidental ulceration in the ileocecal valve or colon. With a mean follow-up of 30 months fully two thirds of patients (62/93) showed resolution of the ulcers, all but two with no therapy (the other two had antituberculous therapy). In the remaining 31 patients, only 1 developed typical Crohn's disease, whereas the other 30 showed no significant changes in the lesions (n = 22), partial improvement (n = 6), or waxing and waning endoscopic appearance (n = 2). The risk of patients progressing to Crohn's disease even when patients taking NSAIDs were excluded was about 1% [27]. The careful history of NSAIDs and long-term aspirin is therefore critical – but remember to ask about all OTC and herbals also.

Beware of the "helpful" pathologist. Regrettably some pathologists are only too willing to agree with suggestions on the requisition forms, but as chronic active inflammation can have a variety of causes, a question of "? Crohn's disease" may get an answer "consistent with Crohn's disease," which is not wrong but shows the issues of signing out something a "consistent with." If there are no granulomas, the same biopsies are also consistent with aspirin, NSAIDs, Behçet's disease, and even TB. The danger is that the patient is reinterpreted as "Crohn's disease," histologically proven, and treated as such. Unless it looks like Crohn's disease endoscopically as well, the chances are very strong that it is not.

Theoretically ileitis can occur in ulcerative colitis but usually as part of backwash ileitis in which the changes are identical on both sides of the ileocecal valve and apparent endoscopically and ideally demonstrated in biopsies.

Large Bowel Biopsies (Boxes 7.7, 7.8, and 7.9: These Can Be Combined)

1. Always biopsy the rectum and if possible the terminal ileum. Put sites in different bottles:
   (a) For possible microscopic colitis at least TI, right colon, left colon, and rectum.
   (b) For a primary diagnosis of IBD at least TI, right colon, transverse, descending, sigmoid colon, and rectum.
   (c) In isolated large bowel inflammation (e.g., segmental colitis or diverticular colitis), always biopsy above and below the abnormal area, and especially include rectal biopsies. In IBD, the job of the endoscopist at the first (diagnostic) colonoscopy is to demonstrate the severity and distribution of the disease – where it is not as well as where it is. When the diagnosis has been established, the question and possibly the biopsies required to answer that question may also change.
2. In a new patient with IBD, ensure there is no concomitant medication that can cause a picture resembling IBD.
3. If a lesion is biopsied within colitic mucosa, ensure it is completely removed if possible and take biopsies around the base of the lesion.
4. Don't ask questions that cannot be answered and may even be misleading, e.g., is there evidence of Crohn's disease in this pouch/diverted bowel?

Box 7.7 Large bowel biopsies – 1

- Always biopsy the rectum and if possible the terminal ileum. Put sites in different bottles.
- For possible microscopic colitis at least TI, right colon, left colon, and rectum.
- For a primary diagnosis of IBD at least TI, right colon, transverse, descending, sigmoid colon, and rectum.
- In isolated large bowel inflammation (e.g., segmental colitis or diverticular colitis), always biopsy above and below the abnormal area and especially include rectal biopsies.

Box 7.8 Large bowel biopsies – 2

- In IBD, at the first (diagnostic) colonoscopy the endoscopist needs to demonstrate the severity and distribution of the disease – where it is not (at least endoscopically) as well as where it is.
- In a new patient with IBD, ensure there is no concomitant medication that can cause a picture resembling IBD.
- If a lesion is biopsied within colitic mucosa, ensure it is completely removed if possible, and take biopsies around the base of the lesion.

Box 7.9 Large bowel biopsies – 3

- Don't ask questions that cannot be answered and may even be misleading, e.g., is there evidence of Crohn's disease in this pouch/diverted bowel?

1. **Biopsying the large bowel for IBD or microscopic colitis.** The most frustrating things for pathologists in looking at diagnostic biopsies for a possible diagnosis of IBD are:
   (a) No rectal biopsies. Yes, the left colon may all look involved to you, but if the biopsies stop at the sigmoid, we have no way of knowing whether the rectum really was involved or not. If the more proximal biopsies have features of IBD but the rectal biopsies proved to be absolutely normal, we can virtually exclude ulcerative colitis. Demonstrating that segmental diseases really are segmental and are normal both endoscopically and histologically makes our lives much easier.
   (b) No terminal ileal biopsies. This is more contentious as normal terminal ilea are usually normal histologically also. In patients with IBD, demonstrating this is a useful baseline. However an intraepithelial lymphocytosis can be part of lymphocytic colitis and can sometimes be seen in patients with celiac disease.
   (c) All biopsies in one container for microscopic colitis. The right and left colon are different histologically. It is not uncommon to see a busy lamina propria with basal plasma cells in the right colon and especially around the ileocecal valve, but in the left colon, this indicates a chronic colitis. If they are all in one pot, we are left to guess the site. Similarly, if one biopsy also has architectural distortion (the combination of chronic inflammation with architectural distortion is IBD or a mimic until proven otherwise), we have no way of knowing whether the abnormal biopsy was rectal (possible ulcerative colitis), sigmoid (possible diverticular colitis), or from around the ileocecal valve – most likely medication injury. So avoid the temptation. As a corollary, at least 10% of lymphocytic colitis are medication associated, so a careful history for the drugs that can cause this is required. However, just as frustrating for the pathologist is when a single biopsy is taken from the large bowel to "R/O microscopic colitis," especially when the biopsy is from the right colon where a lot of chronic inflammation may be physiological or if from the rectum, which is often spared.
   (d) From the pathologists' viewpoint, the job of the endoscopist is to take a series of biopsies to demonstrate the distribution/location and severity of IBD. We are just as interested in knowing which parts of the bowel are not involved, as well as which are, and, if there are ulcers or erosions, whether they are taking place on a background of inflamed mucosa (typical of UC) or relatively normal mucosa (usually Crohn's disease until proven otherwise – Fig. 7.8).
2. **In a new patient with IBD, ensure there is no concomitant medication that can cause a picture resembling IBD.** A variety of medications can produce a picture mimicking IBD. These are primarily chemotherapeutic agents including:

CTL4 antagonists such as ipilimumab (Yervoy) and tremelimumab.

Anti-programmed death-ligand 1 [anti-PD1/PDL-1 compounds (prembrolizumab, nivolumab)], pembrolizumab (Keytruda), lambrolizumab, and nivolumab (Opdivo) used primarily for refractory melanoma but also for some other cancers.

Anti-CD20 medications such as rituximab (rituxan, MabThera).

PI3K inhibitors (Idelalisib/Zydelig) are used for hematological malignancies with p53 mutations.

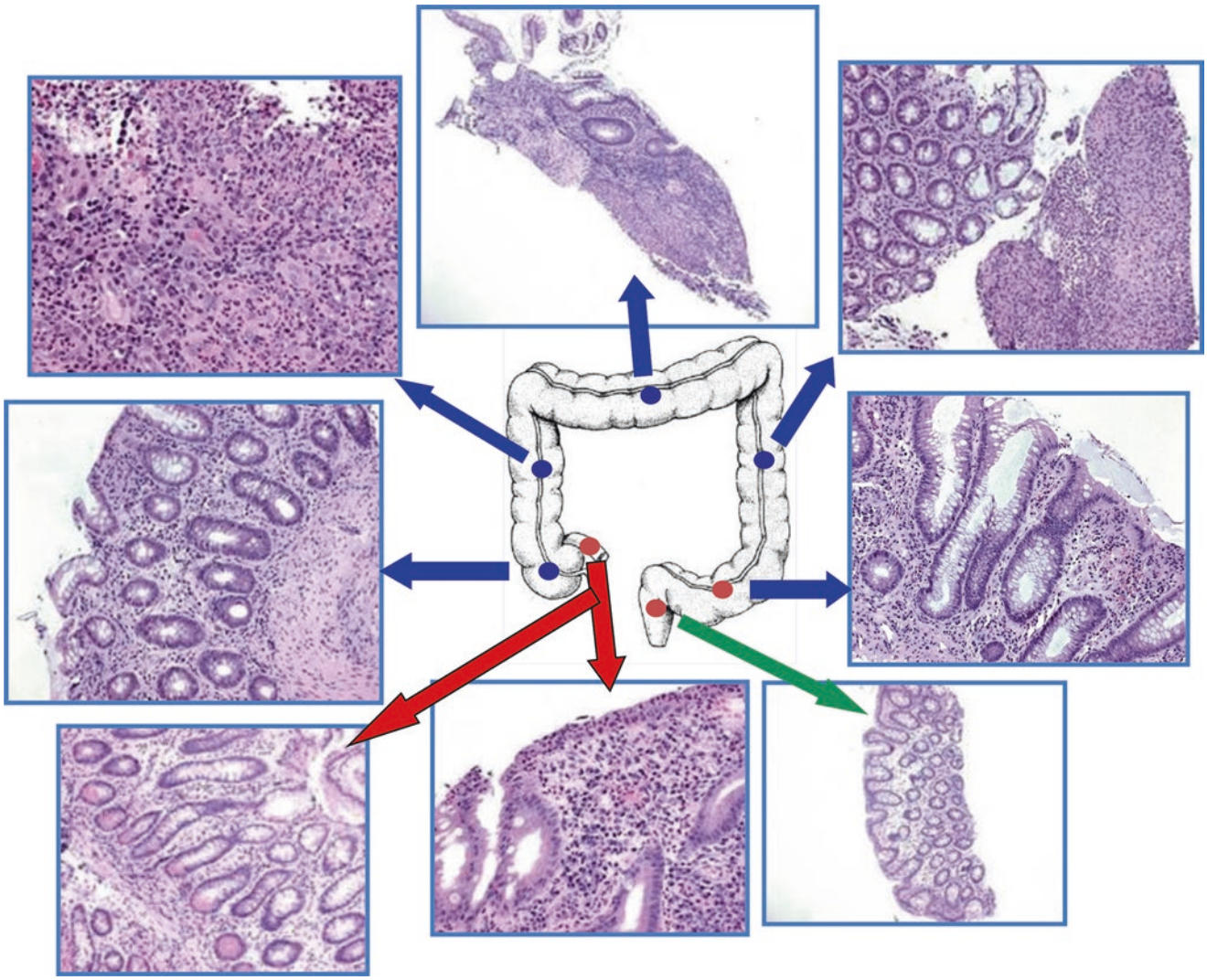

Fig. 7.8 Biopsies from ileum (red arrows) shows marked focal inflammation. Those from cecum and rectum are normal, but the reminder have focal erosions and ulcers – a typical distribution and morphology for Crohn's disease. Demonstrating the distribution of the large bowel disease, the ileal disease but normal cecum and rectum really assists in making a firm daignosis of Crohn's disease histologically

A variety of medications used in following transplantation can also produce GI symptoms, although most of these (mycophenolate mofetil, tacrolimus cyclosporine, etc.) produce changes in the GI tract, but these do not usually include an overt colitis but may cause ulceration.

In patients with apparent new onset IBD, if there is a history of malignancy, the possibility that the colitis is medication-associated needs to be considered as the colitis disappears rapidly when the drug is discontinued – or sometimes treated with steroids.

3. **If a lesion is biopsied within colitic mucosa, ensure it is removed completely but also biopsy around the base.** The concern in this situation is that if these prove to be part of flat/invisible dysplasia, it may be impossible to find again and ensure that the area of dysplasia was dealt with completely. Most of these lesions prove to be atypical inflammatory polyps or sporadic adenomas. It is quite important to ensure this is the case, especially in a patient with multiple polyps. In practice it is uncommon to see dysplasia around the base of these lesions [28], but leaving residual dysplasia that one may know even exists seems not a good idea.
4. **Don't ask questions that cannot be answered and may even be misleading, e.g., is there evidence of Crohn's disease in this pouch/diverted bowel.** The latter refers to patients with residual large bowel distal to an ileostomy or a colostomy, e.g., Hartmann's pouch.

In both of these situations, changes can be found in biopsies (focal erosions or ulcers, granulomas) or resections (fissures, fistulas, transmural lymphoid hyperplasia), all of which can

mimic Crohn's disease. What is worse, should the endoscopist not be aware of this but take biopsies to ask this question, and a "helpful" pathologist says these changes are "consistent with Crohn's disease"; we suddenly have a patient in whom the "consistent with" evolves to "this patient with histologically proven Crohn's disease of the pouch (ileal or Hartmann's). In a patient waiting for an ileal pouch, the diagnosis of "C/W Crohn's disease" in a Hartmann's pouch could well be enough to prevent an ilea pouch anal anastomosis in a patient who has previously undergone subtotal colectomy for severe or unresponsive colitis, which until this time was thought to be ulcerative colitis or indeterminate colitis. Don't make this request! The changes present can invariably be explained by diversion disease or pouchitis. The criteria for making the diagnosis of Crohn's disease under these circumstances are poorly defined and tend to be in the eye of the beholder.

Conclusions

Pathologists assume that endoscopists, during their training, are taught how to ask the right question when they are doing endoscopy or colonoscopy and then to take the appropriate biopsies to answer that question ("endoscopic biopsies 101"). However teachers and training programs vary in their ability to teach these, and the process is dynamic, so that continued learning is required by both endoscopists and pathologists to continually update their skills (mental database) – pathology and endoscopic biopsies 201. Most pathologists understand that good clinicians usually have a good understanding of the role of pathology and vice versa. Nevertheless, the interaction between pathologist and clinician is mutually expectant. Specific questions require specific biopsies to answer that question, even if as simple as "R/O *Helicobacter*, celiac disease, microscopic colitis, or IBD"; if they are not obtained, pathologists make do with what they have but mentally may note the deficiency. However, the other side of the coin is that when the question is accompanied by the appropriate biopsies to answer that question, but the answer is not forthcoming and there is no explanation, the opinion and acumen of the pathologist is eroded. Pathologists also tend to be as good as their teachers, and if taught only to use descriptions (e.g., "chronic active colitis" – which could equally apply to some infections, all forms of IBD and microscopic colitis, and some drug-associated changes) and not interpret them or suggest a possible etiology or answering the specific questions, then there tends to be a downward spiral in the relationship and expectations are diminished. This chapter hopes to achieve an elevation of this relationship so that "endoscopic biopsies 201" becomes the norm. By thinking in advance in situations which are often quite common, and often "bread and butter", endoscopists in training, as well as their teachers, and also those in active practice that take a pride in their clinical skills and acumen, can potentially raise their level of practice, and also stimulate the pathologists with whom they work to do the same. Or, as Henry Ford was purported to have said, "Anyone who stops learning is old, whether at 20 or 80. Anyone who keeps learning stays young." May we all try to stay young.

References

1. Dellon ES, Gonsalves N, Hirano I, Furuta GT, Liacouras CA, Katzka DA. ACG clinical guideline: evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). Am J Gastroenterol. 2013;108(5):679–92; quiz 93. PubMed PMID: 23567357. Epub 2013/04/10. eng
2. Liacouras CA, Furuta GT, Hirano I, Atkins D, Attwood SE, Bonis PA, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. J Allergy Clin Immunol. 2011;128(1):3–20 e6; quiz 1-2. PubMed PMID: 21477849. Epub 2011/04/12. eng
3. Shah A, Kagalwalla AF, Gonsalves N, Melin-Aldana H, Li BU, Hirano I. Histopathologic variability in children with eosinophilic esophagitis. Am J Gastroenterol. 2009;104(3):716–21. PubMed PMID: 19209168. Epub 2009/02/12. eng
4. Dellon ES, Collins MH, Bonis PA, Leung J, Capocelli KE, Dohil R, et al. Substantial variability in biopsy practice patterns among gastroenterologists for suspected eosinophilic gastrointestinal disorders. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2016;14(12):1842–4. PubMed PMID: 27112108. Pubmed Central PMCID: PMC5075280. Epub 2016/04/27. eng
5. Shaheen NJ, Falk GW, Iyer PG, Gerson LB. ACG çlinical guideline: diagnosis and management of barretts esophagus. Am J Gastroenterol 2016;111(1):30–50; quiz 1. PubMed PMID: 26526079. Epub 2015/11/04. eng.
6. Gerson LB, Shetler K, Triadafilopoulos G. Prevalence of Barrett's esophagus in asymptomatic individuals. Gastroenterology. 2002;123(2):461–7. PubMed PMID: 12145799. Epub 2002/07/30. eng
7. Nandurkar S, Talley NJ, Martin CJ, Ng TH, Adams S. Short segment Barrett's oesophagus: prevalence, diagnosis and associations. Gut. 1997;40(6):710–5. PubMed PMID: 9245922. Pubmed Central PMCID: PMC1027193. Epub 1997/06/01. eng
8. Yang YX, Brill J, Krishnan P, Leontiadis G. American Gastroenterological Association Institute Guideline on the role of upper gastrointestinal biopsy to evaluate dyspepsia in the adult patient in the absence of visible mucosal lesions. Gastroenterology. 2015;149(4):1082–7. PubMed PMID: 26283143. Epub 2015/08/19. eng
9. Qumseya BJ, Wani S, Gendy S, Harnke B, Bergman JJ, Wolfsen H. Disease progression in Barrett's low-grade dysplasia with radiofrequency ablation compared to surveillance: systematic review and meta-analysis. Amer J Gastroenterol. 2017;112:849–65.
10. Duits LC, Phoa KN, Curvers WL, Ten Kate FJ, Meijer GA, Seldenrijk CA, et al. Barrett's oesophagus patients with low-grade dysplasia can be accurately risk-stratified after histological review by an expert pathology panel. Gut. 2015;64(5):700–6. PubMed PMID: 25034523. Epub 2014/07/19. eng
11. Vieth M, Montgomery EA, Riddell RH. Observations of different patterns of dysplasia in barretts esophagus – a first step to harmonize grading. Ceskoslovenska Patologie. 2016;52(3):154–63. PubMed PMID: 27526016. Epub 2016/08/16. Rozlisovani ruznych typu dysplazie v Barrettove jicnu – prvni krok k harmonizaci gradingu. eng

12. El-Zimaity H, Serra S, Szentgyorgyi E, Vajpeyi R, Samani A. Gastric biopsies: the gap between evidence-based medicine and daily practice in the management of gastric Helicobacter pylori infection. Canadian J Gastroenterol = J Canadien De Gastroenterol. 2013;27(10):e25–30. PubMed PMID: 24106732. Pubmed Central PMCID: PMC3805342. Epub 2013/10/10. eng
13. Kimura K, Takemoto T. An endoscopic recognition of the atrophic border and its significance in chronic gastritis. Endoscopy. 1969;1:87–97.
14. Masuyama H, Yoshitake N, Sasai T, Nakamura T, Masuyama A, Zuiki T, et al. Relationship between the degree of endoscopic atrophy of the gastric mucosa and carcinogenic risk. Digestion. 2015;91(1):30–6. PubMed PMID: 25632914. Epub 2015/01/31. eng
15. Miike T, Yamamoto S, Miyata Y, Hirata T, Noda Y, Noda T, et al. Surrounding gastric mucosa findings facilitate diagnosis of gastric neoplasm as gastric adenoma or early gastric cancer. Gastroenterol Res Pract. 2016;2016:6527653. PubMed PMID: 26858751. Pubmed Central PMCID: PMC4706934. Epub 2016/02/10. eng
16. Vannella L, Lahner E, Osborn J, Bordi C, Miglione M, Delle Fave G, et al. Risk factors for progression to gastric neoplastic lesions in patients with atrophic gastritis. Aliment Pharmacol Ther. 2010;31(9):1042–50. PubMed PMID: 20175768. Epub 2010/02/24. eng
17. Park YH, Kim N. Review of atrophic gastritis and intestinal metaplasia as a premalignant lesion of gastric cancer. J Cancer Prev. 2015;20(1):25–40. PubMed PMID: 25853101. Pubmed Central PMCID: PMC4384712. Epub 2015/04/09. eng
18. Vannella L, Lahner E, Annibale B. Risk for gastric neoplasias in patients with chronic atrophic gastritis: a critical reappraisal. World J Gastroenterol. 2012;18(12):1279–85. PubMed PMID: 22493541. Pubmed Central PMCID: PMC3319954. Epub 2012/04/12. eng
19. Vyas M, Yang X, Zhang X. Gastric hamartomatous polyps-review and update. Clin Med Insights Gastroenterol. 2016;9:3–10. PubMed PMID: 27081323. Pubmed Central PMCID: PMC4825775. Epub 2016/04/16. eng
20. Memeo L, Jhang J, Hibshoosh H, Green PH, Rotterdam H, Bhagat G. Duodenal intraepithelial lymphocytosis with normal villous architecture: common occurrence in H. pylori gastritis. Modern Pathol : Off J United States Canadian Acad Pathol, Inc. 2005;18(8):1134–44. PubMed PMID: 15803187. Epub 2005/04/02. eng
21. Pace LA, Crowe SE. Duodenal bulb biopsies remain relevant in the diagnosis of adult celiac disease. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2016;14(11):1589–92. PubMed PMID: 27565522. Epub 2016/10/19. eng
22. Shmidt E, Smyrk TC, Boswell CL, Enders FT, Oxentenko AS. Increasing duodenal intraepithelial lymphocytosis found at upper endoscopy: time trends and associations. Gastrointest Endosc. 2014;80(1):105–11. PubMed PMID: 24565068. Epub 2014/02/26. eng
23. Rubio-Tapia A, Herman ML, Ludvigsson JF, Kelly DG, Mangan TF, Wu TT, et al. Severe spruelike enteropathy associated with olmesartan. Mayo Clin Proc. 2012;87(8):732–8. PubMed PMID: 22728033. Pubmed Central PMCID: PMC3538487. Epub 2012/06/26. eng
24. Kulai T, Arnason T, MacIntosh D, Igoe J. Duodenal villous atrophy in a TTG-negative patient taking olmesartan: a case report and review of the literature. Canadian J Gastroenterol Hepatol. 2016;2016:6091571. PubMed PMID: 27446852. Pubmed Central PMCID: PMC4904703. Epub 2016/07/23. eng
25. Endo H, Sakai E, Kato T, Umezawa S, Higurashi T, Ohkubo H, et al. Small bowel injury in low-dose aspirin users. J Gastroenterol. 2015;50(4):378–86. PubMed PMID: 25501289. Epub 2014/12/17. eng
26. Iwamoto J, Mizokami Y, Saito Y, Shimokobe K, Honda A, Ikegami T, et al. Small-bowel mucosal injuries in low-dose aspirin users with obscure gastrointestinal bleeding. World J Gastroenterol. 2014;20(36):13133–8. PubMed PMID: 25278707. Pubmed Central PMCID: PMC4177492. Epub 2014/10/04. eng
27. Chang HS, Lee D, Kim JC, Song HK, Lee HJ, Chung EJ, et al. Isolated terminal ileal ulcerations in asymptomatic individuals: natural course and clinical significance. Gastrointest Endosc. 2010;72(6):1226–32. PubMed PMID: 21111872. Epub 2010/11/30. eng
28. ten Hove JR, Mooiweer E, Dekker E, van der Meulen-de Jong AE, Offerhaus GJA, Ponsioen CY, et al. Low rate of dysplasia detection in mucosa surrounding dysplastic lesions in patients undergoing surveillance for inflammatory bowel diseases. Clin Gastroenterol Hepatol. 2017;15(2):222–8.

Complications Related to Gastrointestinal Endoscopy

8

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Introduction

More than 200,000,000 gastrointestinal procedures are performed in the United States every year. As with other therapeutic modalities, complications are inherent to gastrointestinal endoscopy. Endoscopists need to be aware of the different types and the expected frequencies of these complications, in order to use strategies to minimize their occurrence and to recognize and treat them appropriately when they occur. Furthermore, it is essential to recognize patients with a higher likelihood of developing complications. Attention must be paid to patients' preexisting medical conditions and their ability to cope with potential complications.

In this chapter, we describe the potential complications of upper and lower endoscopy, together with the adverse effects related to endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasound (EUS), and certain advanced therapeutic techniques such as mucosal resection.

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It is important to keep in mind that one should always consider the risk/benefit ratio of a procedure and make sure that the benefits outweigh the risks.

Complications Related to Preparation for Endoscopy

General GI Procedure Preparation

Prior to gastrointestinal (GI) procedures, patients are usually advised to avoid eating and drinking for about 6–8 h. The American Society of Anesthesiologists (ASA) guidelines recommend that patients should fast a minimum of 2 h after consuming clear liquids and 6 h after consuming light meals before the administration of sedation. This fasting period can be a potential problem for the diabetics who take oral hypoglycemic medications or insulin injection. The general recommendation is that patients should stop their oral hypoglycemic drugs [51] and their fast-acting insulin on the day of procedure. However, they will need some baseline insulin during the procedure to prevent hyperglycemia. For this purpose it has been recommended that patients receive half of their usual dose of the long-acting insulin in the morning of the procedure [23]. A brief history and physical examination, with particular emphasis on sedation-oriented issues, should be performed at the time of endoscopy including risk stratify patients for sedation (ASA classification). Furthermore, a pregnancy test should be perform for all childbearing age women unless they have had a bilateral tubal ligation, total hysterectomy, or absent menstruation for 1 year (menopause). The verification of patient identification and confirmation of the need of the appropriate procedure, we call this *time-out*, should be performed by the procedural team in a *quiet room* before the endoscopic procedure is commenced. It is important to note that all the involved members of the team should be present prior to the *time-out*.

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Practical Considerations

- Patients should fast a minimum of 2 h after consuming clear liquids and 6 h after consuming light meals prior to the endoscopic procedure.
- It is important to consider diabetic patients and their requirements.
- Exclude pregnancy in childbearing female patients.
- *Time-out* should be performed in a quiet room by the endoscopy team prior to the planned endoscopic procedure, and all the involved members should be present.

Colonoscopy Preparation

One of the essential steps before colonoscopy is bowel preparation, the lack of which can greatly hinder the detection of colonic abnormalities. Poor or suboptimal bowel preparation has a significant role in increased adenoma miss rate, prolonged procedure time, and unnecessary need for repeat procedures [23]. Available bowel preparation regimens can be divided into two categories: isosmotic and hyperosmotic.

The isosmotic agents generally contain a nonabsorbable solute (e.g., polyethylene glycol [PEG]) and rely on high volume to clean the bowel and, therefore, do not cause a significant shift in fluid and electrolytes. The volume used is about 2–4 L which can lead to frequent nausea, vomiting, and abdominal cramps. As a result, Mallory-Weiss tears and aspiration have been reported. Furthermore, there are isolated reports of pancreatitis and exacerbation of congestive heart failure (CHF) following large volume preparations with a polyethylene glycol (PEG)-based solution. More recent isosmotic preparations have applied a decreased volume of about 2 L together with laxatives such as bisacodyl. Bisacodyl use as a laxative has been associated with episodes of ischemic colitis in young adults [23].

In contrast, hyperosmotic agents induce a net fluid shift into the bowel lumen causing significant fluid and electrolyte abnormalities, which can usually be tolerated in healthy subjects. However, in patients who have conditions more vulnerable to fluid and electrolyte shifts like renal failure, congestive heart failure (CHF), or chronic liver disease, these agents are contraindicated. A typical hyperosmotic agent is a hyperosmotic sodium phosphate solution. These solutions induce a net influx of water into the bowel lumen due to their hyperosmolar effect, and the water helps with bowel cleansing. Therefore, patients are instructed to increase their fluid intake in order to prevent dehydration [23].

Several case reports have described nephrotoxicity attributed to sodium phosphate-based preparations in the form of acute phosphate nephropathy, leading to chronic renal failure and in some cases end-stage renal disease ending in hemodialysis [36]. Furthermore, there have been reports of aphthous ulceration, similar to Crohn's disease following sodium phosphate-based preparations [23]. Special care should be taken with older patients using diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, and possibly nonsteroidal anti-inflammatory drug (NSAID). It is reasonable to avoid sodium phosphate preparations in these patients. Hyperphosphatemia following use of sodium phosphate preparations has been associated with symptomatic hypocalcemia leading to perioral tingling and numbness and even tetany [23]. As stated above an underlying renal insufficiency can predispose to these electrolyte abnormalities. Magnesium citrate, another hyperosmotic agent, is also excreted via the kidneys. This preparation should be avoided in kidney and elderly patient.

Overall, caution is reasonable when using sodium phosphate and magnesium citrate preparations especially in cases with the abovementioned risk factors. Patients should be instructed on adequate hydration during and after the procedure. Allowing a longer interval between the two doses of the preparation might further decrease the risk of complications.

Practical Considerations

- Isosmotic high-volume preparation is preferred in general population (polyethylene glycol-based solution).
- Sodium phosphate and magnesium citrate preparations should be avoided in elderly and kidney disease population.

Complications Related to Sedation and Anesthesia

Sedation has been used to decrease the discomfort associated with endoscopic procedures. Sedation helps reduce patient anxiety and the pain and increase the acceptability of procedures by the patients, resulting in greater willingness to undergo repeat procedures when needed. A combination of narcotics and benzodiazepines is commonly used for endoscopy. Sedation regimens include benzodiazepines (e.g., midazolam and diazepam), opiates (e.g., morphine, meperidine, and fentanyl), and propofol.

The adverse effects range from allergic reactions to drug interactions, respiratory depression, and hypotension. A detailed history of patient's allergies together with a list of medications should be obtained prior to procedure. The spectrum of allergic reactions can include a minor local reaction, which can be controlled with IV diphenhydramine, to more severe anaphylactic reactions [19]. Anaphylaxis can present with mild dyspnea in mild cases or lead to hypotension and shock in more severe ones. Epinephrine can be used as an intramuscular injection together with IV diphenhydramine to con-

trol the anaphylactic reactions. In severe cases, patients will need to be transferred quickly to an emergency department.

Hypotension has been reported with midazolam at therapeutic doses of 0.15–0.3 mg/kg. A significant fall in the blood pressure can be seen in patients with underlying cardiovascular disease. One should be cautious about combining benzodiazepines and opioids which can lead to pronounced decreases in blood pressure [53]. Furthermore, drug interactions between benzodiazepines and azole antifungals and protease inhibitors can lead to increase serum levels of benzodiazepines and, therefore, more exaggerated hypotension and respiratory depression.

Several studies have reported respiratory depression occurring with benzodiazepines during endoscopy which can lead to oxygen desaturation, respiratory acidosis, hyperkalemia, myocardial depression, and arrhythmias [23]. Consequently, the routine use of supplemental oxygen during endoscopy can be beneficial. However, higher levels of carbon dioxide can also occur with hypoventilation and may potentially be masked by supplemental oxygen. A study by Nelson et al. showed that adding transcutaneous CO_2 monitoring during endoscopy led to fewer episodes of severe CO_2 retention but no clinically significant difference in the outcome [40]. Oxygen supplementation can be even more important when doing endoscopy on the elderly population due to their decreased baseline oxygen saturation, their blunted cardiovascular response to hypercarbia and hypoxia, and their more pronounced response to opioid induced respiratory depression.

According to American Society of Gastrointestinal Endoscopy (ASGE) guidelines, blood pressure, pulse, and oximetry monitoring are recommended in all patients undergoing a procedure with conscious sedation [Gastrointest Endosc 68 [3]]. In patients with a low baseline oxygen saturation, supplemental oxygen can be used through a nasal cannula. The ASA Task Force recommends that supplemental oxygen should be considered for moderate sedation and should be administered during deep sedation unless specifically contraindicated for a particular patient or procedure. Capnography, a noninvasive tool, can immediately detect hypoventilation and has still not become a standard monitoring. However, capnography should be considered for all patients receiving deep sedation and for patients whose ventilation cannot be observed directly during moderate sedation. The endoscopist needs to be familiar with signs and symptoms of overdose related to sedation and be able to administer appropriate reversal agents if needed. In case of benzodiazepine overdose, flumazenil can be administered at 0.2 mg IV and can be repeated every 3–5 min up to a total dose of 3 mg. In the event of opioid overdose, naloxone can be used at 0.4 mg IV and can be repeated every 3–5 min. In patients with chronic benzodiazepine or opioid use, these reversal medications may lead to withdrawal symptoms which can manifest as seizures in chronic benzodiazepine users, sweating, tremor, and agitation with chronic opioid users.

In cases in which local anesthetics are used in the oropharynx, attention needs to be paid during the recovery period due to impaired gag reflex. Therefore, resumption of oral intake should be delayed until the gag reflex has recovered. Furthermore, methemoglobinemia has been reported as a rare complication due to topical anesthetics [25]. This should be suspected in an alert patient with a low level of oxygen after the procedure while on supplemental oxygen. Methemoglobin is a form of hemoglobin that does not bind oxygen or CO_2. When its concentration is elevated in red blood cells, tissue hypoxia can occur. It is important to be aware of this phenomenon and take prompt diagnostic action in the form of obtaining an arterial blood gas analysis. Methemoglobin concentrations as high as 15% can be managed by O_2 supplementation. However, higher concentrations (>30%) may require intravenous methylene blue (0.1–0.2 mg/kg over 5 min) every hour until the level of methemoglobin falls below 15%. In severe cases, ICU care, ventilator support, and exchange transfusions may be needed.

Aspiration

Another rare complication of upper endoscopy is aspiration of stomach contents. Older patients and those with upper GI bleeding, altered mental status, decreased gag reflex, and hemodynamic instability are at increased risk for aspiration [23]. Avoiding topical anesthetics and oversedation, maintaining the head of the bed at a 30–45° angle, minimizing air insufflation, and thoroughly removing gastric contents prior to the procedure have been recommended to decrease the aspiration risk in these cases [23]. According to ASA recommendations, patients undergoing upper endoscopy will need to avoid solid food for at least 6 h and clear liquids for at least 2 h prior to their procedure. Patients with massive upper GI bleeding have a higher reported risk for aspiration (1% and 4%) and, therefore, require more aggressive airway monitoring during upper endoscopy [23]. Prophylactic endotracheal intubation prior to endoscopy has been recommended by some, but a retrospective study by Rudolph and colleagues [46] on ICU patients, admitted for massive upper GI bleeding and intubated for airway protection, failed to show any significant benefit to endotracheal intubation. It is important to keep in mind that it is up to the endoscopist and the endoscopy team to ensure the adequacy of the airway during the procedure and take prompt action to secure the airway to prevent aspiration.

Practical Considerations

- Blood pressure, pulse, and oximetry monitoring are recommended in all patients undergoing an endoscopic procedure with conscious sedation.
- Supplemental oxygen should be considered for moderate sedation and should be administered during deep sedation.

(continued)

- Capnography should be considered for all patients receiving deep sedation and for patients whose ventilation cannot be observed directly during moderate sedation.
- Recognition of sedative overdose is important and managed promptly.
- Reversal agent for:
  - For benzodiazepine overdose: Flumazenil 0.2 mg IV and repeated every 3–5 min up to a total dose of 3 mg
  - For opioid overdose: Naloxone 0.4 mg IV and repeated every 3–5 min
- Resumption of oral intake should be delayed until the gag reflex has recovered.
- Aspiration can be avoided by:
  - Adequate NPO time described earlier (2 h for liquid, 6 h for solid food).
  - Avoiding topical anesthetics, oversedation, elevate the head of the bed at a 30°–45° angle, minimizing air insufflation, and thoroughly removing gastric contents prior to the procedure in high-risk patients.
  - Massive upper GI bleeding might need prophylactic intubation.

Cardiovascular Complications

There are rare reports of cardiovascular complications related to upper and lower gastrointestinal endoscopy within 24 h of the procedure, including chest pain, myocardial infarction, hypotension, CHF, and arrhythmias. Gangi et al. reviewed 100,000 endoscopies and reported a rate of 0.3% complications [20]. Male gender, higher Goldman score preoperatively, and propofol use were considered independent risk factors for cardiovascular complications.

A careful history and physical before the procedure can help identify patients at higher risk for cardiovascular complications. Attention must be paid to drug interactions with sedatives. Close monitoring of cardiovascular function and blood oxygenation during the procedure is needed for early detection and prompt therapeutic action to control these complications [5]. Early warning signs can include brady- or tachyarrhythmias, hypotension, and oxygen desaturation.

Infection

Infectious complications of endoscopy can be categorized in two main groups: one, transmission of microorganisms by contaminated endoscopy equipment "between patients," and, two, "within patient" translocation of bacteria from the gastrointestinal tract to the blood and then to the other organs or prosthetic devices.

There are case reports of hepatitis B and C, salmonella, pseudomonas, and even *Helicobacter pylori* and *Clostridium difficile* transmission through contaminated endoscopy equipments. However, HIV transmission following endoscopy has never been reported. It is worth mentioning that all of these reports were made prior to the publication of current reprocessing guidelines [6, 41].

In order to protect against transmission of microorganisms by an endoscopy between patients, the endoscopy team must adhere to high-level disinfection (HLD) in reprocessing of endoscopes after use, with careful adherence to the multisociety guidelines. The processing involves three major steps that begin with manual cleaning of the endoscope with detergent solution and brushes [7]. Manual cleansing minimizes the chances of bacterial biofilm developing within the endoscope channels. It is important to keep in mind that manual cleansing is personnel dependent and is different for each type of scope. Therefore, training and quality control is a must, and manufacturers' recommendations should be adhered to for each type of endoscope. The US Food and Drug Administration (FDA) approved new labeling for an automated endoscope reprocessors (AERs) for processing endoscopes. Most of the AERs require first step manual cleaning and brushing. In 2006, one device (EvoTech System; Advanced Sterilization Products, Irvine, Calif) has received labeling clearance for use after bedside precleaning only, without previous manual cleaning and channel brushing. However, at this time, there are no independent confirmatory data regarding the efficacy of this machine. The second step is HLD which is operationally defined by the FDA as a 6-log reduction of mycobacteria (FDA. Guidance on the content and format of premarket notification [510 (k)] submissions for liquid chemical germicides. Rockville (MD), Food and Drug Administration et al. [17]). HLD is often performed using an automated washer/disinfector and involves submerging the endoscope in a liquid chemical germicide (often 2% glutaraldehyde solution at room temperature for 20 min). Both the temperature of the solution and the duration of the soak are critical in ensuring adequate disinfection. The third step includes proper rinsing and drying of the endoscope channels. Here, the scope will be rinsed with large volumes of water through all working channels to expel the chemical disinfectant. The importance of adequate rinsing is emphasized by a case report describing glutaraldehyde-induced colitis that was attributed to inadequate rinsing of the endoscopes. After rinsing with water, a 70% alcohol flush promotes drying and inhibits the growth of organisms in stored instruments. After the instruments are dried, they should be stored in an upright hanging position according to the manufacturers' recommendations.

In rare circumstances where sterilization of endoscopy equipment is necessary, as in the case of intraoperative endoscopy to avoid contamination of an open surgical field, ethylene oxide gas treatment has been used. Furthermore, in these cases reusable biopsy forceps, snares, sphincterotomes, and other accessories designed to breach the GI mucosal surface all require sterilization. Similarly, water bottles should also be disinfected or sterilized, and sterile water should be used in the water bottle. Overall, achieving sterilization is a difficult task due to the complex channel design of the endoscope. There is no evidence for any demonstrable benefits to the further reduction in endoscope bacterial spore counts achieved by sterilization instead of HLD [38].

Another infectious complication related to endoscopy is translocation of gut bacteria to other sites in the body. Bacteremia occurring during endoscopy has been demonstrated in several reports with rates as high as 20–25% during colonoscopy and esophageal dilation [39]. According to the revised guidelines from the American Heart Association (AHA) for prevention of infective endocarditis, antimicrobial prophylaxis should be given only to patients with high-risk heart valve lesions if they undergo high-risk procedures that are likely to result in a bacteremia with a microorganism that has the potential ability to cause endocarditis. *The 2007 AHA guidelines no longer consider any GI procedure high risk, and, therefore, administration of prophylactic antibiotics solely to prevent IE was no longer recommended for patients undergoing GI endoscopy* [60]. However, The AHA also outlined cardiac conditions associated with the highest risk of an adverse outcome from IE, including (1) prosthetic (mechanical or bioprosthetic) cardiac valves, (2) history of previous IE, (3) cardiac transplant recipients who develop cardiac valvulopathy, and (4) patients with congenital heart disease (CHD) including those with unrepaired cyanotic CHD including palliative shunts and conduits; those with completely repaired CHD with prosthetic material or devices, placed surgically or by catheter, for the first 6 months after the procedure; and those with repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or device. For the patients with abovementioned high-risk cardiac condition who suspected having GI tract infection and need for endoscopic procedure which may increase the risk of bacteremia (such as ERCP), the AHA suggests that inclusion of an agent active against enterococci in the concurrent antibiotic regimen may be reasonable.

Furthermore, in patients undergoing ERCP for an obstructed biliary system or EUS or ERCP for a pancreatic cystic lesion, the prophylactic use of an antibiotic against enterococcus is recommended. Also, for patients with ascites, procedures associated with higher rates of spontaneous and sustained bacteremia including variceal sclerotherapy, and esophageal stricture dilation, antibiotics prophylaxis is still indicated. In the setting of PEG placement, several prospective trials have shown a reduction in PEG site infections in patients who received a single prophylactic dose of antibiotics prior to PEG insertion. Therefore, ASGE recommended that all patients undergoing PEG placement should receive antibiotic prophylaxis with cefazolin 1 g IV (or an equivalent antibiotic) 30 min prior to the procedure [7]. Summarized population who requires antibiotic prophylaxis prior to GI procedure is showed in Table 8.1.

Practical Considerations

- Cardiovascular complications related to GI procedures could occur within 24 h of the procedure.
- Close monitoring of cardiovascular function and blood oxygenation during the procedure is needed for early detection of complications.
- The infectious transmission through contaminated endoscopy equipment can be prevented by strictly following to high-level disinfection (HLD) in reprocessing of endoscopes after use.
- To prevent bacterial translocation, antibiotic prophylaxis for GI endoscopic procedure is recommended in patients who have:
  - High-risk cardiac conditions who need high-risk GI procedure (ERCP, esophageal dilation, and sclerotherapy of varices)
  - Known or suspected biliary obstruction or have had liver transplantation that need ERCP procedure where there is a possibility of incomplete biliary drainage
  - Mediastinal cysts requiring EUS-FNA
  - Pancreatic or peripancreatic cysts requiring EUS-FNA
  - Need for PEG/PEJ tube placement (cefazolin 1 gm IV or equivalent).
  - Patients on continuous ambulatory peritoneal dialysis who will undergo lower GI tract endoscopy
  - Patients with cirrhosis presenting with GI bleeding requiring a GI procedure

Perforation

Upper Endoscopy

The reported rate for perforation during upper endoscopy has been 0.02–0.2% [23]. In spite of the relatively rare occurrence, the mortality rate can be as high as 25%. The most common location reported is the distal third of the esophagus. However, perforations at the site of piriform sinus in

Table 8.1 Summarized population who requires antibiotic prophylaxis prior to GI procedure

High-risk cardia condition requiring IE prophylaxis
Prosthetic (mechanical or bioprosthetic) cardiac valve
History of previous IE
Cardiac transplant recipients who develop cardiac valvulopathy
Congenital heart disease (CHD) including those with unrepaired cyanotic CHD including palliative shunts and conduits Repaired CHD with prosthetic material or devices, placed surgically or bycatheter, for the first 6 months after the procedure Repaired CHD with residual defects at the site or adjacent to the site of aprosthetic patch or device
GI procedures which recommend periprocedural antibiotic prophylaxis
Mediastinal cyst requiring EUS-FNA
Pancreatic cyst requiring EUS-FNA
Suspected obstructing cholangitis or incomplete drainage requiring ERCP
Percutaneous endoscopic feeding tube placement
Cirrhotic patients with acute GI bleeding requiring upper GI procedure
Peritoneal dialysis patients requiring lower GI procedure

Adapted from Allison et al. [2] ASGE guideline
IE infective endocarditis, *CHD* congenital heart disease, *EUS-FNA* endoscopic-guided fine needle aspiration, *ERCP* endoscopic retrograde cholangiopancreatography

patients with Zenker's diverticulum have also been reported. The risk of perforation increases in cases with underlying tissue abnormalities like cancers and if therapeutic interventions including dilation or stent placement are performed. Blind passage of bougies carry the highest reported rate of perforation of 0.3–0.4% [27]. In terms of the underlying pathology, caustic strictures have the highest risk of post-dilation perforation (17%), followed by malignant strictures (10%), and achalasia with pneumatic dilation (4–7%) [23]. It is important to inform and educate the patients about the high risk for perforation prior to dilatation and have surgical backup. A routine post-procedure esophagogram is recommended in these high-risk cases to rule out perforation. Mallory-Weiss tears have been reported as rare complications especially in the setting of large hiatal hernias. These usually present with fresh bleeding during endoscopy and resolve spontaneously.

Patients with a perforation during an upper GI endoscopy can present with severe chest pain, tachypnea, and tachycardia followed by fever and leukocytosis. Crepitus may develop which can be detected by palpation of the anterior chest wall or the neck. The diagnostic test of choice is barium esophagogram with a water-soluble oral contrast or CT scan of chest. Treatment can range from conservative (nothing per mouth, IV fluids, and antibiotics) to surgery in most cases. There are reports of covered metallic esophageal stents used to cover tears and facilitate healing [22]. Also, placement of immediate endoscopic clips has been reported as a possible modality in order to avoid surgery [23]. Clip application might be especially beneficial in cases with a retroperitoneal perforation like during endoscopic ampullectomy. In cases undergoing a nonsurgical management for perforation, very close follow-up with serial physical exams and CT scans is recommended, and surgery needs to be considered in case of clinical deterioration.

Colonoscopy

Perforation is seen in about 0.2% of all diagnostic colonoscopies [23]. These can be caused by direct force from the tip of the endoscope against the mucosa, lateral pressure form a loop of colonoscope inside a loop of bowel, or excessive distention with air. Polyp removal, decompression of colonic pseudo-obstruction, or reduction of a volvulus can increase the risk of perforation. The most commonly reported sites are rectosigmoid and cecum. Polypectomy can lead to perforation especially if a large (>1 cm) sessile polyp is being removed from a portion of the colon where the wall is thin. Furthermore, using electrocautery or presence of an invasive lesion within the polyp can increase the risk of perforation during polypectomy. In these cases, injection of saline at the base of the polyp prior to polypectomy has been recommended to decrease the risk of perforation. There is also a relatively higher risk of perforation with a reported rate of 3% when colonoscopy is performed in the setting of colonic pseudo-obstruction not responding to conservative measures. In the setting of sigmoid volvulus, the reported rate of perforation during colonoscopy is 5–7% [23].

Patients with perforation after colonoscopy usually present with abdominal pain (acute abdomen) and distention. Fever and leukocytosis develop subsequently due to peritonitis. A plain upright X-ray of chest and abdomen will need to be obtained to look for free air under the diaphragm followed by a CT of the abdomen. Conservative management with serial abdominal exams and X-rays can only be pursued in a subset of relatively healthy patients. However, most patients will need surgical intervention for removal of the perforated segment or repair of a perforation, followed by IV antibiotics and bowel rest. As in upper endoscopy, immediate clipping of a perforation followed by frequent monitoring and IV antibiotics has been reported as an alternative to avoid surgery in patients in whom perforation was identified during the procedure [23].

Practical Considerations

- Risk of perforation related to EGD and colonoscopy in general are low.
- Risk of perforation is substantially increased in subgroup of patients requiring special procedure.
- Education of patients and their family is important to procedure.
- Early recognition of perforation is important.
- Sign of perforation includes severe chest pain, tachypnea, tachycardia abdominal pain (acute abdomen), and distention followed by fever and leukocytosis.
- Diagnostic imaging:
  - For the esophageal perforation: Barium esophagogram with a water-soluble oral contrast or CT scan of chest
  - For colonic perforation: A plain upright X-ray of chest and abdomen or CT abdomen
- Treatment—NPO, IV antibiotic:
  - For the esophageal perforation: Endoscopic clip application, covered metallic esophageal stents should be considered in early perforation or surgery.
  - For the colonic perforation: Surgical intervention or conservative management in selective cases.

Post-polypectomy Syndrome

Occasionally 1–5 days after the procedure, after polypectomy, patients present with significant abdominal pain including local peritoneal signs on abdominal exam, mimicking colonic perforation. They may also develop fever and leukocytosis. However, imaging including abdominal X-ray and CT will not show any evidence of perforation. The etiology can be due to the use of electrocautery during polypectomy leading to a full-thickness electrical burn. The treatment is mainly supportive with IV fluids, antibiotics, and bowel rest [23].

Bleeding

Upper Endoscopy

Bleeding after upper endoscopy has been reported as a relatively uncommon complication occurring in 0.15% of cases [14]. There has been no documented increase in bleeding complications in patients using aspirin or NSAIDs during a routine upper endoscopy and biopsy. Therefore, procedures can be performed without any modification in these drugs. In the setting of patients with low platelets, it is believed that upper endoscopy can be performed with platelets as low as 20,000 [50]. Performing dilation during an upper endoscopy can be associated with a minor increase in the risk of bleeding.

Colonoscopy

Colonoscopy is associated with a relatively low rate of bleeding (0.07%). However, higher rates have been reported when biopsy (0.3%) or polypectomy (1.5–2%) was performed [58]. In the setting of post-polypectomy bleeding, the site can be identified by repeat colonoscopy or by tagged red blood cell nuclear scan. The bleeding can occur up to 2 weeks after polypectomy (delayed) and can usually be managed endoscopically by electrocautery or epinephrine injection and clipping. There are also reports of angiography to identify and selectively embolize the bleeding vessel [23].

For GI procedure, patients who are taking antithrombotic medications including aspirin, clopidogrel, ticlopidine, low-molecular-weight heparin (LMWH), warfarin, and novel oral anticoagulation (NOAC) may need some modification in their drug regimen. ASGE guidelines recommend that aspirin (up to 325 mg/day) and NSIADs may not be held before any procedure. However, clopidogrel, ticlopidine, LMWH, warfarin, and NOAC may need modification in a certain subset of patients. Table 8.2 shows patients with a higher risk of bleeding or thromboembolic events. Patients undergoing a procedure with low risk for bleeding need no modification in their antithrombotics. Patients undergoing a high-risk procedure need some modification depending on their risk for thrombotic event. In those with a low risk of thrombotic events, the medication can be held for 3–5 days prior to their procedure. In the high risk for thrombotic event group, bridging with LMWH can be provided for those on warfarin and NOAC, and then LMWH will be held on the day of the procedure (thus minimizing the amount of time that the patient is off anticoagulation) [14, 61].

Practical Considerations

Low risk procedures:

- No antiplatelet or anticoagulation adjustment needed.

High-risk procedure with low thrombotic risk:

- Aspirin/NSAID can be continued.

(continued)

- Thienopyridines (i.e., clopidogrel) should be discontinued at least 5 days before switch to aspirin.
- If the patient on dual antiplatelet:
  - Continue aspirin.
  - Discontinue thienopyridines.
- If the patient on anticoagulation (including warfarin and NOAC):
  - Discontinue anticoagulation *without* bridge therapy.

High-risk procedure with high-thrombotic risk:

- Aspirin/NSAID can be continued.
- Thienopyridines (i.e., clopidogrel) should be discontinued at least 5 days before switch to aspirin.
- If the patient on dual antiplatelet:
  - Continue aspirin.
  - Discontinue thienopyridines.
- If the patient on anticoagulation (including warfarin and NOAC):
  - Discontinue anticoagulation *with* bridge therapy.
  - In moderate-risk patients, the decision to use bridge therapy and the degree of intensity should be individualized, and the patient's wishes should be considered.

Vasovagal Reactions

Patients can occasionally develop bradycardia, hypotension, or loss of consciousness during upper endoscopy or colonoscopy. This has been attributed to distention of the bowel together with pressure from loop formation and possibly hypovolemia [23]. Therefore, partial or complete withdrawal of the scope and IV fluids may usually rectify the situation. However, severe cases might need atropine or reversal or the sedation.

Splenic Injury

Injury to the spleen has been rarely reported as a complication of colonoscopy [54]. These patients may present with pain in the left upper quadrant of the abdomen after the procedure. The mechanism is thought to be due to shear forces from pushing a colonoscope against splenocolic ligament leading to avulsion injury to the splenic capsule. Most cases can be managed with conservative measures.

Table 8.2 Bleeding and thromboembolic risks

Procedure bleeding risk
High
Polypectomy
Biliary or pancreatic sphincterotomy
Pneumatic or bougie dilation
PEG placement
Endosonographic-guided fine needle aspiration
Laser ablation and coagulation
Treatment of varices Therapeutic balloon-assisted enteroscopy EUS with FNA Endoscopic hemostasis Tumor ablation Cystogastrostomy Ampullary resection Endoscopic mucosal resection
Low
Diagnostic (EGD, colonoscopy, flexible sigmoidoscopy) including mucosal biopsy
ERCP with stent (biliary or pancreatic) placement without sphincterotomy or papillary balloon dilation without sphincterotomy
Push enteroscopy and diagnostic balloon-assisted enteroscopy Capsule endoscopy Enteral stent deployment (controversial)
EUS without FNA Argon plasma coagulation Barrett's ablation
Thromboembolic event risk
High
Any mitral valve prosthesis
Any caged ball or tilting disc aortic valve prosthesis
Recent (within 6 months) CVA or TIA Recent (within 3 months) VTE Severe thrombophilia (deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate
Bileaflet aortic valve prosthesis and one or more of the following risk factors: AF, prior CVA or TIA, hypertension, diabetes, congestive heart failure, age 75 years VTE within the past 3–12 months or recurrent VTE Nonsevere thrombophilia (heterozygous factor V Leiden or prothrombin gene mutation) Active cancer (treated within 6 months or palliative)
Low
Bileaflet aortic valve prosthesis without AF and no other risk factors for CVA
VTE > 12 months previous and no other risk factors

Adapted from Acosta et al. [1]

Entrapment of the Endoscope

There are rare case reports describing entrapment of the endoscope during upper endoscope or colonoscopy. Huang and colleagues presented a case of entrapment of the upper endoscope in a 24-year-old man which happened when the patient belched during a retroflex examination of the gastric

fundus, pushing the U-turned shaft into the distal esophagus [29]. Eventually, the entrapped endoscope was released, using another endoscope in parallel, inserting pressure on the U-turned shaft, and pushing it into the stomach.

Entrapment of the colonoscope can also happen during a routine procedure in a similar manner. Koltun and Coller have described a case with right-sided inguinal hernia [32]. In this case, the colonoscope was entrapped in a loop of colon inside the hernia sac, and the authors were not able to reduce the hernia. They eventually managed to withdraw the scope with gentle pressure support on the loop inside the hernia.

Practical Considerations

Vasovagal reaction:

- Requires partial or complete withdrawal of the scope.
- IV fluids.
- Atropine might need to reverse the sedation.

Splenic injury:

- Left upper quadrant abdominal pain
- Conservative management in the most cases

Entrapment of the endoscope:

- Rare complication which could occur in both EGD and colonoscopy

Complications of Percutaneous Endoscopic Gastrostomy

Since its introduction in 1980 by Ponsky and Gauderer [21, 44], percutaneous endoscopic gastrostomy (PEG) has gained wide acceptance as a safe and efficient method of providing enteral alimentation in patients who cannot swallow due to dementia, stroke, or other causes [23]. The pull method, introduced by Ponsky and his colleagues, is the most widely used technique. There are several other modifications of the original procedure. The push technique differs from the pull method in that the PEG tube is pushed over a guidewire into its final position [23]. All of these techniques require the introduction of a flexible endoscope into the stomach and then percutaneous placement of a cannula through the abdominal wall into the stomach. Complications of the PEG placement is reported up to 4.9–10.3%, although most are relatively minor [34]. PEG-related mortality was reported to be 0.53% [56].

Peristomal Wound Infection

Infection around the PEG site has been reported in about one-third of cases [23]. In most of these patients, infection is minor and can be managed by 1 week of oral antibiotics. However, IV antibiotics or tube removal may be necessary in certain situations. A single dose of cephalosporin- or penicillin-based prophylaxis resulted in a clinically significant reduction in PEG site wound infections, and antibiotic prophylaxis for PEG placement is both cost-effective and recommended for routine use (Jafri and Kulling et al.). Additional attention will need to be paid to patients with a higher risk of infection such as those with diabetes mellitus, renal insufficiency, and alcohol abuse, where necrotizing fasciitis has been reported as a result of severe infection at the PEG site [23].

Fistula

A rare complication of PEG placement involves development of a fistula between the stomach, colon, and skin or the so-called gastrocolocutaneous fistula. This can be prevented by careful identification of the site by transillumination and positioning of the PEG tube to provide good apposition of the stomach with the anterior abdominal wall. The presentation can range from an acute manifestation with peritonitis or colonic obstruction to a more chronic picture with leakage of stool from the stoma or diarrhea resembling tube feeds. This can be diagnosed radiographically. The fistula usually resolves with removal of the tube. However, surgery needs to be considered if the patient develops signs of peritonitis.

Buried Bumper Syndrome

Occasionally, the gastric mucosa can grow over the internal bolster (bumper) after PEG placement and result in migration of the internal bumper along the length of the sinus tract in 1–2% of cases [55]. These patients can present with multiple episodes of abdominal pain, tube blockage, or leakage around the tube during feedings. This can be managed by removing the old PEG tube and placing a new one. A new location should be tried if the bumper is completely covered by the mucosa.

Stoma Leak or Enlargement

This is a common problem with PEG tubes and is leakage around the stoma which has been reported in 1–3% of patients [23]. Several factors have been associated with this condition including infection at the PEG site, high gastric

acid output, loose or absent external bolster, torsion of the tube, buried bumper, or excessive cleaning with hydrogen peroxide. The treatment mainly involves correcting the underlying factors and proper site care. Depending on the cause, these patients can benefit from acid suppression with a proton pump inhibitor, antibiotics to control infection, and increasing tension on the tube by adjusting the external bolster [23]. In cases where stoma enlargement has led to leakage, some authors have recommended replacing the PEG with a large-size tube. However, based on our experience, when the abovementioned measure to control the leakage fail, the original PEG will have to be removed, and a new site for a new PEG will need to be chosen. Another proposed method involves leaving a smaller-sized catheter at the old PEG site, allowing partial closure of the site and then placing a new replacement tube when the stoma enlargement has resolved [23].

Tube Dislodgement

Occasionally, PEG tubes may be removed accidentally (up to 5%). Generally, in cases where the tube was placed more than 4 weeks prior to an accidental removal, the sinus tract has matured. Therefore, a new replacement PEG tube can be placed at the bedside through the original tract without need for endoscopy. However, this reinsertion should be done within 24 h of the original tube removal. Otherwise, the tract may close which may necessitate dilatation or an endoscopic replacement. The tube insertion should be verified by aspiration of gastric contents, and if there is any doubt about the tube placement, a Gastrografin study via the new gastrostomy tube should be performed.

Pneumoperitoneum

More than one-third of PEG insertions have been reported to show some evidence of pneumoperitoneum on radiology. In the setting of a clinically stable patient, the finding of pneumoperitoneum does not appear to have any clinical significance. In fact, it has been shown that these patients can be fed and discharged uneventfully within 24 h [23]. However, the presence of peritoneal signs points to the possibility of clinically significant perforation and will require more aggressive evaluation.

Bleeding

Bleeding from the wound and abdominal wall vessels have also been reported, less than 1%, following PEG placement. As expected, bleeding is more common in patients on anticoagulation or those with an underlying coagulopathy. The treatment is usually conservative including local pressure and adequate external bolster placement. A hematoma may form in some cases due to injury to abdominal wall vessels. Spontaneous resolution happens in most cases. However, there has been a case report of massive ulcerated hematoma following PEG placement that eventually led to a partial gastrectomy in order to stop the bleeding [11].

Practical Considerations

PEG tube placement:

Peristomal wound infection:

- Most common
- Single dose of cephalosporin- or penicillin-based prophylaxis recommended (cefazolin 1 gm IV)

Fistula:

- Prevented by careful transillumination and positioning of the PEG tube (good apposition).
- Surgery needs to be considered if the patient develops signs of peritonitis.

Buried bumper syndrome:

- Present with multiple episodes of abdominal pain, tube blockage, or leakage around the tube during feedings.
- Remove the old PEG tube and placing a new one.
- A new location should be tried if the bumper is completely covered by the mucosa.

Stoma leak or enlargement:

- Conservative management base on causes such as proton pump inhibitor, antibiotics to control infection, and increasing tension on the tube by adjusting the external bolster.
- PEG with a large-sized tube.
- The original PEG will have to be removed, and a new site for a new PEG will need to be chosen.
- Smaller-sized catheter at the old PEG site, allowing partial closure of the site and then placing a new replacement tube.

Tube dislodgement

- If the PEG tube has been placed >4week, bedside replacement PEG tube can be done within 24 h.

(continued)

Otherwise, replacement needs to be done endoscopically.
- If uncertain about location of new PEG, consider Gastrografin study.

Pneumoperitoneum: No clinical significance unless patient developed peritoneal signs.

Hemorrhage: Local pressure and adequate external bolster placement.

Endoscopic Retrograde Cholangiopancreatography (ERCP)

ERCP has been widely used as both a diagnostic and therapeutic modality in pancreaticobiliary disorders. There are many reports of ERCP complications providing a rate of 5–10%, which is higher compared to other endoscopic procedures [57]. The majority of these complications are of mild to moderate severity. However, a significant number can be severe leading to a reported mortality rate of about 1% [57]. Andriulli and colleagues performed a systematic review of 21 prospective studies covering 16,800 patients undergoing ERCP [4]. Overall, complications attributed to ERCP occurred in 1154 patients (6.8%), including in a decreasing order of frequency: pancreatitis 585 cases (3.5%), infection in 242 cases (1.4%), bleeding in 226 (1.3%), and perforations in 101 (0.6%). One hundred seventy-three cases (1.3%) developed cardiovascular and/or analgesia-related complications. The overall mortality rate was 0.07% (nine cases).

Pancreatitis

Post-ERCP pancreatitis (PEP) has been reported as the most common ERCP-related complication. From 21 prospective studies meta-analysis, the incident of PEP was approximately 3.5% but ranged widely from 1.6% to 15.7% [13]. It is important to keep in mind that transient elevation of amylase and lipase, which is extremely common after ERCP (up to 75%), does not necessarily constitute pancreatitis. According to the standards of practice committee statement of ASGE, the consensus definition for ERCP pancreatitis (1) is a new or worsened abdominal pain; (2) is a serum amylase that is three or more times the upper limits of normal, measured 24 h after the procedure; and (3) requires at least 2 days of hospitalization [35]. Pancreatitis is usually of mild to moderate severity in more than 80% of cases. However, severe pancreatitis has been reported in up to 11% of all post-ERCP pancreatitis cases [4].

Several factors have been attributed to increased risk of post-ERCP pancreatitis. Based on a recent prospective study by Wang and colleagues involving 14 centers in China over the course of 1 year, the younger age of the patient (< 60 years), female gender, presence of periampullary diverticulum, cannulation time of more than 10 min, more than one pancreatic deep wire pass, and performing needle-knife precut were found to play a significant role in the development of post-ERCP pancreatitis [57].

Preventive measures for post-ERCP pancreatitis include:

1. Patient selection: Avoid diagnostic ERCP if other imaging modalities (MRCP or EUS) are possible unless patient will likely need therapeutic intervention with ERCP
2. Pharmacologic prophylaxis: Rectal indomethacin or diclofenac immediately before or soon after the procedure
3. Modifications in technique to prevent pancreatitis:
   (a) Pancreatic duct stent in high-risk patient
   (b) Biliary wire-guided cannulation before contrast injection avoiding pancreatic duct contrast injection

Infection

The main infectious complications reported after ERCP include cholangitis (up to 1%) and cholecystitis (up to 0.5%) [35]. Several factors have been considered to increase the rate of post-ERCP cholangitis including the use of combined percutaneous endoscopic procedures (rendezvous technique), stent placement in malignant strictures, and presence of jaundice, low patient volume, and incomplete or failed biliary drainage. Accordingly, placement of plastic stents has been proposed as a means of reducing cholangitis in cases with incomplete or unsuccessful stone extraction. In patients with a malignant hilar obstruction, some endoscopists have recommended to avoid filling all intrahepatic segments and to try to drain all intrahepatic segments that are filled with contrast.

Several studies have evaluated the role of antibiotic prophylaxis in decreasing post-ERCP cholangitis. Most studies including a meta-analysis failed to show any benefit for routine prophylaxis with antibiotics [26]. However, in cases with known cholangitis, incomplete drainage, or inadvertent filling of a pancreatic pseudocyst, prophylactic use of antibiotics is recommended [35].

Cholecystitis has also been reported as a post-ERCP complication. The presence of stones in the gallbladder and the filling of the gallbladder with contrast during ERCP have been proposed as possible factors that increase the risk of cholecystitis [18].

Bleeding

Bleeding during or after ERCP has been reported in 0.7–2% of patients [35]. It usually happens in the setting of sphincterotomy and may present as melena, hematochezia, or hematemesis. Half of these cases present with delayed bleeding that can happen up to 1–2 weeks after the procedure. The majority are of mild to moderate severity with severe hemorrhage (i.e., requiring two or more units of blood, surgery, or angiography) occurring in 0.1–0.5% [4, 35]. Similar to other procedures, the presence of an underlying coagulopathy and anticoagulants used within 72 h can increase the risk of bleeding. Furthermore, the presence of acute cholangitis or papillary stenosis, use of precut sphincterotomy, and low case volume of the endoscopist (one sphincterotomy per week or fewer) have been considered as risk factors. The use of aspirin or NSAIDs does not appear to significantly increase the risk of bleeding.

Perforation

ERCP procedure-related perforation ranges from 0.3% to 0.6% [18, 35]. Three different types of perforation have been reported post-ERCP: guidewire-induced perforation, periampullary perforation during sphincterotomy, and perforation at a site remote from the papilla [28]. Early diagnosis of periampullary perforations is important, since prompt initiation of biliary and duodenal drainage (nasobiliary and nasogastric tubes) together with broad spectrum antibiotics can prevent more aggressive operative interventions in up to 86% of cases [16].

Other types of perforations, that are remote from the papilla, are frequently diagnosed later and will need surgery. Several factors have been recognized to increase the risk of post-ERCP perforation including the history of a Billroth II partial gastrectomy, performance of a sphincterotomy, intramural injection of contrast, duration of the procedure, biliary stricture dilation, and sphincter of Oddi (SOD) [16].

Cardiopulmonary Complications

Although rarely reported, cardiopulmonary complications can lead to a significant number of mortalities from ERCP [35]. These may arise from arrhythmias, hypoventilation, aspiration, or other underlying conditions. Furthermore, medications used for sedation and analgesia might play a role in precipitating these complications. Such complications might be reduced by careful preoperative evaluation and collaboration with anesthesiologists for high-risk or difficult-to-sedate patients.

Mortality

Death associated with ERCP has been reported in about 0.2% of cases (1 in 500) [4]. Mortality rate is twice more frequent after therapeutic procedures compared with diagnostic ERCP [4, 18]. Any of the abovementioned complications can be associated with mortality.

Miscellaneous Complications

There are several other complications reported to be associated with ERCP including ileus, antibiotic-related diarrhea, hepatic abscess, pneumothorax/pneumomediastinum, perforation of the colonic diverticulum, duodenal hematoma, portal venous air, and impaction of therapeutic devices such as stone retrieval baskets [37]. Infection of pseudocysts has been reported especially after filling of pseudocysts during ERCP. Therefore, it is recommended to avoid filling of pseudocysts in the absence of subsequent drainage.

Practical Considerations

ERCP complications:

- Incident is up to 5–10%.
- Common complications include post-ERCP pancreatitis (PEP), infection, bleeding, and perforation.
- PEP is the most common complication. Prevention modalities for PEP include:
  - Careful patient selection.
  - Pre-procedure rectal indomethacin or diclofenac may prevent PEP.
  - Placement of pancreatic duct stent should be considered in high-risk patients.
  - Biliary wire-guided cannulation before contrast injection.
- Early detection of periampullary perforations is important.
- Bleeding complications may be immediate or delayed.

Endoscopic Ultrasound (EUS)

EUS shares the risks and complications of other endoscopic procedures including risks of conscious sedation, cardiorespiratory events, and allergic reaction to medication. There are other complications specifically associated with performance

of EUS due to unique properties of echoendoscopes along with risks of fine needle aspiration (FNA), true-cut biopsy (TCB), and other therapeutic interventions.

Perforation

The reported frequency of GI perforation during EUS ranges between 0.03% and 0.4% with a mortality rate of 0.002% [42]. The increased risk is partly due to long non-flexible rigid transducers and oblique-viewing optics of both radial and linear echoendoscopes. The risk of perforation is particularly higher in patients with esophageal cancer and esophageal strictures, if dilation is performed to traverse the obstructing esophageal tumor. Initial studies reported perforation rates as high as 24%. But, recently, sequential dilation to no more than 16 mm without use of undue force has been reported to be safe without any perforation in 120 patients [43]. The risk can be reduced if a mini-probe or a small caliber echoendoscope is used. But, the depth of penetration of the tumor cannot be assessed accurately with these instruments.

Bleeding

Clinically significant bleeding is rare with EUS and EUS-guided FNA as most endosonographers use Doppler to avoid the path of visible vessel when FNA is considered. The incidence of EUS-related bleeding was 0.4% in two prospective studies and 1.3% in a retrospective analysis. FNA of pancreatic cystic lesions is associated with 6% rate of self-limited bleeding [59].

Infection

The frequency of bacteremia as a complication of EUS and EUS-FNA was reported in 3 prospective studies which collectively included over 250 patients [59]. These studies did not find a statistically significant increase in the rate of bacteremia when compared with that seen after upper endoscopy, and none of the patients who developed bacteremia manifested clinical signs or symptoms of illness. Similarly, a study of 52 patients who underwent EUS-FNA of solid lesions of upper GI tract showed bacteremia in 6% of patients. None of these patients developed signs or symptoms of infection. However, an infection rate of 9% was reported after EUS-guided FNA of cystic lesions of pancreas, mediastinum, and other areas, and pre-procedure antibiotics administration has been recommended in these cases [47]. At present, there are no guidelines regarding antibiotics prophylaxis by ASGE or American Heart Association in patients undergoing EUS or EUS-guided FNA of solid lower GI lesions and non-pancreatic cystic lesions, although antibiotic prophylaxis is recommended by ASGE for FNA of pancreatic cystic lesions but not for solid upper GI lesions.

Pancreatitis

Pancreatitis may occur after EUS-FNA of both cystic and solid lesions with the incidence rate of 0.3–0.6% in two prospective studies. EUS-FNA-induced pancreatitis is usually mild, but severe pancreatitis with fatal complications has been reported. The risk is higher if multiple passes are made or large amount of pancreatic parenchyma or the pancreatic duct is traversed [15].

Miscellaneous

Other rare complications reported with EUS include bile peritonitis and tumor seeding of the needle track. The EUS-guided celiac block and neurolysis are associated with transient diarrhea (4–15%), orthostasis (1%), transient increase in pain (9%), abscess formation, as well as lower extremity weakness with or without paresthesias, paraplegia, perforation, and chronic gastroparesis [10, 48].

Practical Considerations

- EUS assume larger roles in the management of GI and non-GI disorders; the potential for adverse events will likely increase.
- Complications include perforation, bleeding, infection, pancreatitis, and bleeding.
- Mediastinal and pancreatic cystic lesions require antibiotic prophylactic prior to procedure.

Advanced Therapeutic Techniques

Endoscopic Mucosal Resection

Endoscopic mucosal resection (EMR), first introduced in Japan, has been shown to be a promising therapeutic option for removal of superficial benign, potentially malignant and malignant gastrointestinal tract lesions. EMR allows histologic assessment of the entire specimen, in contrast to other ablative methods such as photodynamic therapy (PDT) and argon plasma coagulation (APC). In cases of malignant

lesions, patients need to be carefully selected to include only those with superficial lesions and no lymph node involvement. In comparison with other endoscopic procedures, EMR carries higher complication rate. Bleeding and perforation are the most common complications. Overall, bleeding has been reported in 4–20% of esophageal squamous cell carcinomas, 10% of patients with Barrett's esophagus, and 12% of early gastric cancers (EGC) [12]. In the colon, bleeding has been reported in 1–9% of cases, although rates as high as 12–45% have been recorded [12]. Most of the bleeding occurs during the procedure, but sometimes it is delayed. Bleeding after polypectomy using EMR has been reported to occur after a median of 5 days with a range of 0–17 days [52]. Gastroenterologists will need to have more training and experience in the procedure and be able to cope with its procedural complications including bleeding and perforation.

Radiofrequency Ablation

Radiofrequency ablation (RFA) entails using high frequency alternating current to ablate dysfunctional tissue. It has been used in a variety of clinical situations including management of tumors, abnormal electrical pathways in heart tissue in cases of arrhythmias, and more recently in eradication of Barrett's esophagus. In a recent study comparing RFA with sham procedure in ablative therapy for dysplastic Barrett's esophagus, 77% patients in the RFA group had complete eradication of intestinal metaplasia, as compared with 2.3% in the control group ($P < 0.001$), and patients in the RFA group had less disease progression (3.6% vs. 16.3%, $P = 0.03$) and fewer cancers (1.2% vs. 9.3%, $P = 0.045$). The side effects of RFA reported in this study of 127 patients include chest pain (two patients), upper gastrointestinal hemorrhage (in one patient on antiplatelet therapy for heart disease), and esophageal stricture (6%). No perforations or procedure-related deaths were reported. Overall, RFA appears to be a relatively safe method for ablation of Barrett's esophagus and treatment of various gastrointestinal tumors [45]. Further studies regarding the long-term efficacy and safety of RFA will need to be performed.

Practical Considerations

- The major complications attributed to endoscopic mucosal resection are infection and bleeding.
- The main reported complications of radiofrequency ablation are chest pain, upper GI bleeding, and esophageal stricture.

Endoscopy in Pregnant or Lactating Women

Most of the studies on pregnant women are limited to case series. The general consensus is that endoscopy in pregnancy is safe when the clear indication for endoscopy is necessary and care is taken with sedation. However, a number of potential risks have been reported for endoscopy during pregnancy. Oversedation may cause maternal hypotension and hypoxia which can lead to fetal hypoxia and potentially fatal consequences. The fetus can be exposed to potentially teratogenic drugs and radiation (ERCP). Fetal hypoxia can occur due to inappropriate maternal positioning leading to compression of inferior vena cava by the pregnant uterus, therefore compromising uterine blood flow.

According to ASGE guidelines for endoscopy during pregnancy or lactation [49], the clinician should always have a strong indication for the procedure especially in high-risk pregnancies. Whenever possible the procedure should be deferred to the second trimester. The lowest possible dose of sedative medications (category A or B drugs) should be used during the procedure. The procedure time should be minimized; the patient should be positioned in the left pelvic tilt or left lateral position to avoid vena caval or aortic compression, and fetal heart sounds should be monitored before the initiation of sedation and at the completion of the procedure. Obstetric support should be available in the event of a pregnancy-related complication. Finally, endoscopy is contraindicated in the setting of obstetric complications such as placental abruption, imminent delivery, ruptured membranes, or preeclampsia.

Cappell et al. [8] reported on safety and diagnostic yield of upper endoscopy in 83 pregnant women. The diagnostic yield was 95%, and there were no cases of premature labor or other complications related to the fetus. The same group reported the outcomes of 48 sigmoidoscopies (46 patients) and 8 colonoscopies (8 patients) during pregnancy [9]. They reported no adverse effect or complications related to the procedures. However, it seems a reasonable recommendation to try to avoid excessive abdominal pressure during colonoscopy (especially during late pregnancy) and prone or decubitus positioning of the pregnant patient. There are no reports on the safety of different bowel preparation agents during pregnancy. Therefore, polyethylene glycol solutions and sodium phosphate are considered category C. Sodium phosphate preparations may cause fluid and electrolyte abnormalities and should be used with caution. Tap water enemas should be sufficient for flexible sigmoidoscopy in a pregnant patient.

Jamidar et al. [31] reported 29 ERCPs in 23 pregnant patients (only 3 diagnostic ERCPs). There was only one post-procedure complication (acute pancreatitis) and no adverse effects on the fetus. It is important to protect the fetus from radiation by lead sheets placed under the pelvis and the lower abdomen. The fluoroscopy time should be minimized with

the X-ray beam strictly focused on the area of interest. To confirm successful bile duct cannulation, one can demonstrate bile aspirate instead of fluoroscopy. Overall, fetal exposure should be kept below 5–10 rad level which is the level associated with radiation induced teratogenesis.

Sedation for endoscopy has also been addressed in the 2012 ASGE guidelines. Generally, sedation should be attempted with the lowest effective dose of the safest medication available. To avoid the critical time of organogenesis, all endoscopic procedures should be deferred to the second trimester if possible. Meperidine (category B) is preferred over fentanyl (category C) for initial sedation. Benzodiazepines are uniformly classified as category D; however, in cases where meperidine alone is insufficient, benzodiazepines may be added. There are no reports of midazolam causing congenital abnormalities or fetal demise, making midazolam a preferred adjunct to meperidine.

In the case of lactating women, the main concern is drug excretion in breast milk. In this case fentanyl appears to be the preferred opiate since it is only excreted in pharmacologically insignificant quantities in breast milk. Midazolam may be used as an adjunct, but breastfeeding should be avoided for 4 h afterward. In cases where meperidine is used, the drug can be detected in breast milk up to 24 h after administration.

Conclusion

- Endoscopy is an important diagnostic and therapeutic modality.
- The spectrum of complications can range from adverse effects related to the preparation and anesthesia to procedure-related complications including cardiovascular, infection, bleeding, perforation, post-polypectomy syndrome, aspiration, vasovagal reactions, and splenic injury.
- Percutaneous endoscopic gastrostomy (PEG) can be associated with fistula, buried bumper syndrome, stoma leak and/or enlargement, tube dislodgement, wound/tube infection, pneumoperitoneum, and bleeding.
- Endoscopic retrograde cholangiopancreatography (ERCP) can lead to similar pattern of complications as upper endoscopy together with an added risk of pancreatitis.
- EUS also shares the complications of other upper endoscopic procedures together with an added risk associated with fine needle aspiration (FNA) and true-cut biopsies and mildly increased risk of perforation due to long non-flexible rigid transducers and oblique-viewing optics.
- The major complications attributed to endoscopic mucosal resection are infection and bleeding.
- The main reported complications of radiofrequency ablation are chest pain, upper GI bleeding, and esophageal stricture.
- Overall endoscopy during pregnancy is a safe procedure when done with appropriate indication and careful sedation.
- The risks from endoscopy can be minimized by careful patient selection, extensive training, and adherence to proper techniques.
- Prompt recognition and appropriate management of complications are essential to ensure the best patient outcomes.

Practical Considerations

Endoscopy in pregnant:

- Endoscopy during pregnancy should be performed for a strong indication and should be postponed to the second trimester whenever possible.
- Meperidine is the first-line agent followed by small doses of midazolam as needed.
- Therapeutic ERCP is generally safe in pregnancy. Minimize radiation exposure to the fetus is recommended.
- In late pregnancy, women should be in the lateral decubitus position before, during, and after the procedure
- Quinolones, streptomycin, and tetracyclines are contraindicated during pregnancy.

(continued)

Endoscopy in lactating women:

- Breastfeeding may be continued base on anesthetic agents describe below:
  - Fentanyl: No need to hold breastfeeding.
  - Midazolam: Hold breastfeeding at least 4 h after maternal midazolam administration.
  - Propofol: Breastfeeding can be continued as soon as the mother has recovered sufficiently from general anesthesia.
- Quinolones and sulfonamides should be avoided.
- Penicillins, cephalosporins, tetracyclines, and erythromycin are compatible with breastfeeding.

References

1. Acosta RD, Abraham NS, Chandrasekhara V, Chathadi KV, Early DS, Eloubeidi MA, Evans JA, Faulx AL, Fisher DA, Fonkalsrud L, Hwang JH. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc. 2016 Jan;83(1):3.

2. Allison MC, Sandoe JA, Tighe R, Simpson IA, Hall RJ, Elliott TS. Antibiotic prophylaxis in gastrointestinal endoscopy. Gut. 2009;58(6):869–80.
3. American Society for Gastrointestinal Endoscopy. Sedation and anesthesia in GI endoscopy. Gastrointest Endosc. 2008;68:815–26.
4. Andriulli A, Loperfido S, Napolitano G, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Am J Gastroenterol. 2007;102:1781–8.
5. Arrowsmith JB, Gerstman BB, Fleischer DE, Benjamin SB. Results from the American Society for Gastrointestinal Endoscopy/U.S. Food and Drug Administration collaborative study on complication rates and drug use during gastrointestinal endoscopy. Gastrointest Endosc. 1991;37:421–7.
6. ASGE. Infection control during gastrointestinal endoscopy: guidelines for clinical application. From the ASGE. American Society for Gastrointestinal Endoscopy. Gastrointest Endosc. 1999;49:836–41.
7. Banerjee S, Shen B, Nelson DB, et al. Infection control during GI endoscopy. Gastrointest Endosc. 2008;67:781–90.
8. Cappell MS, Colon VJ, Sidhom OA. A study of eight medical centers of the safety and clinical efficacy of esophagogastroduodenoscopy in 83 pregnant females with follow-up of fetal outcome with comparison control groups. Am J Gastroenterol. 1996a;91:348–54.
9. Cappell MS, Colon VJ, Sidhom OA. A study at 10 medical centers of the safety and efficacy of 48 flexible sigmoidoscopies and 8 colonoscopies during pregnancy with follow-up of fetal outcome and with comparison to control groups. Dig Dis Sci. 1996b;41:2353–61.
10. Chen HY, Lee CH, Hsieh CH. Bile peritonitis after EUS-guided fine-needle aspiration. Gastrointest Endosc. 2002;56:594–6.
11. Chikamori F, Kuniyoshi N, Kawashima T, Takase Y. Huge submucosal hematoma of the stomach after accidental removal of the percutaneous endoscopic gastrostomy tube. Dig Endosc. 2003;15:341–3.
12. Conio M, Ponchon T, Blanchi S, Filiberti R. Endoscopic mucosal resection. Am J Gastroenterol. 2006;101:653–63.
13. Cotton PB, Garrow DA, Gallagher J, et al. Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. Gastrointest Endosc. 2009;70:80–8.
14. Eisen GM, Baron TH, Dominitz JA, et al. Guideline on the management of anticoagulation and antiplatelet therapy for endoscopic procedures. Gastrointest Endosc. 2002;55:775–9.
15. Eloubeidi MA, Gress FG, Savides TJ, et al. Acute pancreatitis after EUS-guided FNA of solid pancreatic masses: a pooled analysis from EUS centers in the United States. Gastrointest Endosc. 2004;60:385–9.
16. Enns R, Eloubeidi MA, Mergener K, et al. ERCP-related perforations: risk factors and management. Endoscopy. 2002;34:293–8.
17. FDA. Guidance on the content and format of premarket notification [510 (k)] submissions for liquid chemical germicides. Rockville: Food and Drug Administration, Infection control devices branch, division of general and restorative devices, office of device evaluation; 1992.
18. Freeman ML, Nelson DB, Sherman S, et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med. 1996;335:909–18.
19. Fujita Y, Ishikawa H, Yokota K. Anaphylactoid reaction to midazolam. Anesth Analg. 1994;79:811–2.
20. Gangi S, Saidi F, Patel K, Johnstone B, Jaeger J, Shine D. Cardiovascular complications after GI endoscopy: occurrence and risks in a large hospital system. Gastrointest Endosc. 2004;60:679–85.
21. Gauderer MW, Ponsky JL, Izant RJ Jr. Gastrostomy without laparotomy: a percutaneous endoscopic technique. J Pediatr Surg. 1980;15:872–5.
22. Gelbmann CM, Ratiu NL, Rath HC, et al. Use of self-expandable plastic stents for the treatment of esophageal perforations and symptomatic anastomotic leaks. Endoscopy. 2004;36:695–9.
23. Ginzburg L, Greenwald D, Cohen J. Complications of endoscopy. Gastrointest Endosc Clin N Am. 2007;17:405–32.
24. Gossner L, Keymling J, Hahn EG, Ell C. Antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG): a prospective randomized clinical trial. Endoscopy. 1999;31:119–24.
25. Gunaratnam NT, Vazquez-Sequeiros E, Gostout CJ, Alexander GL. Methemoglobinemia related to topical benzocaine use: is it time to reconsider the empiric use of topical anesthesia before sedated EGD? Gastrointest Endosc. 2000;52:692–3.
26. Harris A, Chan AC, Torres-Viera C, Hammett R, Carr-Locke D. Meta-analysis of antibiotic prophylaxis in endoscopic retrograde cholangiopancreatography (ERCP). Endoscopy. 1999;31:718–24.
27. Hernandez LV, Jacobson JW, Harris MS. Comparison among the perforation rates of maloney, balloon, and savary dilation of esophageal strictures. Gastrointest Endosc. 2000;51:460–2.
28. Howard TJ, Tan T, Lehman GA, et al. Classification and management of perforations complicating endoscopic sphincterotomy. Surgery. 1999;126:658–63. discussion 64–5
29. Huang PM, Wang HP, Chen CN, Chen LH, Lee YC. Impaction of an upper gastrointestinal endoscope in the distal esophagus: alternative method of removal by double endoscopy without fluoroscopic assistance. Endoscopy. 2006;38:293.
30. Jafri NS, Mahid SS, Minor KS, et al. Meta-analysis: antibiotic prophylaxis to prevent peristomal infection following percutaneous endoscopic gastrostomy. Aliment Pharmacol Ther. 2007;25:647–56.
31. Jamidar PA, Beck GJ, Hoffman BJ, et al. Endoscopic retrograde cholangiopancreatography in pregnancy. Am J Gastroenterol. 1995;90:1263–7.
32. Koltun WA, Coller JA. Incarceration of colonoscope in an inguinal hernia. "Pulley" technique of removal. Dis Colon Rectum. 1991;34:191–3.
33. Kulling D, Sonnenberg A, Fried M, et al. Cost analysis of antibiotic prophylaxis for PEG. Gastrointest Endosc. 2000;51:152–6.
34. McClave SA, Chang WK. Complications of enteral access. Gastrointest Endosc. 2003;58:739–51.
35. Mallery JS, Baron TH, Dominitz JA, et al. Complications of ERCP. Gastrointest Endosc. 2003;57:633–8.
36. Markowitz GS, Stokes MB, Radhakrishnan J, D'Agati VD. Acute phosphate nephropathy following oral sodium phosphate bowel purgative: an underrecognized cause of chronic renal failure. J Am Soc Nephrol. 2005;16:3389–96.
37. Masci E, Toti G, Mariani A, et al. Complications of diagnostic and therapeutic ERCP: a prospective multicenter study. Am J Gastroenterol. 2001;96:417–23.
38. Muscarella LF. High-level disinfection or "sterilization" of endoscopes? Infect Control Hosp Epidemiol. 1996;17:183–7.
39. Nelson DB, Sanderson SJ, Azar MM. Bacteremia with esophageal dilation. Gastrointest Endosc. 1998;48:563–7.
40. Nelson DB, Freeman ML, Silvis SE, et al. A randomized, controlled trial of transcutaneous carbon dioxide monitoring during ERCP. Gastrointest Endosc. 2000;51:288–95.
41. Nelson DB, Jarvis WR, Rutala WA, et al. Multi-society guideline for reprocessing flexible gastrointestinal endoscopes. Society for Healthcare Epidemiology of America. Infect Control Hosp Epidemiol. 2003;24:532–7.
42. O'Toole D, Palazzo L, Arotcarena R, et al. Assessment of complications of EUS-guided fine-needle aspiration. Gastrointest Endosc. 2001;53:470–4.
43. Pfau PR, Ginsberg GG, Lew RJ, Faigel DO, Smith DB, Kochman ML. Esophageal dilation for endosonographic evaluation of malignant esophageal strictures is safe and effective. Am J Gastroenterol. 2000;95:2813–5.
44. Ponsky JL, Gauderer MW. Percutaneous endoscopic gastrostomy: a nonoperative technique for feeding gastrostomy. Gastrointest Endosc. 1981;27:9–11.
45. Pouw RE, Sharma VK, Bergman JJ, Fleischer DE. Radiofrequency ablation for total Barrett's eradication: a description of the endoscopic technique, its clinical results and future prospects. Endoscopy. 2008;40:1033–40.

46. Rudolph SJ, Landsverk BK, Freeman ML. Endotracheal intubation for airway protection during endoscopy for severe upper GI hemorrhage. Gastrointest Endosc. 2003;57:58–61.
47. Ryan AG, Zamvar V, Roberts SA. Iatrogenic candidal infection of a mediastinal foregut cyst following endoscopic ultrasound-guided fine-needle aspiration. Endoscopy. 2002;34:838–9.
48. Shah JN, Fraker D, Guerry D, Feldman M, Kochman ML. Melanoma seeding of an EUS-guided fine needle track. Gastrointest Endosc. 2004;59:923–4.
49. Shergill AK, Ben-Menachem T, Chandrasekhara V, Chathadi K, Decker GA, Evans JA, Early DS, Fanelli RD, Fisher DA, Foley KQ, Fukami N. Guidelines for endoscopy in pregnant and lactating women. Gastrointest Endosc. 2012 Jul 31;76(1):18–24.
50. Silvis SE, Nebel O, Rogers G, Sugawa C, Mandelstam P. Endoscopic complications. Results of the 1974 American Society for Gastrointestinal Endoscopy Survey. JAMA. 1976;235:928–30.
51. Sivak M, editor. Gastroenterologic endoscopy. Philadelphia: WB Saunders; 2000.
52. Sorbi D, Norton I, Conio M, Balm R, Zinsmeister A, Gostout CJ. Postpolypectomy lower GI bleeding: descriptive analysis. Gastrointest Endosc. 2000;51:690–6.
53. Soysal S, Karcioglu O, Demircan A, et al. Comparison of meperidine plus midazolam and fentanyl plus midazolam in procedural sedation: a double-blind, randomized controlled trial. Adv Ther. 2004;21:312–21.
54. Taylor FC, Frankl HD, Riemer KD. Late presentation of splenic trauma after routine colonoscopy. Am J Gastroenterol. 1989;84:442–3.
55. Venu RP, Brown RD, Pastika BJ, Erikson LW Jr. The buried bumper syndrome: a simple management approach in two patients. Gastrointest Endosc. 2002;56:582–4.
56. Wollman B, D'Agostino HB, Walus-Wigle JR, et al. Radiologic, endoscopic, and surgical gastrostomy: an institutional evaluation and meta-analysis of the literature. Radiology. 1995;197:699–704.
57. Wang P, Li ZS, Liu F, et al. Risk factors for ERCP-related complications: a prospective multicenter study. Am J Gastroenterol. 2009;104:31–40.
58. Waye JD, Lewis BS, Yessayan S. Colonoscopy: a prospective report of complications. J Clin Gastroenterol. 1992;15:347–51.
59. Wiersema MJ, Vilmann P, Giovannini M, Chang KJ, Wiersema LM. Endosonography-guided fine-needle aspiration biopsy: diagnostic accuracy and complication assessment. Gastroenterology. 1997;112:1087–95.
60. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation. 2007;116:1736–54.
61. Zuckerman MJ, Hirota WK, Adler DG, et al. ASGE guideline: the management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures. Gastrointest Endosc. 2005;61:189–94.

Anticoagulants and Therapeutic Endoscopy

9

Andrew M. Veitch

Introduction

Anticoagulants are very widely prescribed and are of great benefit to patients with a number of conditions including thromboembolic disease, stroke, and mechanical heart valves. Warfarin and heparin have been the mainstays of treatment for many years. Patients on these drugs are frequently encountered in endoscopy services, and previous American [1] and British [2] guidelines have provided advice in these situations. More recently, a new class of anticoagulants has been introduced: NOACs (novel oral anticoagulants or non-vitamin K oral anticoagulants), also termed DOACs (direct oral anticoagulants). The latter two descriptions are more relevant as they refer to their mechanism of action, and these drugs are no longer new. DOACs have advantages compared to warfarin as they have a rapid onset of action and reliable dosing regimens and do not require laboratory monitoring of anticoagulation. They do, however, pose particular challenges to therapeutic endoscopy as the level of anticoagulation cannot be simply measured by standard techniques, and there are no simple reversal measures in the event of hemorrhage. Moreover, there is an increased risk of spontaneous gastrointestinal hemorrhage compared to warfarin therapy for two of these drugs, dabigatran [3] and rivaroxaban [4]. Guidance on the management of patients on NOACs/DOACs has been produced by the American Society for Gastrointestinal Endoscopy (ASGE) [5], and jointly by the British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) [6], and will form the basis of much of the advice given in this chapter. It is important to consider that for the management of endoscopy patients on warfarin and heparin, there are very few prospective trials and no studies at all of endoscopy patients on DOACs. Many of the recommendations in guidelines have therefore been made on very limited evidence, and consensus opinions have often been made by extrapolating known levels of risks in other situations.

Patient Factors

Endoscopists are rightly concerned with the risk of hemorrhage in a patient on anticoagulants undergoing therapeutic procedures, but conversely there is a risk of thrombosis to the patient if anticoagulation is discontinued. Hemorrhage as a result of endoscopic therapy can often be managed with hemostatic techniques and is rarely fatal. The statistical risk of thrombosis in a patient with a short, temporary, cessation of anticoagulation may be low, but if this resulted in a stroke, then this may be considered a catastrophic event for the patient. In a retrospective study of patients with atrial fibrillation (AF) whose anticoagulation with warfarin was adjusted for endoscopy, the subsequent risk of stroke was low but was significantly higher in those patients with added cardiovascular risk factors [7]. The risk ranged from 0.31% for patients with uncomplicated AF to 2.93% for complex patients with advanced age and severe illness. Alternatives to diagnostic endoscopy include radiological investigations, but if endoscopic therapy is indicated, then it may be possible to defer this for patients who are anticoagulated for a defined period such as those with venous thromboembolism. Those that require temporary cessation of long-term anticoagulation will require counseling regarding the risks of discontinuation of therapy versus the benefits of the procedure.

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Drug Factors

Warfarin

Warfarin is used for the prevention and treatment of venous thromboembolism (VTE) and for the prevention of embolism in atrial fibrillation or prosthetic heart valves. It is a coumarin derivative that inhibits vitamin K metabolism, which is essential for production of certain clotting factors. It has a half-life of greater than 40 h, and levels can be detected in the blood up to 120 h after a single dose. The level of anticoagulation achieved is measured by the international normalized ratio (INR), which is dependent on the prothrombin time.

Heparin

Heparin is usually used for short-term prophylaxis or treatment of thromboembolism and as interim measure in patients being established on anticoagulation with warfarin. The anticoagulant action of heparin is due to a combination of indirect antithrombin and anti-Xa activity. Low molecular weight heparin (LMWH) is less protein bound than unfractionated heparin (UFH) and has a predictable dose–response profile. For UFH the level of anticoagulation is monitored by the activated partial thromboplastin time (APTT). LMWH is administered once or twice daily by subcutaneous injection and does not need routine monitoring. Effective anticoagulation is achieved with the first dose. Its short half-life results in loss of anticoagulant effect by 12–24 h, hence its usefulness in bridging regimens when warfarin is discontinued.

Direct Oral Anticoagulants

Drugs that directly inhibit thrombin (dabigatran) [3, 8] and factor Xa (rivaroxaban [4, 9], apixaban [10, 11], and edoxaban [12]) are licensed for prevention of stroke and systemic embolus in patients with non-valvular AF and for prevention of VTE. These drugs are not indicated for patients with metal heart valves. Compared to warfarin, these drugs have relatively short half-lives and a rapid onset of action, with full anticoagulant effect at approximately 3 h. It is therefore important to delay reintroduction of DOACs after a therapeutic procedure, usually for 24–48 h depending on the risk of post-procedure bleeding.

All DOACs are excreted to some extent by the kidneys, and dosage regimens are adjusted according to renal function. This is most important for dabigatran, which is 80% excreted by the kidneys, and plasma levels of which are most sensitive to impairment of renal function. Only approximately 30% of rivaroxaban and 50% of apixaban and edoxaban are cleared by the kidneys. The ideal interval to discontinue DOACs prior to therapeutic procedures would allow anticoagulation effects to drop to a safe level for therapy and also expose the patient to the minimum time at risk of thromboembolism. This has not been studied for endoscopy, and variable intervals have been recommended dependent on renal function for each of the DOACs [5]. In practice, stopping the drug at least 48 h before the procedure is likely to ensure minimal residual anticoagulant effect for rivaroxaban, apixaban, and edoxaban in patients with stable renal function [6]. This also applies to dabigatran but with the exception that the interval should be extended to 72 h if creatinine clearance is 30–50 mL/min. In any patient with unstable, or rapidly deteriorating, renal function, then a hematologist should be conducted for a specific advice prior to endoscopy.

Reversal of Anticoagulation

Anticoagulation may need to be reversed, rather than just discontinued, in an emergency situation such as gastrointestinal hemorrhage, either spontaneous or following endoscopic therapy. A detailed advice on management of anticoagulants in the context of acute upper gastrointestinal hemorrhage is set out in ESGE guidelines on the management of non-variceal hemorrhage [13], and these principles can be applied to other settings. For warfarin, the level of anticoagulation can be quickly assessed by measurement of the INR. Reversal of anticoagulation can be achieved with intravenous infusion of fresh frozen plasma (FFP), but prothrombin complex (PCC) has a more rapid onset of action, and superior efficacy, and is therefore preferred [14]. Intravenous vitamin K is administered with either agent but has a longer onset of action. Intravenous heparin therapy has a short half-life, and discontinuation is usually all that is required, but if rapid reversal is required, then an infusion of protamine sulfate can be given. This can also be used for LMWH heparin but is less effective.

DOACs have short half-lives (9–17 h), and the anticoagulation effect will have usually dissipated by 12 h. Discontinuation of the drug may be all that is necessary, though half-lives will be prolonged particularly for dabigatran if there is impaired renal function. Adequate resuscitation, including blood transfusion, and early endoscopic hemostatic intervention are required. Protamine sulfate, vitamin K, and FFP are ineffective. Administration of PCC has been suggested for life-threatening hemorrhage, but this has not yet been proven to be clinically effective [15, 16]. In dabigatran patients with impaired renal function, hemodialysis is a potential therapeutic option [17]. Specific antidotes to DOACs are in development [18–20], and one of these, idarucizumab, has been approved by the FDA for management of life-threatening hemorrhage on dabigatran.

Bridging of Anticoagulant Therapy

"Bridging" of anticoagulant therapy with heparin is utilized in patients at high risk of thromboembolic disease if oral anticoagulation is temporarily discontinued for procedures with a risk of significant hemorrhage. Bridging with heparin can be performed with a continuous intravenous infusion of unfractionated heparin (UFH) or with subcutaneous low molecular weight heparin (LMWH) given once or twice daily. The former requires an inpatient stay in hospital while warfarin is discontinued and then reintroduced; the latter can often be managed in an outpatient setting. Some clinicians have a preference for UFH in the context of metal heart valves, but a multicenter registry study found no difference in adverse events between patients bridged with UFH or LMWH in this context [21], and bridging with LMWH is now commonplace. At one extreme, AF without valvular heart disease or other cardiovascular comorbidities is considered low risk for thromboembolism should anticoagulation be temporarily discontinued for endoscopy; at the other extreme, AF with mitral stenosis would be considered high risk and bridging instituted. The risk of thromboembolism with AF increases with additional cardiovascular factors such as hypertension, heart failure, and diabetes, and this risk can be quantified by the $CHADS_2$ score (annual risk of stroke 1.9% with score of 1–18.2% with score of 6) [22]. This has since been updated with the CHA_2DS_2VASc scoring system in which the annual risk of stroke increases from 1.3% with a score 1–15.2% with score of 9. Patients with the highest CHA_2DS_2VASc scores have risks of thromboembolic disease comparable to AF with mitral valve disease, and there has been uncertainty and concern as to whether these patients need bridging with LMWH for therapeutic endoscopic procedures. The most recent ASGE guidelines on antithrombotic agents [5] recommend bridging with LMWH for $CHA_2DS_2VASc \geq 2$. Until recently there were few high-quality studies of perioperative management of anticoagulation. A randomized, prospective, double-blind placebo-controlled trial was conducted in 1884 patients with atrial fibrillation undergoing operative procedures, approximately half of which were gastroenterological endoscopic procedures [23]. They were randomized to LMWH or placebo. Risk factors were well matched in each arm of the study; 38% of the patients had $CHADS_2$ scores ≥ 3, $\leq 2\%$ had mitral stenosis, and $\leq 3.4\%$ had $CHADS_2$ scores of 5 or 6. There was no significant difference in rates of thromboembolism between the LMWH and placebo groups, but there was a significant increase in major hemorrhagic events in the LMWH group vs placebo (3.2% vs 1.3%). Caution should be exercised when interpreting the results in the high-risk thromboembolic groups as the study was not designed or powered to specifically examine these categories of patients.

Bridging with LMWH has also been studied in patients on DOACs. In a German registry, heparin bridging for rivaroxaban patients did not reduce the incidence of thromboembolism and led to higher rates of major hemorrhage (2.7% vs 0.5% $p = 0.01$) [24]. Similarly, in the RE-LY trial, bridging of dabigatran with LMWH resulted in major hemorrhage rates compared to no bridging (6.5% vs 1.8% $p < 0.001$) [25]. Bridging with heparin can therefore not be recommended for DOACs, and in any case, the short half-lives and fast on–off effects of these drugs render it unnecessary.

Procedure Factors

Diagnostic endoscopic procedures have a minimal risk of hemorrhage, as does biliary or pancreatic stenting (without sphincterotomy). Endoscopic biopsies on warfarin therapy have long been considered safe, although there has been little study of this. A Japanese study found no significant hemorrhage after biopsy at gastroscopy or colonoscopy [26]. Only small numbers of biopsies were taken, and this has not been tested in the context of, for example, multiple biopsies in Barrett's esophagus. The safety of endoscopic biopsies in patients on DOACs has not been tested. ASGE guidelines [5] indicate that biopsies may be taken in this context, but the BSG/ESGE guidelines [6] take a more conservative approach. In the latter guidelines, a pragmatic approach is taken to recommend omitting the dose of DOAC on the morning of the procedure. For warfarin we can measure the level of anticoagulation by INR and easily reverse its effects in the event of hemorrhage. For DOACs there is no simple test of the level of anticoagulation and no straightforward effective method of reversal. Also, the pharmacology of DOACs can vary so that some individuals have higher peak levels 2–6 h after administration [27]. Omitting the morning dose may therefore mitigate against this effect. Specific studies of DOACs in the context of endoscopy are, however, required.

Therapeutic procedures have an intrinsic risk of hemorrhage, and data regarding this is presented in Table 9.1. Comparison of data is, however, confused by inconsistency in definitions of severity of hemorrhage and variable rates of intra-procedural and post-procedural hemorrhage. The risk category for hemorrhage with regard to anticoagulants is inferred from these data in studies of patients not taking anticoagulants. Due to the increased risk of hemorrhage on anticoagulants, there are few studies of therapeutic endoscopy in this context. The risks presented in Table 9.1 can sometimes underestimate the risk on anticoagulants; for example, the baseline risk of hemorrhage for EUS with FNA was 0.13% in a meta-analysis, but in a study of EUS with FNA on LMWH, the risk of hemorrhage was 33.3% [28]. For diagnostic colonoscopy, the risk of hemorrhage on anticoagulants would be expected to be low, but polypectomy has been required in 22.5%–32.1% [29, 30] of patients in routine practice and

42% in a bowel cancer screening program [31]. A study of polypectomy <1 cm in patients on continued warfarin therapy found a rate of hemorrhage requiring transfusion in 0.8%, despite routine clipping of polypectomy sites. A pragmatic approach for endoscopy services may be to treat all colonoscopy patients as high risk.

Table 9.1 Risk of hemorrhage associated with therapeutic endoscopic procedures in patients not taking anticoagulants

Procedure	Risk of hemorrhage	References
Colonoscopic polypectomy	0.07–1.7%	[30, 32–35]
Colonic EMR (>10 mm)	3.7–11.3%%	[36–38]
Esophageal EMR	0.6–0.9%	[39, 40]
Duodenal EMR	6.3–12.3%	[40, 41]
Endoscopic submucosal dissection	2–6.9%	[42–45]
ERCP + sphincterotomy	0.1–2%	[46, 47]
ERCP + sphincteroplasty	0.19%	[48]
Ampullectomy	1–7%	[49, 50]
Esophageal dilatation	0–1.7%	[51–53]
Esophageal/duodenal/enteral stent	0.5–1%	[54–57]
Colonic stent	0–4.5%	[58, 59]
Percutaneous endoscopic gastrostomy	≤2%	[60]
EUS with FNA	0.13%	[61]
EUS with brushing of pancreatic cysts	0–3.3%	[62–66]

EMR endoscopic mucosal resection, *ERCP* endoscopic retrograde cholangiopancreatography, *EUS* endoscopic ultrasound, *FNA* fine needle aspiration

Intra-procedural hemorrhage is readily identified and can usually be managed at the time of the procedure. Post-procedural hemorrhage may be delayed by several days and presents a particular problem for patients on anticoagulant therapy, as this will often have been reestablished with full anticoagulation at the time of delayed hemorrhage. Additional measures such as routine clipping of polypectomy sites, or use of endoloops, may be employed. Clip closure of EMR sites has also been advocated to help prevent delayed hemorrhage. It would be prudent to warn anticoagulated patients of an increased risk of post-procedural bleeding.

Management of Endoscopy Patients on Anticoagulants

Management of patients on warfarin or DOACs requiring therapeutic endoscopy is a balance between the risk of hemorrhage due to the procedure and the risk of thrombosis if anticoagulation is discontinued. Bridging with LMWH may reduce the risk of thrombosis in high-risk patients, but this has not been specifically tested in high-quality studies in the context of endoscopy. Pragmatic recommendations based on a risk–benefit analysis are presented in Table 9.2. For patients on anticoagulants for a relatively short duration, such as following deep vein thrombosis, it may be possible to defer

Table 9.2 Management of anticoagulants in patients undergoing endoscopy

Low-risk procedure			High-risk procedure
Diagnostic procedures ± biopsy Biliary stenting without sphincterotomy			Therapeutic procedures (Table 9.1)
Warfarin	*Low-risk indication* Prosthetic metal aortic heart valve Xenograft heart valve AF without valvular disease >3 months after VTE Thrombophilia syndromes[a]	Continue warfarin Ensure INR in therapeutic range prior to procedure	Stop warfarin 5 days before procedure Ensure INR ≤ 1.5 Restart warfarin on the evening of procedure at usual daily dose
	High-risk indication Prosthetic metal mitral heart valve Prosthetic heart valve and AF AF and mitral stenosis <3 months after VTE	Continue warfarin Ensure INR in therapeutic range prior to procedure	Stop warfarin 5 days before procedure Commence LMWH 3 days before procedure Restart warfarin on evening of procedure at usual daily dose Continue LMWH until INR in therapeutic range
DOAC Dabigatran Rivaroxaban Apixaban Edoxaban	*Indications* AF + additional risk factors Prevention or treatment of VTE	Consider omitting DOAC on morning of procedure	Take last dose of DOAC ≥48 h before procedure (except dabigatran with CrCl 30–50 mL/min take last dose 72 h before procedure) Seek hematology advice for any DOAC in patient with rapidly deteriorating renal function Restart DOAC 24–48 h post procedure

Recommendations adapted from Veitch et al. [6]

AF atrial fibrillation, *VTE* venous thromboembolism, *INR* international normalized ratio, *DOAC* direct oral anticoagulant, *CrCl* creatinine clearance

[a]Most thrombophilia syndromes will not require heparin bridging if warfarin is temporarily discontinued, but hematologic advice should be sought in each instance

endoscopic therapy until anticoagulation treatment has ceased. This would be applicable, for example, to small colonic polyps with a low risk of invasive neoplasia. This policy could also be applied to obstructive jaundice due to biliary stones when a temporary biliary stent could be placed as an alternative to sphincterotomy, though this needs to be balanced against a risk of subsequent cholangitis. Further prospective studies are required to better define the risks and management strategies in patients on anticoagulants requiring therapeutic endoscopy.

Box 9.1 Anticoagulants in Therapeutic Endoscopy: Management Considerations

- Therapeutic endoscopic procedures confer benefit to the patient.
- Anticoagulation protects against thromboembolic disease.
- Discontinuation of anticoagulants has a risk of thrombosis, including risk of stroke.
- Therapeutic endoscopic procedures have a risk of hemorrhage, which ranges from minor to life-threatening.
- Post-procedure hemorrhage may be delayed and present after anticoagulation is restarted.

Box 9.2 Direct Oral Anticoagulants (DOACs)

Rivaroxaban, dabigatran, apixaban, edoxaban
Advantages
- Predictable dose response
- Rapid onset of action
- No need for routine monitoring
- Less need for dose adjustment than for warfarin
- Few drug interactions

Disadvantages
- No simple measurement of anticoagulant activity
- Increased risk of spontaneous gastrointestinal hemorrhage for rivaroxaban and dabigatran

Box 9.3 Reversal of Anticoagulant Therapy

For life-threatening gastrointestinal hemorrhage:
Warfarin
- IV prothrombin complex
- IV vitamin K

Heparin
- IV protamine sulfate: More effective for UFH than LMWH

DOACS
- No proven benefit with clotting factors.
- Resuscitate and transfuse pending diminution of effect (DOACs have relatively short half-lives).
- Idarucizumab for dabigatran if available (antidotes for other DOACs in development).

Box 9.4 Bridging Therapy for Anticoagulants

- Bridging of warfarin with LMWH may be used for patients with a high risk of thrombosis.
- Bridging of warfarin with LMWH in AF patients (without mechanical heart valves) increases the risk of hemorrhage without reducing the risk of thrombosis.
- Bridging of DOACs with LMWH increases the risk of hemorrhage without reducing the risk of thrombosis.

References

1. ASGE Standards of Practice Committee, Anderson MA, Ben-Menachem T, et al. Management of antithrombotic agents for endoscopic procedures. Gastrointest Endosc. 2009;70:1060–70.
2. Veitch AM, Baglin TP, Gershlick AH, et al. Guidelines for the management of anticoagulant and antiplatelet therapy in patients undergoing endoscopic procedures. Gut. 2008;57:1322–9.
3. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361:1139–51.
4. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365:883–91.

5. ASGE Standards of Practice Committee, Acosta RD, Abraham NS, et al. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc. 2016;83:3–16.
6. Veitch AM, Vanbiervliet G, Gershlick AH, et al. Endoscopy in patients on antiplatelet or anticoagulant therapy, including direct oral anticoagulants: British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) guidelines. Gut. 2016;65:374–89.
7. Blacker DJ, Wijdicks EF, McClelland RL. Stroke risk in anticoagulated patients with atrial fibrillation undergoing endoscopy. Neurology. 2003;61:964–8.
8. Schulman S, Kearon C, Kakkar AK, et al. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. N Engl J Med. 2009;361:2342–52.
9. Bauersachs R, Berkowitz SD, et al. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med. 2010;363:2499–510.
10. Agnelli G, Buller HR, Cohen A, et al. Oral apixaban for the treatment of acute venous thromboembolism. N Engl J Med. 2013;369:799–808.
11. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981–92.
12. Giugliano RP, Ruff CT, Braunwald E, et al. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2013;369:2093–104.
13. Gralnek IM, Dumonceau JM, Kuipers EJ, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2015;47:a1–a46.
14. Karaca MA, Erbil B, Ozmen MM. Use and effectiveness of prothrombin complex concentrates vs fresh frozen plasma in gastrointestinal hemorrhage due to warfarin usage in the ED. Am J Emerg Med. 2014;32:660–4.
15. Schulman S, Crowther MA. How I treat with anticoagulants in 2012: new and old anticoagulants, and when and how to switch. Blood. 2012;119:3016–23.
16. Weitz JI, Quinlan DJ, Eikelboom JW. Periprocedural management and approach to bleeding in patients taking dabigatran. Circulation. 2012;126:2428–32.
17. Desai J, Granger CB, Weitz JI, et al. Novel oral anticoagulants in gastroenterology practice. Gastrointest Endosc. 2013;78:227–39.
18. Ansell JE, Bakhru SH, Laulicht BE, et al. Use of PER977 to reverse the anticoagulant effect of edoxaban. N Engl J Med. 2014;371:2141–2.
19. Lu G, DeGuzman FR, Hollenbach SJ, et al. A specific antidote for reversal of anticoagulation by direct and indirect inhibitors of coagulation factor Xa. Nat Med. 2013;19:446–51.
20. Pollack CV Jr, Reilly PA, Eikelboom J, et al. Idarucizumab for Dabigatran Reversal. N Engl J Med. 2015;
21. Spyropoulos AC, Turpie AG, Dunn AS, et al. Perioperative bridging therapy with unfractionated heparin or low-molecular-weight heparin in patients with mechanical prosthetic heart valves on long-term oral anticoagulants (from the REGIMEN Registry). Am J Cardiol. 2008;102:883–9.
22. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA. 2001;285:2864–70.
23. Douketis JD, Spyropoulos AC, Kaatz S, et al. Perioperative bridging anticoagulation in patients with atrial fibrillation. N Engl J Med. 2015;373:823–33.
24. Beyer-Westendorf J, Gelbricht V, Forster K, et al. Periinterventional management of novel oral anticoagulants in daily care: results from the prospective Dresden NOAC registry. Eur Heart J. 2014;35:1888–96.
25. Douketis JD, Healey JS, Brueckmann M, et al. Perioperative bridging anticoagulation during dabigatran or warfarin interruption among patients who had an elective surgery or procedure. Substudy of the RE-LY trial. Thromb Haemost. 2015;113:625–32.
26. Ono S, Fujishiro M, Kodashima S, et al. Evaluation of safety of endoscopic biopsy without cessation of antithrombotic agents in Japan. J Gastroenterol. 2012;47:770–4.
27. Baglin T. Clinical use of new oral anticoagulant drugs: dabigatran and rivaroxaban. Br J Haematol. 2013;163:160–7.
28. Kien-Fong Vu C, Chang F, Doig L, et al. A prospective control study of the safety and cellular yield of EUS-guided FNA or Trucut biopsy in patients taking aspirin, nonsteroidal anti-inflammatory drugs, or prophylactic low molecular weight heparin. Gastrointest Endosc. 2006;63:808–13.
29. Gavin DR, Valori RM, Anderson JT, et al. The national colonoscopy audit: a nationwide assessment of the quality and safety of colonoscopy in the UK. Gut. 2013;62:242–9.
30. Wexner SD, Garbus JE, Singh JJ, et al. A prospective analysis of 13,580 colonoscopies. Reevaluation of credentialing guidelines. Surg Endosc. 2001;15:251–61.
31. Ellul P, Fogden E, Simpson CL, et al. Downstaging of colorectal cancer by the National Bowel Cancer Screening programme in England: first round data from the first centre. Color Dis. 2010;12:420–2.
32. Bowles CJ, Leicester R, Romaya C, et al. A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? Gut. 2004;53:277–83.
33. Gibbs DH, Opelka FG, Beck DE, et al. Postpolypectomy colonic hemorrhage. Dis Colon Rectum. 1996;39:806–10.
34. Rosen L, Bub DS, Reed JF 3rd, et al. Hemorrhage following colonoscopic polypectomy. Dis Colon Rectum. 1993;36:1126–31.
35. Sieg A, Hachmoeller-Eisenbach U, Eisenbach T. Prospective evaluation of complications in outpatient GI endoscopy: a survey among German gastroenterologists. Gastrointest Endosc. 2001;53:620–7.
36. Burgess NG, Metz AJ, Williams SJ, et al. Risk factors for intraprocedural and clinically significant delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. Clin Gastroenterol Hepatol. 2014;12:651–61 e1-3.
37. Cipolletta L, Rotondano G, Bianco MA, et al. Endoscopic resection for superficial colorectal neoplasia in Italy: a prospective multicentre study. Dig Liver Dis. 2014;46:146–51.
38. Heresbach D, Kornhauser R, Seyrig JA, et al. A national survey of endoscopic mucosal resection for superficial gastrointestinal neoplasia. Endoscopy. 2010;42:806–13.
39. Namasivayam V, Prasad GA, Lutzke LS, et al. The risk of endoscopic mucosal resection in the setting of clopidogrel use. ISRN Gastroenterol. 2014;2014:494157.
40. Qumseya BJ, Wolfsen C, Wang Y, et al. Factors associated with increased bleeding post-endoscopic mucosal resection. J Dig Dis. 2013;14:140–6.
41. Nonaka S, Oda I, Tada K, et al. Clinical outcome of endoscopic resection for nonampullary duodenal tumors. Endoscopy. 2015;47:129–35.
42. Kim JS, Kim BW, Shin IS. Efficacy and safety of endoscopic submucosal dissection for superficial squamous esophageal neoplasia: a meta-analysis. Dig Dis Sci. 2014;59:1862–9.
43. Miyahara K, Iwakiri R, Shimoda R, et al. Perforation and postoperative bleeding of endoscopic submucosal dissection in gastric tumors: analysis of 1190 lesions in low- and high-volume centers in Saga, Japan. Digestion. 2012;86:273–80.
44. Repici A, Hassan C, De Paula PD, et al. Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review. Endoscopy. 2012;44:137–50.
45. Takeuchi T, Ota K, Harada S, et al. The postoperative bleeding rate and its risk factors in patients on antithrombotic therapy who undergo gastric endoscopic submucosal dissection. BMC Gastroenterol. 2013;13:136.
46. Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointest Endosc. 1991;37:383–93.

47. Freeman ML, Nelson DB, Sherman S, et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med. 1996;335:909–18.
48. Zhao HC, He L, Zhou DC, et al. Meta-analysis comparison of endoscopic papillary balloon dilatation and endoscopic sphincteropapillotomy. World J Gastroenterol. 2013;19:3883–91.
49. Bohnacker S, Seitz U, Nguyen D, et al. Endoscopic resection of benign tumors of the duodenal papilla without and with intraductal growth. Gastrointest Endosc. 2005;62:551–60.
50. Catalano MF, Linder JD, Chak A, et al. Endoscopic management of adenoma of the major duodenal papilla. Gastrointest Endosc. 2004;59:225–32.
51. Metman EH, Lagasse JP, d'Alteroche L, et al. Risk factors for immediate complications after progressive pneumatic dilation for achalasia. Am J Gastroenterol. 1999;94:1179–85.
52. Polese L, Angriman I, Bonello E, et al. Endoscopic dilation of benign esophageal strictures in a surgical unit: a report on 95 cases. Surg Laparosc Endosc Percutan Tech. 2007;17:477–81.
53. Williams VA, Watson TJ, Zhovtis S, et al. Endoscopic and symptomatic assessment of anastomotic strictures following esophagectomy and cervical esophagogastrostomy. Surg Endosc. 2008;22:1470–6.
54. Dormann A, Meisner S, Verin N, et al. Self-expanding metal stents for gastroduodenal malignancies: systematic review of their clinical effectiveness. Endoscopy. 2004;36:543–50.
55. Johnson E, Enden T, Noreng HJ, et al. Survival and complications after insertion of self-expandable metal stents for malignant oesophageal stenosis. Scand J Gastroenterol. 2006;41:252–6.
56. Ramirez FC, Dennert B, Zierer ST, et al. Esophageal self-expandable metallic stents–indications, practice, techniques, and complications: results of a national survey. Gastrointest Endosc. 1997;45:360–4.
57. Telford JJ, Carr-Locke DL, Baron TH, et al. Palliation of patients with malignant gastric outlet obstruction with the enteral Wallstent: outcomes from a multicenter study. Gastrointest Endosc. 2004;60:916–20.
58. Dionigi G, Villa F, Rovera F, et al. Colonic stenting for malignant disease: review of literature. Surg Oncol. 2007;16(Suppl 1):S153–5.
59. Khot UP, Lang AW, Murali K, et al. Systematic review of the efficacy and safety of colorectal stents. Br J Surg. 2002;89:1096–102.
60. Schapiro GD, Edmundowicz SA. Complications of percutaneous endoscopic gastrostomy. Gastrointest Endosc Clin N Am. 1996;6:409–22.
61. Wang KX, Ben QW, Jin ZD, et al. Assessment of morbidity and mortality associated with EUS-guided FNA: a systematic review. Gastrointest Endosc. 2011;73:283–90.
62. Al-Haddad M, Wallace MB, Woodward TA, et al. The safety of fine-needle aspiration guided by endoscopic ultrasound: a prospective study. Endoscopy. 2008;40:204–8.
63. Bruno M, Bosco M, Carucci P, et al. Preliminary experience with a new cytology brush in EUS-guided FNA. Gastrointest Endosc. 2009;70:1220–4.
64. Lozano MD, Subtil JC, Miravalles TL, et al. EchoBrush may be superior to standard EUS-guided FNA in the evaluation of cystic lesions of the pancreas: preliminary experience. Cancer Cytopathol. 2011;119:209–14.
65. Sendino O, Fernandez-Esparrach G, Sole M, et al. Endoscopic ultrasonography-guided brushing increases cellular diagnosis of pancreatic cysts: a prospective study. Dig Liver Dis. 2010;42:877–81.
66. Thomas T, Bebb J, Mannath J, et al. EUS-guided pancreatic cyst brushing: a comparative study in a tertiary referral centre. JOP. 2010;11:163–9.

Confocal Laser Endomicroscopy

10

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Introduction

Confocal laser endomicroscopes (CLEs) provide the highest magnification in clinical endoscopy and have been commercially available since 2005 [1]. A CLE is an instrument providing ×1,000 black and white imaging that is comparable to standard microscopic examination. The principle technique is a summary of display images that are reconstructed from a pinhole that filters only a focused light and reflected plane. In addition, the pinhole reduces light scatter below and above the plane (Fig. 10.1). Therefore, only a single point in one plane, called "confocal," can be seen at once [2]. During the examination, the confocal system can display a stream of images with 1–12 frames/second. In other words, it resembles real-time endoscopic histology images [3–7].

Instruments, Accessories, and Procedure

Currently, there are two types of CLE systems: a) endoscopic-based confocal laser endomicroscope (eCLE, Pentax-Hoya, Tokyo, Japan) and b) probe-based confocal laser endomicroscope (pCLE, Cellvizio Technology, Mauna Kea Company, Paris, France). Both require an intravenous (IV) contrast injection (2.5 ml of 10% fluorescein sodium) or topical dye spray (e.g., acriflavine hydrochloride) to enhance the visibility of all vascular supplied mucosal structures during CLE examination [2].

The eCLE is an endoscopic-based CLE that integrates the microscope onto the distal tip of a conventional 12.8 mm diameter flexible endoscope (Hoya cooperation, Tokyo, Japan). The tool was primarily developed to evaluate the esophagus, stomach, and colon by applying the tip of the scope to the surface of the lesion after fluorescein injection or topical dye spray. The scanning field is 1,024 × 1,024 pixels, and the adjustable depth of examination ranges from 0 to 250 μm [8] (Table 10.1). The other system is a probe-based CLE (pCLE) (Figs. 10.2 and 10.3) provided by Mauna Kea Company (Paris, France), which is a 0.6–2.5 mm ultrahigh definition (UHD) catheter probe transported laser beam with 10,000 or 30,000 sensors [2, 7, 9] (Table 10.1). This probe can be inserted in any accessory channel that accepts a 2.5 mm catheter. The probe can examine the upper and lower GI tract and the bile duct by a gentle contact of the probe to the suspicious lesion. Moreover, pCLE can evaluate pancreatic lesions or nearby lymph nodes using a 0.632 mm miniprobe (needle-based confocal laser endomicroscopy; nCLE or AQ-Flex) after removing the stylet of the 19 G endoscopic ultrasound (EUS) needle. The tip of the nCLE probe should be placed 2–3 mm outside the tip of the needle and secured with a locking device to maintain an accurate distance from the EUS-FNA needle sheet. To prevent AQ-Flex damage while adjusting for the appropriate position of the 19 G needle in the tissue, it is recommended to unlock and retract the AQ-Flex probe inside the needle a little while puncturing the target with the needle. After the endosonographer adjusts the needle to the most appropriate area followed by an injection of 2.5 ml of 10% fluorescein into the patient, the AQ-Flex is pushed forward and again fixed by a locking device at the same position before performing the nCLE examination to ensure the focus is stable [9] (Fig. 10.4). Although it is possible, it may be difficult to examine lesions located at the head of the pancreas. Practically, the technique is not different between examining cystic and solid pancreatic lesions.

Fluorescein, a slightly acidic and hydrophilic dye, has been used intravenously as a staining substance. The recommended dosage is 2.5–5.0 ml of 10% fluorescein [10]. Within 30 s of injection, fluorescein distributes through all the epithelial cells and lasts for 12 min [11]. Fluorescein

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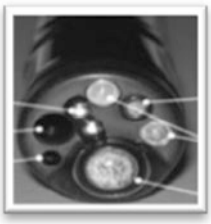
Table 10.1 A comparison between eCLE and pCLE

	eCLE 	pCLE 			
		GastroFlex UHD	ColoFlex UHD	CholangioFlex	AQ-Flex
Lateral resolution	0.7 μm	1 μm		3.5 μm	
Field of view	475 × 475 μm	240 × 240 μm		325 × 325 μm	
Scanning filed	1,000,000 pixels	30,000 sensors in UHD probe			10,000 sensors
Z-axis	Yes	No			
Adjustable for use in different organs	No	Yes			
Imaging plane depth	Adjustable from 0 to 250 μm	55–65 μm		40–70 μm	
Number of images/second	±1	9–12			
Operating channel requirement	N/A	≥2.8 mm		≥1 mm	≥0.91 mm (19 gauge)

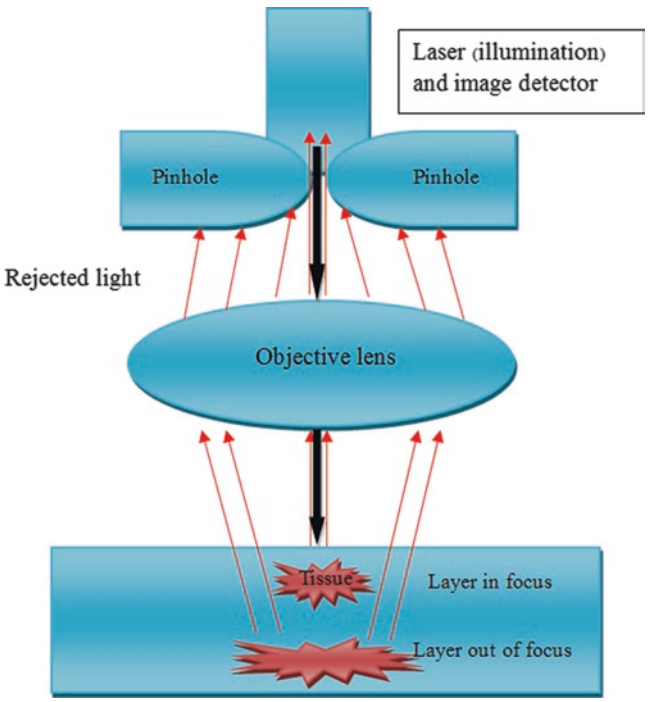


Fig. 10.1 Schematic of the confocal laser endomicroscopy principle

facilitates a real-time histology reading by enhancing structures containing blood vessels, including normal gastric epithelium [3, 12]. In contrast, any structure that has no vascular supply, such as mucin, will not be stained by fluorescein. Presently, fluorescein is proven as a very safe contrast agent, and, reportedly, less than 2% of patients experience mild side effects [13].

Another well-known agent called acriflavine hydrochloride, a topical dye, is not currently recommended for early cancer screening because it only stains the superficial layer of the GI tract mucosa [6], and it is considered teratogenic, with genotoxicity at a concentration as low as 0.025% [14].

Practical Considerations

- eCLE provides better image quality but has limited use only in upper and lower endoscopies, whereas pCLE can be inserted in almost any scope through a standard accessory channel.
- nCLE can be inserted in 19G needle under EUS guidance.
- For safety, fluorescein is preferred over acriflavine hydrochloride as a contrast-enhancing agent.

Contraindications for Fluorescein Injection

1. Fluorescein allergy.
2. Avoid in pregnancy, especially in the first trimester, because there are not enough data on pregnant women.
3. Be careful in lactation; breast-feeding should be discontinued for at least 7 days.
4. Children because there are not enough data on patients below 18 years old.

With today's technology, pCLE is designed to be used in various gastrointestinal endoscopes, including gastroscopes (GastroFlex UHD), colonoscopes (ColoFlex UHD), duodenoscopes (CholangioFlex), and EUS scopes (nCLE or AQ-Flex) [8]. Each probe is specifically developed for use

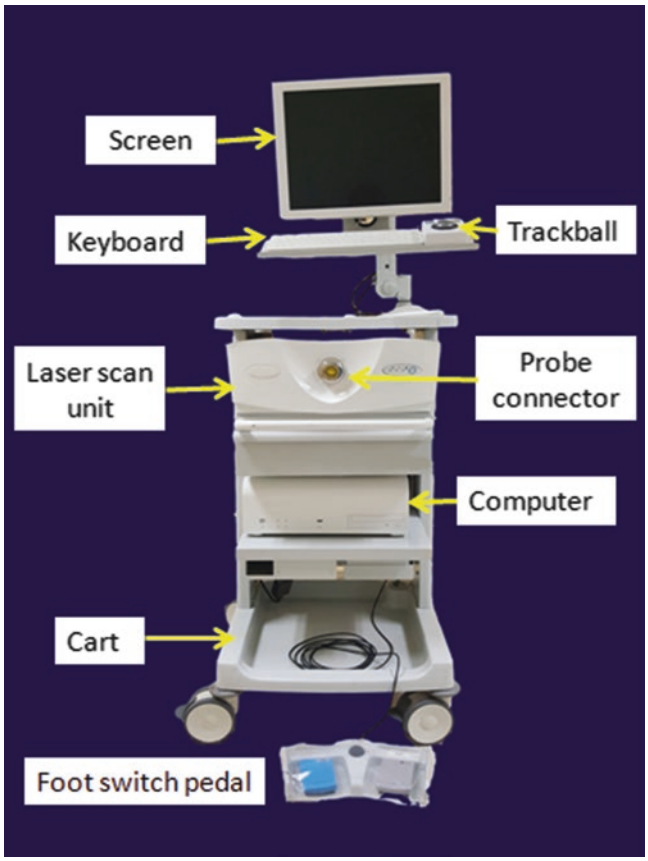


Fig. 10.2 pCLE system

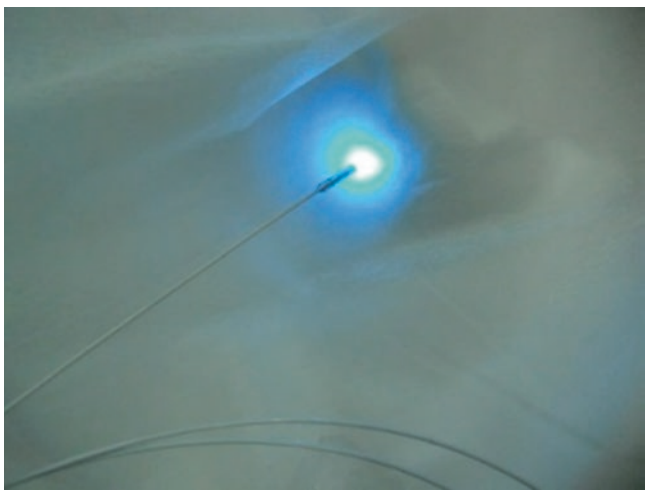


Fig. 10.3 pCLE probe

according to the organ of examination. Conversely, eCLE can only be used in the organ for which the scope is designed, and in the current models, only upper and lower endoscopes are available. In addition, the quality of the confocal image with eCLE is better than pCLE because the eCLE system provides a better (0.7 μm) lateral resolution than pCLE

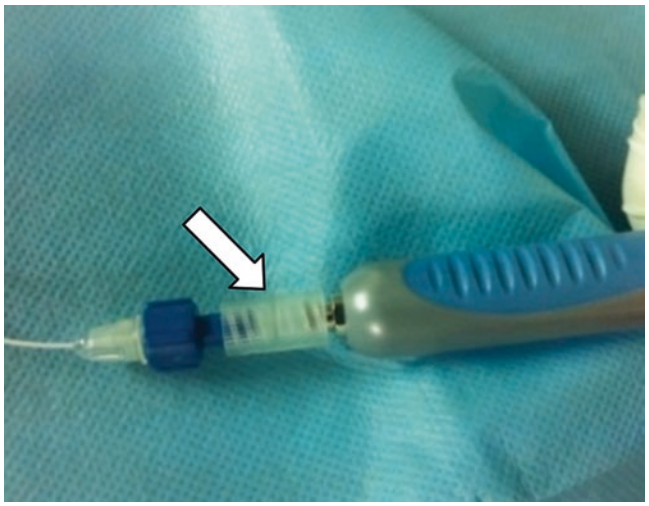


Fig. 10.4 nCLE in a 19 G needle and fixed with a locking device (*arrow*)

(1–3.5 μm) [6–8]. Additionally, with eCLE, the Z-axis can be adjusted to focus at different depths up to 250 μm, whereas pCLE and nCLE systems have a fixed imaging plane depth at 40–70 μm [8]. However, the pCLE system provides a much faster frame rate (9–12 images/second) than eCLE (±1 image/second) [8, 15]. Consequently, the streamline of pCLE images is close to the standard video output (Table 10.1). To date, the eCLE is no longer available for new purchase [8].

Indications

Currently, the role of confocal laser endomicroscopy is not well established in the guidelines of gastrointestinal disease treatment [16–19]. However, there is a growing body of evidence that pCLE can provide valuable diagnostic information in various gastrointestinal diseases, including malignancy and nonmalignancy. Consequently, in the USA, pCLE has been accepted and can be reimbursed in certain CPT codes. For instance, optical endomicroscopy procedures in the esophagus or upper GI tract have been reported using the 43,206 and 43,252 CPT codes.

Over the last decade, confocal laser endomicroscopy has been utilized at different levels, including research and clinical practice in the field of diagnostic endoscopy. Potential indications for confocal laser endomicroscopy in the future are the following [8, 9, 19, 20]:

1. Targeted biopsy of suspicious malignant or premalignant lesions, i.e., gastric intestinal metaplasia and early gastric cancer.
2. Differentiate malignant from nonmalignant lesion in suspected areas that are still questionable by standard tech-

niques, i.e., Barrett's esophagus, indeterminate biliary stricture, and pancreatic mass.
3. Real-time diagnosis for endoscopic management, i.e., colonic polyp and dysplastic change in IBD.
4. Predicting treatment response, i.e., anti-TNF treatment in IBD.

Esophagus

Reflux Esophagitis

The role of confocal laser endomicroscopy is to evaluate micro-alterations in patients with nonerosive reflux disease (NERD) or minimal change esophageal reflux disease (MERD), when white light endoscopy (WLE) fails to detect the lesion. Only two eCLE studies in MERD patients were published in 2012. Chu et al. considered greater than 6 intrapapillary capillary loops (IPCLs) per image (475 × 475 μm), an IPCL diameter greater than 17.2 μm, or a dilated intercellular space greater than 2.4 μm as significant factors predicting MERD [21]. Another eCLE study reported that NERD patients had a significantly smaller distance of surface to papillary than normal controls (0.19 μm/cm vs. 0.44 μm/cm; $p = 0.019$) and proposed this parameter for MERD diagnosis [22]. Our group recently used a pCLE probe to study MERD diagnosis. We reported that more than 5 IPCLs per 500 μm (4 sets of view) in a patient with reflux symptom was appropriate to diagnose MERD. This uncomplicated criterion demonstrated 90% accuracy, 85% sensitivity, 100% specificity, 100% PPV, and 77% NPV [23]. However, future studies on how pCLE predicts treatment response after MERD diagnosis is needed.

Barrett's Esophagus

In 2006, the first study using eCLE in 63 Barrett's esophagus (BE) cases proposed the presence of irregular black cells with a loss of normal cellular pattern and distorted capillaries with fluorescein leakage as criteria to diagnose high-grade intraepithelial neoplasia (HGIN) or cancer. The study reported a sensitivity of 92%, specificity of 98%, and accuracy of 97% in predicting areas associated with neoplasia. The mean kappa value for interobserver agreement in the prediction of histopathological diagnosis was 0.843, whereas the intraobserver agreement showed a mean kappa value of 0.89 [24]. Based on these criteria, the first randomized, controlled, double-blind, crossover trial was conducted to determine the diagnostic yield of eCLE with targeted biopsy compared to the standard endoscopy under a four-quadrant random biopsy protocol [25]. Forty-six suspected BE patients were enrolled and randomized to undergo eCLE-targeted biopsy or the standard protocol, to allow complete healing from the prior biopsy. Two to six weeks later, a crossover endoscopy was performed. This study emphasized the advantage of eCLE over the standard protocol by showing the significant diagnostic yield for neoplasia at 33% with pCLE-targeted biopsy compared to 17% with the standard biopsy protocol ($p = 0.01$). Additionally the study showed a significant 59% decreased in the number of biopsies (9.8 vs. 23.8 biopsies; $p = 0.002$) [25].

Subsequently, a pCLE study on BE was conducted by Pohl et al. [26] and described five parameters to diagnose high-grade intraepithelial neoplasia (HGIN) or early esophageal carcinoma in 15 patients with previously known BE. The criteria to diagnose early adenocarcinoma were (1) irregular epithelial lining, (2) variable width of the epithelial lining, (3) gland fusion, (4) presence of "dark area," and (5) irregular vascular pattern (Fig. 10.5). These criteria were validated in phase 2 of this study in another 53 patients. The accuracy rate was approximately 88–93% if there were at least two positive criteria [26]. Moreover, the interobserver agreement among experienced pCLE and inexperienced pCLE using these criteria was almost perfect (kappa = 0.83) and was substantial (kappa = 0.72) [27]. Recently, Gaddam et al. [28] proposed six novel pCLE criteria for the prediction of high-grade cancer in Barrett's esophagus patients: (1) epithelial surface appears saw-toothed; (2) goblet cells not easily identified; (3) glands are not equidistant; (4) glands are unequal in size and shape; (5) cells are enlarged; and (6) cells are irregular and not equidistant from one another. By following these criteria, experienced endoscopists could perform the examination with near-perfect accuracy at 98% [28]. Furthermore, only a short learning curve was required to train beginners [28].

Even with various criteria for HGIN and esophageal adenocarcinoma diagnosis, the international multicenter, randomized, control trial study showed the benefit of pCLE in Barrett's esophagus patients for neoplasm detection when compared with high-definition white light endoscopy (HD-WLE) or narrow-band imaging (NBI) endoscopy using different criteria. pCLE plus HD-WLE led to an increased sensitivity for HGIN/esophageal adenocarcinoma diagnosis when compared to HD-WLE alone (68% vs. 34%; $p = 0.002$). Moreover, the sensitivity of associated malignancy diagnosis in BE was significantly improved from 45% to 75% when using pCLE plus HD-WLE or NBI [29]. The recent pCLE European consensus in 2015 suggested that Barrett's esophagus should be added to the list of neoplastic conditions for which pCLE may affect management decisions. However, the red flag technique (e.g., chromoendoscopy) is recommended as a supplemental procedure to delineate the area of interest [30]. In the USA, there is a CPT code for BE diagnosis using pCLE.

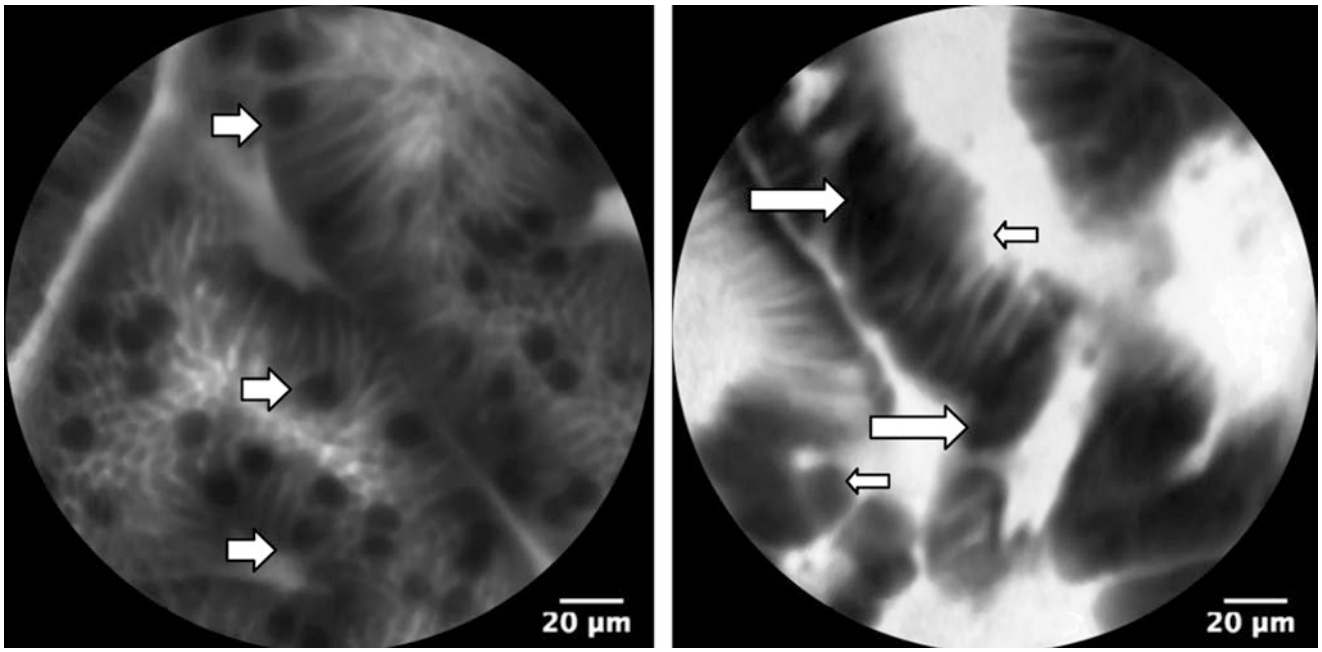


Fig. 10.5 Image of Barrett's esophagus (BE) without dysplasia (*left*; mucin-containing goblet cells; *arrow*) and BE with high-grade dysplasia (*right*; irregular epithelial lining (*short arrows*) with the presence of a dark area (*long arrows*))

Squamous Cell Carcinoma (SCC) of the Esophagus

In 2008, Pech et al. [31] reported 95% accuracy, 100% sensitivity, and 87% specificity when eCLE was used to diagnose superficial esophageal squamous cell carcinoma (SCC) in 21 suspected SCC patients. The criteria included the following: (1) the presence of mucosal abnormalities such as irregular dark cell arrangement of varying size with ill-defined boarders; (2) increased IPCL diameter; and (3) irregular-shaped IPCLs, which were adopted from a case report the year before [32]. In addition, they reported fluorescein leakage as another criterion for SCC diagnosis [31].

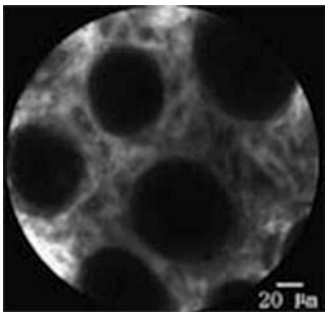
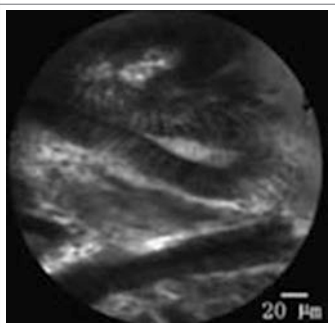
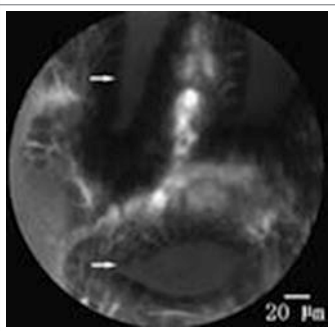
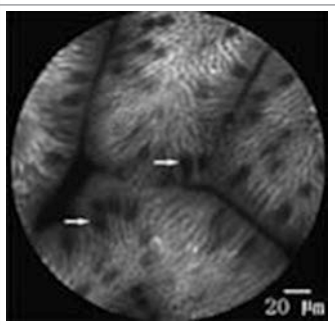
In the same year, a Chinese team proposed another criterion for SCC diagnosis by comparing the different eCLE images between 27 pathology-confirmed SCC cases and 30 normal controls. The significant findings were as follows: (1) irregular cell arrangement, (2) IPCL diameter $\geq$ 22.9 μ, and (3) irregular-shaped IPCLs [33]. In 2015, our group [34] adopted these eCLE criteria [31, 33] to evaluate the value of pCLE in diagnosing early SCC in 44 asymptomatic patients with well-controlled previous head and neck cancer. We compared the diagnostic value of pCLE with dual-focus narrow-band imaging (dNBI) on the Lugol's voiding areas larger than 5 mm. Histology from a targeted biopsy was used as the gold standard. The pCLE vs. dNBI readings revealed 83% vs. 85% sensitivity, 92% vs. 62% specificity, 83% vs. 54% NPV, 92% vs. 89% PPV, and 89% vs. 70% accuracy in diagnosing early SCC on Lugol's voiding areas [34]. The inferior results by dNBI have been speculated from the interference of residual Lugol's stain over the abnormal esophageal mucosa.

Stomach

Gastric Cancer and Premalignant Conditions

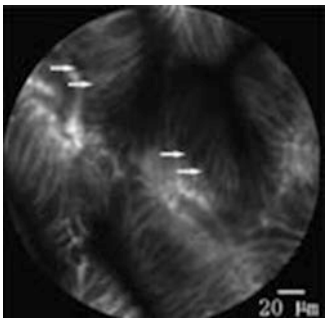
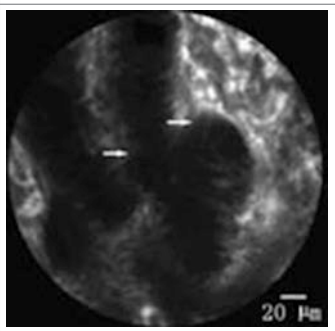
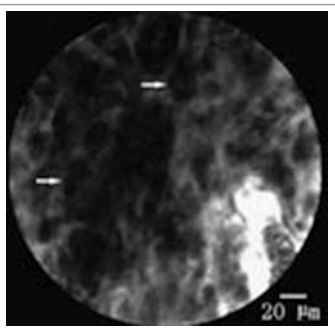
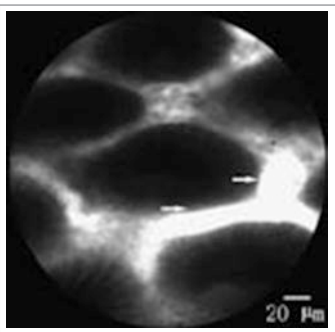
The confocal laser endomicroscopy imaging criteria for early gastric cancer (EGC) detection have not been standardized because nonstructural mitotic glands of the stomach are difficult to recognize. However, the largest eCLE study by Li WB et al. reported a higher accuracy for the diagnosis of gastric superficial cancer/HGIN lesions than that of WLE (98.8% vs. 94.1%) [35]. The simplified two-tiered eCLE classification of noncancerous lesions and EGC/HGIN lesions were based on the architecture (irregularity in glandular size and shape; disorganized or destroyed pits and glands) and the cell characteristics (irregular cells with disordered appearance; severe stratification; loss of cell polarity) as features of gastric cancer lesions [35]. However, the interobserver agreement for EGC reading using eCLE was not reported.

Table 10.2 pCLE classification of gastric pit patterns and vessel architecture

Categories	pCLE appearance	pCLE images[a]	Correlated histology
Gastric pit patterns			
Type 1	Regular pit with wide/round/ slit-like opening		Normal at cardia/corpus/ antrum
Type 2a	Regular pits with elongated openings, increased fluorescein in stroma		Inflammatory gastric mucosa
Type 2b	Reduced pits with dilated openings		Atrophic mucosa
Type 2c	Appearance of goblet cells with dark mucin		Intestinal metaplastic mucosa

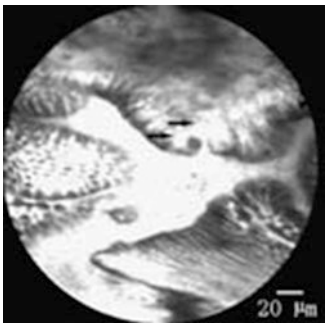
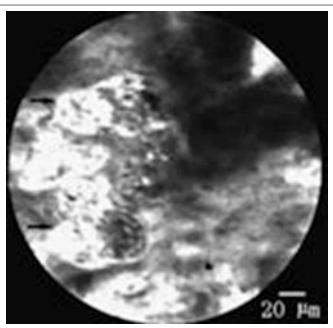
(continued)

Table 10.2 (continued)

Categories	pCLE appearance	pCLE images[a]	Correlated histology
Type 3a	Mild to moderate irregular pits with variable epithelial lining width		Low-grade intraepithelial neoplasia
Type 3b	Prominent distorted pits with irregular epithelial lining		High-grade intraepithelial neoplasia
Type 3c	Appearance of atypical glands/ dispersion of irregular dark cells		Adenocarcinoma
Vessel patterns			
Type 1	Regular capillaries with normal caliber, anfractuous/honeycomb-like/ coil shape		Normal, cardia/corpus/ antrum

(continued)

Table 10.2 (continued)

Categories	pCLE appearance	pCLE images[a]	Correlated histology
Type 2	Increased capillaries with elevated leakage		Inflammatory gastric mucosa
Type 3	Irregular capillaries with heterogeneous leakage/dilated caliber		Neoplastic gastric mucosa

[a]Copyright permission from Wolters Kluwer Health, Inc., License Number: 3802490762895

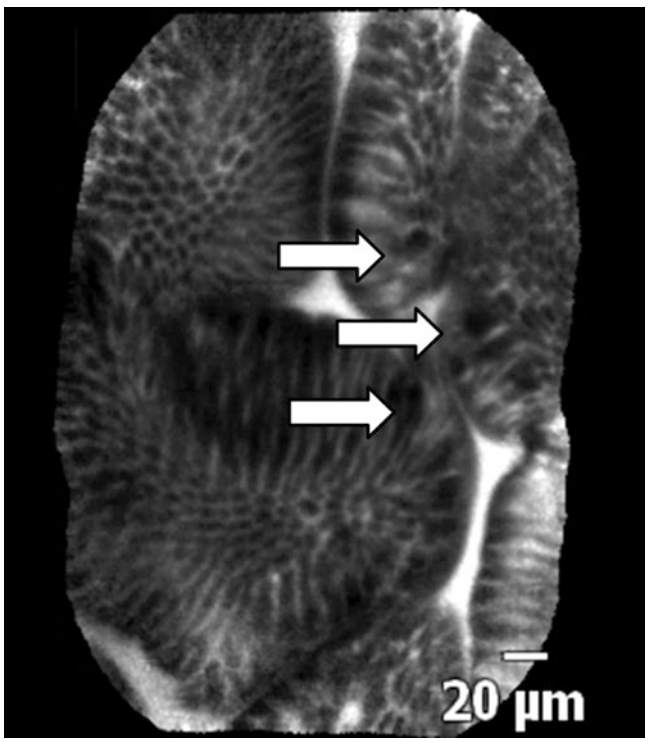


Fig. 10.6 GIM from pCLE image (mucin-containing goblet cells; *arrow*)

In 2016, Li, Z et al. reported a new classification for gastric pit patterns and vessel architecture using pCLE [36]. They reviewed 291 pCLE videos from 32 patients to establish the criteria and then validated these criteria in 240 patients. The criteria contained three types of gastric pit patterns and vessel architecture (Table 10.2). This study demonstrated substantial interobserver agreement regarding gastric pit (kappa = 0.63) and vascular patterns (kappa = 0.64) with excellent intraobserver agreement in both categories (mean kappa = 0.90 and 0.94) [36].

In contrast, there are more studies available on precancerous gastric cancer lesions, especially gastric intestinal metaplasia (GIM), because it is readily recognizable with CLE by demonstrating mucin-containing goblet cells (Fig. 10.6). Many studies have demonstrated good or excellent validity scores for both eCLE [36–39] and pCLE [40, 41] in diagnosing GIM. However, the limitation of current technology is the inability of CLE to distinguish between mature and immature GIMs [39, 40]. This is very important because the risk of gastric cancer in a patient with immature GIM is much higher than a patient with mature GIM [42, 43].

In the authors' opinion, confocal laser endomicroscopy for GIM detection during routine work is more practical because the goblet cell is easy to detect by non-experts and requires only a short learning curve for training [44].

Small Bowel

Celiac Disease

In 2008, the first celiac disease study using eCLE reported a 92% sensitivity and 97% specificity for villous atrophy (the presence of five or fewer blunt-shaped villi seen on superficial scan) and crypt hypertrophy (one or more crypts one

deep scan) criteria [45]. Then, Gunther et al. revealed that eCLE has a correlation with histology in terms of an increased number of intraepithelial lymphocytes (IELs) and villous atrophy assessment but not crypt hyperplasia [46]. Recently, Pohl et al. [47] used pCLE to identify active celiac disease and found that villous atrophy and irregular appearing villi were most predictive of celiac pathology but with poor interobserver agreement (kappa = 0.05–0.26). Unfortunately, IELs and brush boarders cannot be recognized on pCLE due to its lower resolution when compared to eCLE.

In the future, we expect to see more reliable criterion for diagnosing celiac disease using pCLE.

Periampullary Adenoma

Only two pCLE studies demonstrated the efficacy in duodenal and/or ampullary adenoma diagnosis [48, 49]. The results of both studies showed the same trend of insignificant difference when pCLE was used to diagnose duodenal [48, 49] or ampullary [49] adenoma compared to NBI, which already has a high diagnostic yield. For instance, dual-focus NBI (GIF-HQ 190) and pCLE can provide excellent accuracy with 92% and 88%, respectively, for both duodenal and ampullary adenoma diagnosis [49], whereas non-zoom NBI (GIF-H 180) and pCLE were 80% and 83%, respectively, for duodenal adenoma diagnosis [48]. However, NBI plus pCLE in duodenal adenoma can enhance the accuracy to 92% [48]. In our opinion, pCLE may add some benefit on non-magnified NBI in duodenal adenoma diagnoses but not on magnified NBI.

Colon

Inflammatory Bowel Disease (IBD)

Klesslich et al. [50] first reported a 4.75-fold neoplastic detection rate using methylene blue-guided eCLE compared with standard colonoscopy and random biopsy in ulcerative colitis (UC) patients. The authors concluded that chromoscopy-guided eCLE may lead to significant improvements in the clinical management of UC. Furthermore, pCLE can be used to identify disease activity in Crohn's disease [51] and UC [52]. Neumann et al. proposed a specific score, the Crohn's Disease Endomicroscopic Activity Score (CDEAS), to assess CD activity during colonoscopy with pCLE. The CDEAS included six parameters to discriminate active vs. inactive CD as follows: (1) crypt number (increased or decreased, (2) crypt distortion, (3) microerosions, (4) cellular infiltrate, (5) presence of vasculature, and (6) number of goblet cells (increased or decreased) (Fig. 10.7). By assigning one point for each given parameter, the score ranged from 0 to 8. They found that a median CDEAS of 2 was compatible with quiescent CD, and 5 represented active CD [51]. Moreover, pCLE can redefine the term "mucosal healing" in vivo because it shows evidence of residual cellular inflammation by using increased epithelial gap density as a surrogate marker [53, 54]. Two studies evaluated the terminal ileum of IBD patients using pCLE and found that epithelial gap density was significantly increased in IBD patients compared to controls [53, 54].

From the recent consensus in pCLE and gastrointestinal applications published in 2015 [30], CLE is recommended for use in targeted biopsies during surveillance of colorectal cancer in IBD patients, with the goal of replacing random four-quadrant biopsies. Hypothetically, the targeted biopsy may improve the yield of colonoscopy and decrease the number of histological examinations [30].

Recently pCLE has played an additional role in monitoring disease activity and predicting the response to antitumor necrosis factor (anti-TNF) antibody in IBD patients. In this capacity, pCLE was used to detect the membrane-bound TNF (mTNF) after spraying topical fluorescent antibody. It has been reported that a patient with a high number of mTNF ($\geq$ 20 cells per confocal image) had higher response rates at week 12 after anti-TNF therapy when compared with those who had low mTNF values (< 20 cells per confocal image). In addition, the clinical response was sustained during a year of follow-up and also correlated with mucosal healing in follow-up endoscopy [55]. However, the use of CLE to customize management of IBD is still limited to research and is not yet used in clinical practice [30].

A recent systematic review did not recommend the use of CLE for standard clinical practice in IBD patients due to great heterogeneity in the literature. Further, no single approach has been validated and reproduced to the level of general acceptance. Currently, confocal laser endomicroscopy remains experimental, but it is the only method that demonstrates in vivo intestinal barrier function [56].

Colonic Polyp

The American Society of Gastrointestinal Endoscopy (ASGE) proposed the Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) initiative for colonic adenoma diagnosis and recommended at least 90% accuracy to exclude the possibility of adenomatous histology of the polyp and predicting surveillance interval [57]. Under this recommendation, confocal laser endomicroscopy will predict the pathology of colonic polyps using the term "resect and discard" for small adenoma $\leq$5 mm or "diagnose and leave behind" for small distal hyperplastic polyps [58]. From a recent study, pCLE achieved 95% accuracy in predicting neoplastic change colonic polyps when combined with digital chromoendoscopy [59, 60]. However, these studies were conducted on small polyps (less than 10 mm). Therefore, this practice is recommended only for small polyps. A complete examination of a large polyp is impractical due to the risk of missing important pathology. Logically, all large polyps require endoscopic resection regardless of their size [57].

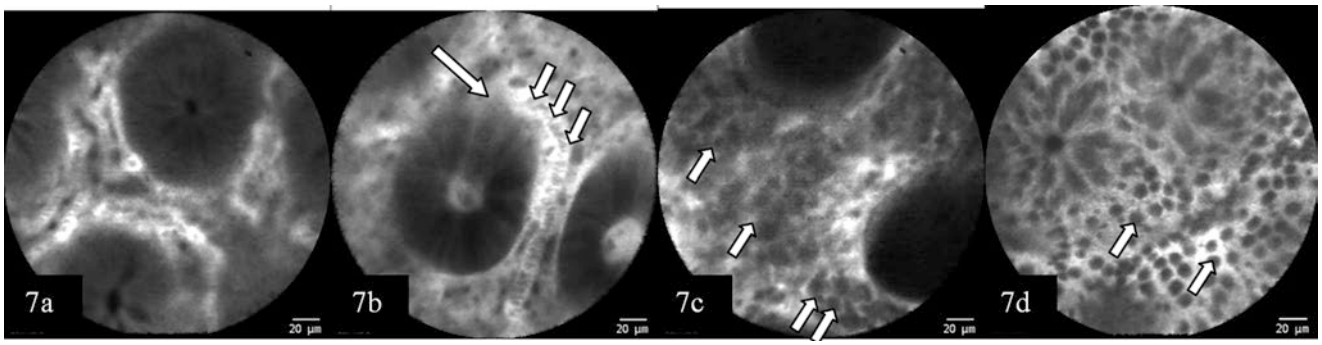
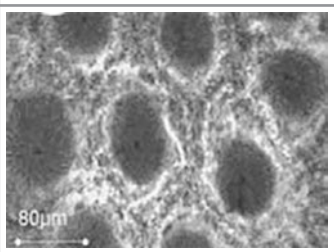
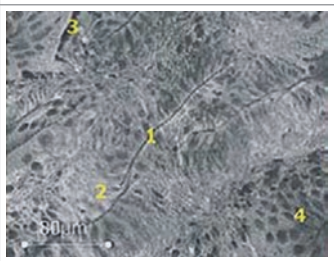
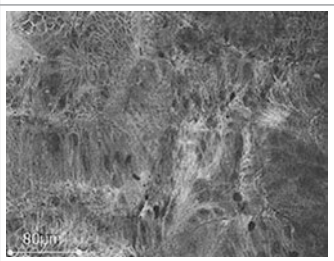


Fig. 10.7 Images of CDEAS by pCLE (**a**) normal (**b**) crypt erosion (*long arrow*) with presence of vasculature (*short arrows*) (**c**) cellular infiltration (*short arrows*) (**d**) increased number of goblet cells (*small black dots*; *short arrows*) (All pictures are provided courtesy of Professor Helmut Neumann, the Interdisciplinary Endoscopy Center, University Medical Center Mainz, Germany)

Table 10.3 Confocal laser endomicroscopy pattern for predicting colonic polyp pathology

Grading	Vascular architecture	Crypt architecture	[a]eCLE
Normal	Hexagonal, honeycomb appearance that presents a network of capillaries outlining the stroma surrounding the luminal openings of the crypts	Regular luminal openings and distribution of the crypts covered by a homogeneous layer of epithelial cells, including goblet cells	
Regeneration (hyperplasia/ inflammation)	Hexagonal, honeycomb appearance with no or mild increase in the number of capillaries	Star-shaped luminal crypt openings [1] or focal aggregation of regular-shaped crypts [4] or loss of cellular junction [3] with a regular or reduced number of goblet cells [2]	
Neoplasia	Dilated and distorted vessels with elevated leakage; irregular architecture with little or no orientation to adjunct tissue	Ridged-lined irregular epithelial layer with loss of crypts and goblet cells; irregular cell architecture with little or no mucin	

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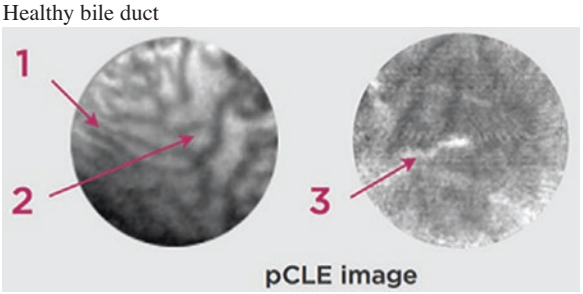
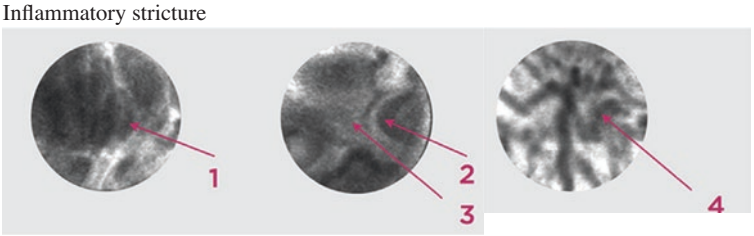
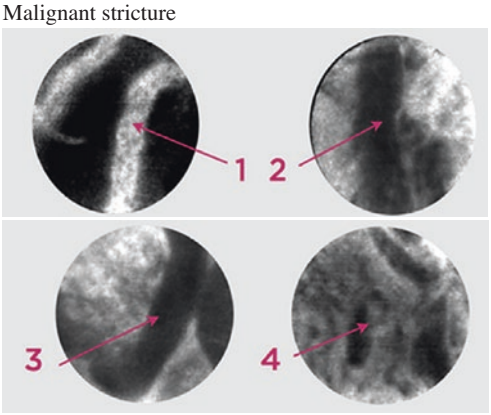
All criteria to diagnose adenomatous colonic polyps in recent studies of pCLE were adopted from the eCLE pilot study [1] (Table 10.3). The learning curve for pCLE use in colorectal neoplasia detection was acceptable and practical. The overall accuracy was reported as 63% during the first examination, and this figure improved to 86% during the last session (fourth session) [61].

From the meta-analysis in 2013, the overall sensitivity of CLE in colonic adenoma diagnosis was 93%, specificity was 90%, and the real-time negative predictive value (NPV) was

Table 10.4 "Paris criteria" from pCLE for indeterminate biliary stricture diagnosis

Diagnosis with images[a]	Criteria	Assumed pathology
Healthy bile duct 	1. Reticular network of thin dark branching bands (<20 μm)	1. Thin collagen bundle
	2. Light gray background	2. Lymphatic sinuses
	3. Vessels (<20 μm)	3. Vessels
Inflammatory stricture 	1. Multiple white bands	1. Vessels
	2. Dark granular pattern in scales	2. N/A
	3. Enlarged space between scales	3. N/A
	4. Thickened reticular structures	4.N/A
Malignant stricture 	1. Thick white bands (>20 μm)	1. Vessels
	2. Thick dark bands (>40 μm)	2. Bundles with increased diameter
	3. Epithelium	3. Epithelium
	4. Dark clumps	4. N/A

Modified from Caillol et al. [66]
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94% [62]. The authors concluded that CLE can be used by well-trained endoscopists but needed additional training to achieve an excellent NPV [62].

Biliary Tract

Indeterminate Biliary Stricture

pCLE can improve the sensitivity of cholangiocarcinoma diagnosis considerably from 50% to 83% by using the presence of irregular vessel criteria when compared to direct cholangioscopy plus histopathology [63]. Recently, the Miami criterion was developed and applied in a multicenter study to demonstrate 81% accuracy, 98% sensitivity, 67% specificity, 71% PPV, and 97% NPV for the diagnosis of malignant change in the bile duct [64]. The low specificity in this study came from the high number of false-positive readings in strictures affected by inflammation, i.e., active cholangitis and post-stenting. Therefore, the criteria are now modified and published as the "Paris criteria" by adding the criteria for inflammatory strictures (Table 10.4) [65]. These new criteria have been validated and demonstrated marginal improvement over the previous criteria with 82% accuracy, 89% sensitivity, 71% specificity, 84% PPV, and 78% NPV for the diagnosis of malignant stricture using pathology from targeted biopsies and clinical of patient as a gold standard [66]. The authors

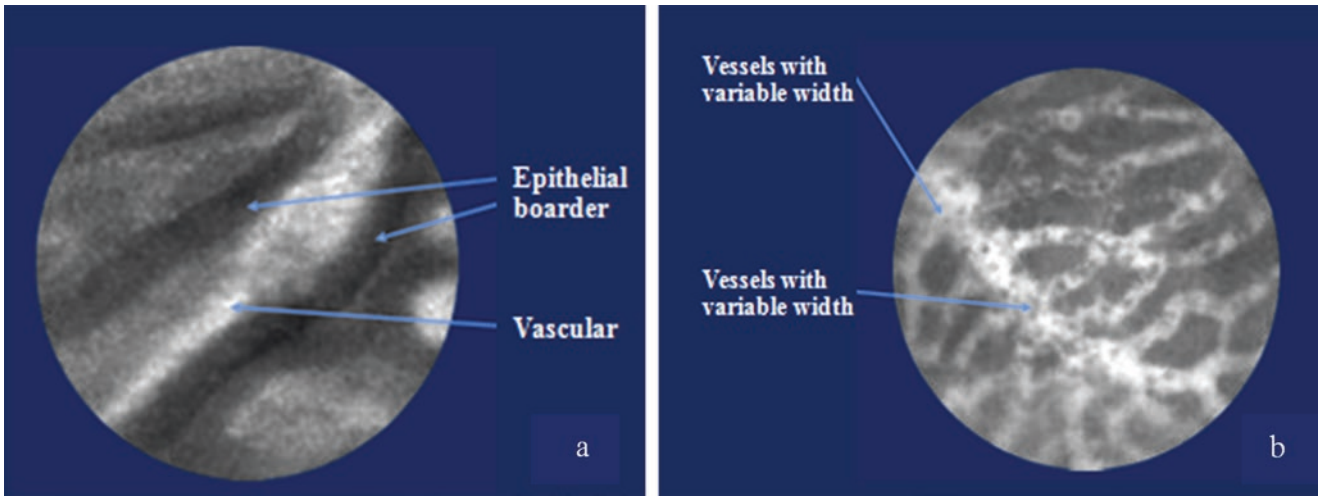

Fig. 10.8 Images of cystic pancreatic lesion by nCLE, villous structure epithelium in (**a**) of intraductal papillary mucinous neoplasm (IPMN) superficial vascular network (**b**) of serous cystadenoma. (**a** Copyright permission from Thieme, License Number: 4093691020842. **b** Copyright permission from ELSEVIER, License Number: 4093690233254)

concluded that pCLE likely provides an accurate assessment by providing a real-time diagnosis and may reduce delayed diagnosis/costly repeat tests due to multiple inconclusive pathologies from the blind biopsy [67].

Additionally, the 2011 guideline for management of patients with biliary neoplasia was developed before the validation of the Paris criteria and stated that pCLE appears to play a useful role in differentiating nonmalignant from malignant biliary strictures, but more validated data are needed to recommend this in daily practice [17].

Pancreas

Pancreatic Cyst

There have been a few studies on the use of nCLE as a real-time diagnostic tool for pancreatic cystic lesions. The first study (INSPECT study) proposed a high potential criterion called "villous structure epithelium" to diagnose pancreatic cystic neoplasm (intraductal papillary mucinous neoplasm (IPMN), mucinous cystic adenoma, or adenocarcinoma). The villous structure is composed of fingerlike papillary projections (Fig. 10.8a), dark rings with a white core, and a crypt-like structure with a perfect specificity and PPV at 100%. However, the sensitivity and NPV were only 59% and 50%, respectively [67]. The other study was conducted in serous cystadenomas (SCA), which are benign lesions. To diagnose serous cystadenoma, superficial vascular network pattern criteria (Fig. 10.8b) form nCLE and corresponded well with a pathological specimen of dense subepithelial capillary lining in pathology with 100% specificity and PPV and acceptable sensitivity, PPV, and accuracy at 69%, 82%, and 87%, respectively [68].

Pancreatic Mass

To date, there have only been a handful of studies assessing pCLE in solid pancreatic lesions. Giovannini et al. conducted a feasibility trial of nCLE in three pancreatic cancer patients and diagnosed pancreatic malignancy using the following

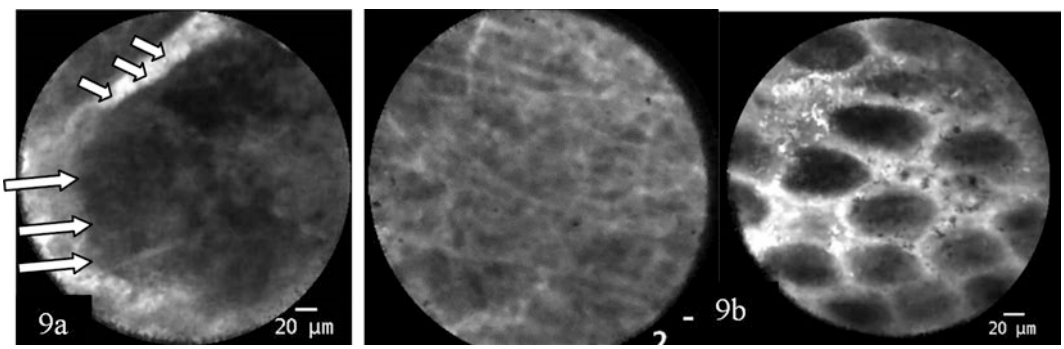

Fig. 10.9 Images of malignant (**a**) and benign (**b**) solid pancreatic masses using nCLE. (**a**) Dark clumping (*short arrow*) with dilated vessel (*long arrow*) (**b**) (*left*) *white* fibrous band, (*right*) normal acini cells

Table 10.5 The summarized confocal laser endomicroscopy evidences in GI disease

Strong evidence for conclusion	More studies in progress	Insufficient data
Barrett's esophagus	Gastric cancer	Reflux esophagitis
Gastric intestinal metaplasia	Squamous cell cancer of esophagus	Celiac disease
Colonic polyp	Anti-TNF response in IBD	Periampullary adenoma
	Cystic pancreatic mass	
	Solid pancreatic mass	
	Targeted biopsy for dysplastic change in IBD	
	Indeterminate biliary stricture	

criteria: large dark clumps (aggregates of malignant cells) and fluorescein leakage [69]. Currently, a multicenter study to further validate these criteria is being conducted (CONTACT study) by the same group [69].

A recent pilot study of solid pancreatic lesion (ENES study) by our group proposed two criteria to diagnose pancreatic malignancy, including dark clumping (>40 μm) and dilated vessels (>20 μm) (Fig. 10.9a), and two criteria to diagnose benign lesions, including white fibrous bands and normal acini cell (Fig. 10.9b). Our preliminary results showed a high accuracy for solid pancreatic mass diagnosis at 90% [70].

Practical Considerations

- The indications for confocal laser endomicroscopy are still limited. The potential indications are:
  1. Targeted biopsy of suspicious malignant or premalignant lesions during endoscopic surveillance in high-risk population
  2. Differentiate malignant from nonmalignant lesion in spotted lesion
  3. Real-time diagnosis for an immediate endoscopic management
  4. Predicting treatment response to biologic or target chemotherapy with the specific antibody-tagged fluorescein

Complications

The adverse effects of confocal laser endomicroscopy are mainly allergic reactions to fluorescein. However, no serious side effects have been reported in humans. Mild adverse events with spontaneous recovery occurred in 1.4% of all cases, and these included nausea/vomiting, diffuse rash, injection site erythema, mild epigastric pain, and transient hypotension [13].

In addition, acute pancreatitis after EUS and nCLE puncture may develop. The incidence of pancreatitis in this procedure was approximately 3% [67, 68]. Moreover, 4% of subjects experienced mild intralesional bleeding, which spontaneously resolved without the need for additional treatment [67].

With the concern of tumor seeding in suspicious pancreatic malignancy, all available studies enrolled only unresectable solid pancreatic mass for evaluation [69, 70]. Due to the anecdotal fear of tumor seeding, we do not recommend nCLE examination in patients with a resectable pancreatic mass.

Practical Considerations

- Fluorescein has only mild adverse events which can resolve spontaneously.
- Pancreatitis and bleeding are the potential complications of pancreatic examination by nCLE.
- Do not recommend nCLE examination in resectable pancreatic mass due to anecdotal fear of tumor seeding unless duodenal access is possible (D1–D2).

Conclusions

Confocal laser endomicroscopy is the latest evolution of endoscopy practice. Without the need for biopsy, CLE can provide real-time confirmation of many precancerous lesions, such as Barrett's esophagus, GIM, and colonic polyps. In contrast, the use of CLE for other malignancy detection is still limited to expert centers due to suboptimal criteria validity; therefore, it is still not practical for day-to-day practice (Table 10.5).

Final Words

CLE is proposed as a real-time diagnosis tool during endoscopy in certain pathologies, such as Barrett's esophagus, gastric intestinal metaplasia, and colonic adenoma; however, it is still impractical but promising to use in other GI diseases, and these need additional studies to validate and simplify the proposed criteria.

References

1. Kiesslich R, Burg J, Vieth M, Gnaendiger J, Enders M, Delaney P. Confocal laser endoscopy for diagnosing intraepithelial neoplasias and colorectal cancer in vivo. Gastroenterology. 2004;127:706–13.
2. Meining A. Confocal endomicroscopy. Gastrointest Endosc Clin N Am. 2009;19(4):629–35.
3. Polglase AL, McLaren WJ, Skinner SA, Kiesslich R, Neurath MF, Delaney PM. A fluorescence confocal endomicroscope for in vivo microscopy of the upper- and the lower-GI tract. Gastrointest Endosc. 2005;62(5):686–95.
4. Kakeji Y, Yamaguchi S, Yoshida D, Tanoue K, Ueda M, Masunari A, et al. Development and assessment of morphologic criteria for diagnosing gastric cancer using confocal endomicroscopy: an ex vivo and in vivo study. Endoscopy. 2006;38(9):886–90.
5. Kitabatake S, Niwa Y, Miyahara R, Ohashi A, Matsuura T, Iguchi Y, et al. Confocal endomicroscopy for the diagnosis of gastric cancer in vivo. Endoscopy. 2006;38(11):1110–4.
6. Hoffman A, Goetz M, Vieth M, Galle PR, Neurath MF, Kiesslich R. Confocal laser endomicroscopy: technical status and current indications. Endoscopy. 2006;38(12):1275–83.
7. Nguyen NQ, Leong RW. Current application of confocal endomicroscopy in gastrointestinal disorders. J Gastroenterol Hepatol. 2008;23(10):1483–91.
8. Committee AT. Confocal laser endomicroscopy. Gastrointest Endosc. 2014;80(6):928–38.
9. Giovannini M. Needle-based confocal laser endomicroscopy. Endosc Ultrasound. 2015;4(4):284–8.
10. Shahid MW, Crook JE, Meining A, Perchant A, Buchner A, Gomez V, et al. Exploring the optimal fluorescein dose in probe-based confocal laser endomicroscopy for colonic imaging. J Interv Gastroenterol. 2011;1(4):166–71.
11. Becker V, von Delius S, Bajbouj M, Karagianni A, Schmid RM, Meining A. Intravenous application of fluorescein for confocal laser scanning microscopy: evaluation of contrast dynamics and image quality with increasing injection-to-imaging time. Gastrointest Endosc. 2008;68(2):319–23.
12. Dunbar KB, Okolo P 3rd, Montgomery E, Canto MI. Confocal laser endomicroscopy in Barrett's esophagus and endoscopically inapparent Barrett's neoplasia: a prospective, randomized, double-blind, controlled, crossover trial. Gastrointest Endosc. 2009;70(4):645–54.
13. Wallace MB, Meining A, Canto MI, Fockens P, Miehlke S, Roesch T, et al. The safety of intravenous fluorescein for confocal laser endomicroscopy in the gastrointestinal tract. Aliment Pharmacol Ther. 2010;31(5):548–52.
14. Obstoy B, Salaun M, Veresezan L, Sesboue R, Bohn P, Boland FX, et al. Safety and performance analysis of acriflavine and methylene blue for in vivo imaging of precancerous lesions using fibered confocal fluorescence microscopy (FCFM): an experimental study. BMC Pulm Med. 2015;15:30.
15. Bisschops R, Bergman J. Probe-based confocal laser endomicroscopy: scientific toy or clinical tool? Endoscopy. 2010;42(6):487–9.
16. Wang KK, Sampliner RE. Practice Parameters Committee of the American College of G. Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett's esophagus. Am J Gastroenterol. 2008;103(3):788–97.
17. American Society for Gastrointestinal Endoscopy Standards of Practice C, Anderson MA, Appalaneni V, Ben-Menachem T, Decker GA, Early DS, et al. The role of endoscopy in the evaluation and treatment of patients with biliary neoplasia. Gastrointest Endosc. 2013;77(2):167–74.
18. Tanaka M, Fernandez-del Castillo C, Adsay V, Chari S, Falconi M, Jang JY, et al. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatol Off J Int Assoc Pancreatol. 2012;12(3):183–97.
19. Sharma P, Brill J, Canto M, DeMarco D, Fennerty B, Gupta N, et al. White paper AGA: advanced imaging in Barrett's esophagus. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2015;13(13):2209–18.
20. Lee SK. Usefulness and future prospects of confocal laser endomicroscopy for gastric premalignant and malignant lesions. Clin Endosc. 2015;48(6):511–5.
21. Chu CL, Zhen YB, Lv GP, Li CQ, Li Z, Qi QQ, et al. Microalterations of esophagus in patients with non-erosive reflux disease: in-vivo diagnosis by confocal laser endomicroscopy and its relationship with gastroesophageal reflux. Am J Gastroenterol. 2012;107(6):864–74.
22. Venkatesh K, Cohen M, Abou-Taleb A, Thomas S, Taylor C, Thomson M. A new method in the diagnosis of reflux esophagitis: confocal laser endomicroscopy. Gastrointest Endosc. 2012;75(4):864–9.
23. Pittayanon R, Aumkaew S, Rerknimitr R, Wisedopas N, Kullavanijaya P. Flexible spectral imaging color enhancement and probe-based confocal laser endomicroscopy in minimal change esophageal reflux disease. Korean J Gastroenterol. 2016;68(1):29–35.
24. Kiesslich R, Gossner L, Goetz M, Dahlmann A, Vieth M, Stolte M, et al. In vivo histology of Barrett's esophagus and associated neoplasia by confocal laser endomicroscopy. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2006;4(8):979–87.
25. Dunbar KB, Canto MI. Confocal laser endomicroscopy in Barrett's esophagus and endoscopically inapparent Barrett's neoplasia: a prospective, randomized, double-blind, controlled, crossover trial. Gastrointest Endosc. 2010;72(3):668.
26. Pohl H, Rosch T, Vieth M, Koch M, Becker V, Anders M, et al. Miniprobe confocal laser microscopy for the detection of invisible neoplasia in patients with Barrett's oesophagus. Gut. 2008;57(12):1648–53.
27. Wallace MB, Sharma P, Lightdale C, Wolfsen H, Coron E, Buchner A, et al. Preliminary accuracy and interobserver agreement for the detection of intraepithelial neoplasia in Barrett's esophagus with probe-based confocal laser endomicroscopy. Gastrointest Endosc. 2010;72(1):19–24.
28. Gaddam S, Mathur SC, Singh M, Arora J, Wani SB, Gupta N, et al. Novel probe-based confocal laser endomicroscopy criteria and interobserver agreement for the detection of dysplasia in Barrett's esophagus. Am J Gastroenterol. 2011;106(11):1961–9.
29. Sharma P, Meining AR, Coron E, Lightdale CJ, Wolfsen HC, Bansal A, et al. Real-time increased detection of neoplastic tissue in Barrett's esophagus with probe-based confocal laser endomicroscopy: final results of an international multicenter, prospective, randomized, controlled trial. Gastrointest Endosc. 2011;74(3):465–72.
30. Wang KK, Carr-Locke DL, Singh SK, Neumann H, Bertani H, Galmiche JP, et al. Use of probe-based confocal laser endomicroscopy (pCLE) in gastrointestinal applications. A consensus report based on clinical evidence. United European Gastroenterol J. 2015;3(3):230–54.
31. Pech O, Rabenstein T, Manner H, Petrone MC, Pohl J, Vieth M, et al. Confocal laser endomicroscopy for in vivo diagnosis of early squamous cell carcinoma in the esophagus. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2008;6(1):89–94.
32. Deinert K, Kiesslich R, Vieth M, Neurath MF, Neuhaus H. In-vivo microvascular imaging of early squamous-cell cancer of the esophagus by confocal laser endomicroscopy. Endoscopy. 2007;39(4):366–8.
33. Liu H, Li YQ, Yu T, Zhao YA, Zhang JP, Zuo XL, et al. Confocal laser endomicroscopy for superficial esophageal squamous cell carcinoma. Endoscopy. 2009;41(2):99–106.

34. Prueksapanich P, Pittayanon R, Rerknimitr R, Wisedopas N, Kullavanijaya P. Value of probe-based confocal laser endomicroscopy (pCLE) and dual focus narrow-band imaging (dNBI) in diagnosing early squamous cell neoplasms in esophageal Lugol's voiding lesions. Endosc Int Open. 2015;3(4):E281–8.
35. Li WB, Zuo XL, Li CQ, Zuo F, Gu XM, Yu T, et al. Diagnostic value of confocal laser endomicroscopy for gastric superficial cancerous lesions. Gut. 2011;60(3):299–306.
36. Li Z, Zuo XL, Li CQ, Liu ZY, Ji R, Liu J, et al. New classification of gastric pit patterns and vessel architecture using probe-based confocal laser endomicroscopy. J Clin Gastroenterol. 2016;50(1):23–32.
37. Li Z, Zuo XL, Yu T, Gu XM, Zhou CJ, Li CQ, et al. Confocal laser endomicroscopy for in vivo detection of gastric intestinal metaplasia: a randomized controlled trial. Endoscopy. 2014;46(4):282–90.
38. Liu T, Zheng H, Gong W, Chen C, Jiang B. The accuracy of confocal laser endomicroscopy, narrow band imaging, and chromoendoscopy for the detection of atrophic gastritis. J Clin Gastroenterol. 2015;49(5):379–86.
39. Guo YT, Li YQ, Yu T, Zhang TG, Zhang JN, Liu H, et al. Diagnosis of gastric intestinal metaplasia with confocal laser endomicroscopy in vivo: a prospective study. Endoscopy. 2008;40(7):547–53.
40. Pittayanon R, Rerknimitr R, Wisedopas N, Ridtitid W, Kongkam P, Treeprasertsuk S, et al. Flexible spectral imaging color enhancement plus probe-based confocal laser endomicroscopy for gastric intestinal metaplasia detection. J Gastroenterol Hepatol. 2013;28(6):1004–9.
41. Lim LG, Yeoh KG, Srivastava S, Chan YH, Teh M, Ho KY. Comparison of probe-based confocal endomicroscopy with virtual chromoendoscopy and white-light endoscopy for diagnosis of gastric intestinal metaplasia. Surg Endosc. 2013;27(12):4649–55.
42. Correa P, Piazuelo MB, Wilson KT. Pathology of gastric intestinal metaplasia: clinical implications. Am J Gastroenterol. 2010;105(3):493–8.
43. Rokkas T, Filipe MI, Sladen GE. Detection of an increased incidence of early gastric cancer in patients with intestinal metaplasia type III who are closely followed up. Gut. 1991;32(10):1110–3.
44. Pittayanon R, Rerknimitr R, Wisedopas N, Khemnark S, Thanapirom K, Thienchanachaiya P, et al. The learning curve of gastric intestinal metaplasia interpretation on the images obtained by probe-based confocal laser endomicroscopy. Diagn Ther Endoscopy. 2012;2012:278045.
45. Leong RW, Nguyen NQ, Meredith CG, Al-Sohaily S, Kukic D, Delaney PM, et al. In vivo confocal endomicroscopy in the diagnosis and evaluation of celiac disease. Gastroenterology. 2008;135(6):1870–6.
46. Gunther U, Daum S, Heller F, Schumann M, Loddenkemper C, Grunbaum M, et al. Diagnostic value of confocal endomicroscopy in celiac disease. Endoscopy. 2010;42(3):197–202.
47. Pohl H, Tanczos BT, Rudolph B, Meining A, Khalifa AC, Rosch T, et al. Probe-based confocal laser microscopy identifies criteria predictive of active celiac sprue. Dig Dis Sci. 2012;57(2):451–7.
48. Shahid MW, Buchner A, Gomez V, Krishna M, Woodward TA, Raimondo M, et al. Diagnostic accuracy of probe-based confocal laser endomicroscopy and narrow band imaging in detection of dysplasia in duodenal polyps. J Clin Gastroenterol. 2012;46(5):382–9.
49. Pittayanon R, Rerknimitr R, Imraporn B, Wisedopas N, Kullavanijaya P. Diagnostic values of dual focus narrow band imaging and probe-based confocal laser endomicroscopy in FAP-related duodenal adenoma. Endoscopy Int Open. 2015;3(5):E450–5.
50. Kiesslich R, Goetz M, Lammersdorf K, Schneider C, Burg J, Stolte M, et al. Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. Gastroenterology. 2007;132(3):874–82.
51. Neumann H, Vieth M, Atreya R, Grauer M, Siebler J, Bernatik T, et al. Assessment of Crohn's disease activity by confocal laser endomicroscopy. Inflamm Bowel Dis. 2012;18(12):2261–9.
52. Li CQ, Xie XJ, Yu T, Gu XM, Zuo XL, Zhou CJ, et al. Classification of inflammation activity in ulcerative colitis by confocal laser endomicroscopy. Am J Gastroenterol. 2010;105(6):1391–6.
53. Liu JJ, Wong K, Thiesen AL, Mah SJ, Dieleman LA, Claggett B, et al. Increased epithelial gaps in the small intestines of patients with inflammatory bowel disease: density matters. Gastrointest Endosc. 2011;73(6):1174–80.
54. Turcotte JF, Wong K, Mah SJ, Dieleman LA, Kao D, Kroeker K, et al. Increased epithelial gaps in the small intestine are predictive of hospitalization and surgery in patients with inflammatory bowel disease. Clin Transl Gastroenterol. 2012;3:e19.
55. Atreya R, Neumann H, Neufert C, Waldner MJ, Billmeier U, Zopf Y, et al. In vivo imaging using fluorescent antibodies to tumor necrosis factor predicts therapeutic response in Crohn's disease. Nat Med. 2014;20(3):313–8.
56. Rasmussen DN, Karstensen JG, Riis LB, Brynskov J, Vilmann P. Confocal laser endomicroscopy in inflammatory bowel disease – a systematic review. J Crohns Colitis. 2015;9(12):1152–9.
57. Rex DK, Kahi C, O'Brien M, Levin TR, Pohl H, Rastogi A, et al. The American society for gastrointestinal endoscopy PIVI (Preservation and incorporation of valuable endoscopic innovations) on real-time endoscopic assessment of the histology of diminutive colorectal polyps. Gastrointest Endosc. 2011;73(3):419–22.
58. Sharma P, Gupta N, Kuipers EJ, Repici A, Wallace M. Advanced imaging in colonoscopy and its impact on quality. Gastrointest Endosc. 2014;79(1):28–36.
59. Shahid MW, Buchner AM, Heckman MG, Krishna M, Raimondo M, Woodward T, et al. Diagnostic accuracy of probe-based confocal laser endomicroscopy and narrow band imaging for small colorectal polyps: a feasibility study. Am J Gastroenterol. 2012;107(2):231–9.
60. Buchner AM, Shahid MW, Heckman MG, Krishna M, Ghabril M, Hasan M, et al. Comparison of probe-based confocal laser endomicroscopy with virtual chromoendoscopy for classification of colon polyps. Gastroenterology. 2010;138(3):834–42.
61. Buchner AM, Gomez V, Heckman MG, Shahid MW, Achem S, Gill KR, et al. The learning curve of in vivo probe-based confocal laser endomicroscopy for prediction of colorectal neoplasia. Gastrointest Endosc. 2011;73(3):556–60.
62. Wanders LK, East JE, Uitentuis SE, Leeflang MM, Dekker E. Diagnostic performance of narrowed spectrum endoscopy, autofluorescence imaging, and confocal laser endomicroscopy for optical diagnosis of colonic polyps: a meta-analysis. Lancet Oncol. 2013;14(13):1337–47.
63. Meining A, Frimberger E, Becker V, Von Delius S, Von Weyhern CH, Schmid RM, et al. Detection of cholangiocarcinoma in vivo using miniprobe-based confocal fluorescence microscopy. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2008;6(9):1057–60.
64. Meining A, Chen YK, Pleskow D, Stevens P, Shah RJ, Chuttani R, et al. Direct visualization of indeterminate pancreaticobiliary strictures with probe-based confocal laser endomicroscopy: a multicenter experience. Gastrointest Endosc. 2011;74(5):961–8.
65. Caillol F, Filoche B, Gaidhane M, Kahaleh M. Refined probe-based confocal laser endomicroscopy classification for biliary strictures: the Paris classification. Dig Dis Sci. 2013;58(6):1784–9.
66. Slivka A, Gan I, Jamidar P, Costamagna G, Cesaro P, Giovannini M, et al. Validation of the diagnostic accuracy of probe-based confocal laser endomicroscopy for the characterization of indeterminate biliary strictures: results of a prospective multicenter international study. Gastrointest Endosc. 2015;81(2):282–90.
67. Konda VJ, Meining A, Jamil LH, Giovannini M, Hwang JH, Wallace MB, et al. A pilot study of in vivo identification of pancreatic cystic neoplasms with needle-based confocal laser endomicroscopy under endosonographic guidance. Endoscopy. 2013;45(12):1006–13.
68. Napoleon B, Lemaistre AI, Pujol B, Caillol F, Lucidarme D, Bourdariat R, et al. A novel approach to the diagnosis of pancreatic

serous cystadenoma: needle-based confocal laser endomicroscopy. Endoscopy. 2015;47(1):26–32.
69. Giovannini M, Caillol F, Poizat F, Bories E, Pesenti C, Monges G, et al. Feasibility of intratumoral confocal microscopy under endoscopic ultrasound guidance. Endosc Ultrasound. 2012;1(2):80–3.
70. Kongkam P, Pittayanon R, Sampatanukul P, Angsuwatcharakon P, Aniwan S, Prueksapanich P, et al. Endoscopic ultrasound-guided needle-based confocal laser endomicroscopy for diagnosis of solid pancreatic lesions (ENES): a pilot study. Endosc Int Open. 2016;4(1):E17–23.

Peroral Endoscopic Myotomy (POEM)

11

Davinderbir Pannu, Dennis Yang, and Peter V. Draganov

Introduction

Achalasia is the most common primary esophageal motility disorder. It is characterized by aperistalsis of the esophageal body and incomplete relaxation of the lower esophageal sphincter (LES). The annual incidence of achalasia is reported to be 1/100000 worldwide [1–4]. Although the incidence is low, the chronic and progressive nature of achalasia significantly affects patients' health-related quality of life, work productivity, and functional status compared with the general population [5].

The diagnosis of achalasia requires recognition of symptoms and appropriate use of diagnostic testing. The patient may present with a varying range of symptoms including progressive dysphagia to solids and liquids (90%), heartburn (75%), regurgitation or vomiting (45%), non-cardiac chest pain (20%), epigastric pain (15%), and odynophagia (<5%) [6]. Extra-esophageal manifestations may include cough, asthma, chronic aspiration, and unintentional weight loss [6]. The type and sequence of index diagnostic testing performed often depends on the patient's clinical presentation. Esophagogastroduodenoscopy (EGD) helps rule out structural and mucosal esophageal lesions and, most importantly, malignancy at the gastroesophageal junction (GEJ) or the cardia masquerading as achalasia ("pseudoachalasia"). Findings of achalasia on barium esophagram include the classic "bird's beak appearance" of the GEJ, retention of contrast with air-fluid levels, and/or a dilated tortuous "sigmoid" esophagus. High-resolution manometry (HRM) evaluates the esophageal pressures and contractions along the length of the esophagus and has become the standard for diagnosis of achalasia. HRM is the most sensitive physiologic test for the diagnosis of achalasia, which is established by the impaired relaxation of the LES after swallowing (defined by a residual integrated relaxation pressure of >15 mm Hg) and the absence of propagating peristaltic esophageal contractions [7].

Given the relatively low efficacy and/or durability of pharmacological intervention with injection of *Clostridium botulinum* toxin or oral calcium channel blockers, procedures aiming to permanently disrupt the LES are now considered first-line therapy for achalasia. Until recently, endoscopic pneumatic balloon dilation and laparoscopic Heller myotomy (LHM) were the only available durable options [8, 9].

A novel endoscopic technique for the treatment of achalasia was conceived by Parsricha and colleagues and described in a porcine model in 2007 [10]. The authors demonstrated the feasibility of endoscopic myotomy by directly accessing the esophageal muscular layers through a submucosal tunnel. In 2010, Inoue and colleagues translated this technique into clinical practice and coined the term peroral endoscopic myotomy (POEM) [11]. Since then, there have been multiple studies demonstrating the excellent technical success, short- and mid-term safety, and clinical success of this endoscopic technique for the treatment of achalasia [12, 13].

Indications

Theoretically, all patients with symptomatic achalasia can be treated with POEM (Table 11.1). While this endoscopic technique was initially reserved for the management of non-sigmoid esophagus-type achalasia [10], the application of POEM has now been expanded to certain special cohorts, including patients with previously failed endoscopic therapy (i.e., Botox injection and pneumatic balloon dilation), surgery (Heller myotomy), and even in those with sigmoid and/or massively dilated esophagus. Furthermore, POEM has been successfully performed in patients with anticipated very difficult laparoscopic approach such as prior Roux-en-Y gastric bypass [14]. More recently, POEM has also

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Table 11.1 Indications for POEM

Indications
Treatment naïve achalasia types I, II, and III
Achalasia with previous treatment failure
Achalasia in patient with prior gastric or GEJ surgery
Potential New Indications
Diffuse esophageal spasm
Jackhammer esophagus
GEJ outflow obstruction
Peroral endoscopic tumor resection (POET)
Luminal patency restoration of completely obstructed esophagus (POETRE)
Pyloromyotomy for gastroparesis

been investigated as a treatment modality for difficult to treat spastic esophageal disorders, including type III achalasia, diffuse esophageal spasm, hypercontractile or jackhammer esophagus, and functional GEJ outflow obstruction. While further studies are needed to corroborate the role of POEM in these settings, initial reports on its technical and clinical success (90–100% success) are promising [15–20].

The introduction of POEM in recent years has not only transformed our approach to the management of esophageal motility disorders, but it has also dramatically changed the landscape of interventional endoscopy by solidifying the concept of endoscopic submucosal tunneling. Based on this gained knowledge and familiarity outside of the confines of the luminal GI tract, there has been a widespread interest in further expanding the applications of submucosal tunneling to include other novel techniques, such as peroral endoscopic tumor resection (POET) [21], peroral endoscopic tunneling for restoration of the esophagus (POETRE) [22], submucosal tunneling and endoscopic resection of submucosal tumor at the GEJ (STER) [23], and pyloroplasty as therapy for gastroparesis (aka pyloric POEM) [24]. Indeed, modified POEM techniques have permitted the exploration of deeper wall layers, including the muscularis propria, once unfathomable by conventional endoscopic techniques [25].

Practical Considerations

- POEM is a procedure with high success in hands of experienced endoscopist; however the decision for procedure should be made taking into consideration clinical history, diagnostic testing, history of previous intervention, and local availability.

Table 11.2 Contraindications for POEM

Relative contraindications
Prior irradiation to the mediastinum
Severe pulmonary disease (example)
Extensive bullous disease
Prior lung resection
Home oxygen dependent
ASA class III
Forced volume/1 sec
Forced vital capacity <70%
pCO2 ≥ 45
pO2 < 75
Coagulopathy
Baseline platelet count <50,000/mm3 (example)
Immune thrombocytopenic purpura
Myelodysplastic syndrome
Hypersplenism
Prior esophageal EMR or other mucosal ablative treatment (examples)
Photodynamic therapy
Radio-frequency ablation
Compensated cirrhosis with portal hypertension even if no or trace esophageal varices on EGD
Patients with contraindication to general anesthesia

Contraindications

There are no consensus guidelines as to the absolute contraindications for POEM. However, a number of relative contraindications have been described based on an international expert survey by Stavropoulos et al. [24]. These include a history of severe pulmonary disease, cirrhosis with portal hypertension, severe coagulopathy, and prior interventions resulting in severe submucosal fibrosis such as esophageal irradiation, ablation therapy, and extensive endoscopic mucosal resection (EMR) (Table 11.2). In a series of 500 patients, Inoue et al. describe exclusion criteria as patients whose general condition of the patient was unfavorable for general anesthesia or if the patient could not stop anticoagulation for the procedure [26] (Table 11.2).

Practical Considerations

- There are no uniformly accepted absolute contraindications for POEM.
- A number of relative contraindications have been described based on expert opinion.

Instruments and Accessories

There are several important aspects that must be carefully delineated before embarking on a program in POEM at any institution or practice. Firstly, several studies have favored using a porcine model for hands-on training prior to human cases [27]. Starting with an ex vivo system reduces costs and permits the trainees to assess the gross specimen following the procedure. Once trainees are comfortable with POEM on the explanted model, progressing to a live animal represents the next natural step. The live pig allows the endoscopist and POEM team members to focus on their respective roles and to monitor/manage any potential complications that may arise (e.g., bleeding, perforation, pneumothorax, abdominal compartment syndrome). Following training in animal models, the endoscopist should be proctored by an experienced operator, who can provide step-by-step supervision and guidance through the initial cases. Adequate training in POEM and, most importantly, ability to recognize and manage all procedural associated adverse events are of paramount importance. The availability of a dedicated "POEM group" of endoscopists, anesthesiologists, nurses, and technicians familiar with their roles is indispensable for successful outcomes [28, 29] .

POEM is an advanced endoscopic technique that requires certain specific instruments and accessories that are not commonly used in day to day basis in an endoscopy unit. Secondly, given the complexity of this technique and intra-procedural monitoring, this procedure should be performed exclusively with the patient under general anesthesia. Overall, the setup needed for the POEM procedure can be divided into the following categories:

- *Location*

POEM was initially described by Dr. Harushiro Inoue [11] in the operating room (OR). To date, two studies have evaluated the feasibility of launching a POEM program and performing this procedure in the endoscopy unit exclusively [28, 30]. While the results from both of these studies are promising, the overall decision of OR versus endoscopy unit depends on various factors specific to each institution, anesthesia equipment availability, and availability of instruments and personnel able to deal with POEM-related complications (e.g., pneumothorax, pneumoperitoneum requiring abdominal decompression) [29].

- *Equipment* (Table 11.3)

In our institution, a pre-procedural checklist for all the necessary equipment and accessories is routinely reviewed by the POEM team prior to each case.

1. Endoscope and accessories

Table 11.3 Instruments and accessories used for POEM

POEM instruments and accessories used at our institution
1. High-definition endoscope with incorporated water-jet function (e.g., Olympus GIF-H-190)[a]
2. Transparent distal cap attachment (D201–10704, Olympus)[a]
3. Hybrid knife (HK)[b]
4. Triangular tip (TT) knife (KD 640 L)[a]
5. Coag grasper (FD410-R)[a]
6. Electrosurgical generator VIO 300 D[b]
7. Resolution clip[c]
8. Over-the-scope clips (OTSC)
9. OverStitch[d]
10. Fully covered esophageal stents
11. Angiocath needle (14 gauge)
12. Veress needle

[a]Olympus America, Center Valley, PA, USA
[b]ERBE USA, Marietta, GA, USA
[c]Boston Scientific, Natick, Massachusetts, USA; and Instinct Clip, Cook Medical, Winston-Salem, North Carolina, USA
[d]Apollo Endosurgery, Austin, TX, United States
[e]OvescoEndoscopy AG, Tubingen, Germany

A standard forward-viewing upper endoscope with integrated water-jet function is recommended. The water-jet irrigation is advantageous since it facilitates identification and targeting of bleeding vessels, which can be challenging in the confined submucosal space during tunneling or myotomy.

A soft, transparent plastic, distal attachment cap should be used (Distal attachment, D201–10704; Olympus America, Center Valley, PA, USA). The attached cap on the endoscope allows for easier entry into the submucosal domain, improved visualization, and potential protection against inadvertent mucosal injury. An esophageal overtube (Guardus overtube; US Endoscopy, Mentor, OH, USA) can be used for repeat endoscope insertions and to stabilize the endoscope, potentially reducing trauma and undesired stretching of the mucosotomy [31].

The use of carbon dioxide gas (CO_2) for insufflation is mandatory. Dissection of insufflating gas into the mediastinum and/or peritoneum is commonly encountered due to the leakage through the submucosal space and the thin esophageal muscle fibers in the absence of a serosal layer [32]. The leaking of CO_2 tends to be less problematic because it is readily absorbed by tissue at a rate approximately 25–30 times that of room air [33]. Hence, in most instances, capnoperitoneum does not interfere with the procedure and is often managed expectantly.

2. Injection agents

In most institutions, a mixture of normal saline with a small amount of indigo carmine is used for the submucosal lift at the mucosal entry site. Indigo carmine provides blue staining for easier identification of the submucosal space. In some instances, a high-viscosity solution is used when

normal saline fails to provide a lasting submucosal fluid cushion for the mucosotomy. Ten percent glycerol is often recommended in this setting [34]; however, this is not commercially available in the United States. Alternatively, a mixture containing 85 ml of normal saline solution with 15 ml hydroxypropyl methylcellulose (Gonak 2.5%; Akorn Inc., Somerset, NJ) can be used [35].

3. Devices
   (a) Knives. The devices used for POEM are in essence derived from those currently available for ESD [36]. The two most commonly used knives during POEM are the triangle-tip (TT) knife (KD-640 L; Olympus America, Center Valley, PA) and the Hybrid knife (ERBE USA, Marietta, GA). The TT knife needs to be exchanged with a separate needle injector (23-gauge injection needle NM4004–0423; Olympus America, Center Valley, PA) multiple times during a single session in order to keep the submucosal plane well delineated. On the other hand, the hybrid knife is the only knife available in the United States that allows submucosal injection. The tip of the knife can inject an ultrafine 120-μm saline jet stream that penetrates into the submucosal space but does not extend into the muscle layer. This adjunct capability to inject and perform electrosurgical dissection with the same device reduces the need for exchanges. Indeed, a single-center randomized trial from China reported that the use of the Hybrid knife led to a significant decrease in procedural time and a lower rate of minor intra-procedural bleeding rate when compared to the use of a TT knife [37]. However, this water-jet function requires a separate dedicated computer unit (ERBE Jet; ERBE USA, Marietta, GA) and hence, a potential additional investment in equipment costs for POEM.
   (b) Hemostasis. Small vessel hemostasis is often adequately achieved by using the dissecting knives as described above. Bleeding from large caliber vessels can significantly preclude visualization within the submucosal space, and the coag grasper (FD-410LR; Olympus America) is commonly employed for hemostasis in this setting. Indeed, the coag grasper is often used for the preemptive coagulation of large vessels noted incidentally during submucosal tunneling. It should be emphasized that preemptive hemostasis of larger vessels is highly desirable.
   (c) Mucosal closure. Adequate closure of the mucosal entry site is critical in order to maintain the integrity of the lumen and to prevent full-thickness perforation. This is usually performed with multiple standard endoscopic clips (Resolution Clip, Boston Scientific, Natick, MA, USA; and Instinct Clip, Cook Medical, Winston-Salem, NC, USA, Quick Clip Pro, Olympus America, Center Valley, PA, USA).
   (i) Due to endoscope manipulation and repeated movements through the entry point, swelling and inversion of the sides of the mucosal incision can sometimes occur, making it difficult to approximate the edges with standard clips. Congruent with a previous report [38], we have found that the over-the-scope clip (OTSC, Ovesco; Tuebingen, Germany) can facilitate closure in these technically challenging cases [39]. Other alternatives for mucosal closure, including suturing devices (Overstich; Apollo Endosurgery, Austin, TX, USA), have also been reported [40]. The use of fully covered metal stent has also been described for difficult mucosal closure [41].
4. Electrosurgical generator

A high-frequency electrosurgical generator (ESG) with modulated current options is necessary for POEM. In the United States, the ICC 200E, the VIO 200S and VIO 300D (ERBE), and the ESG 100 (Olympus America) are the ESGs that are commonly used for POEM and ESD procedures. The settings of the ESG (e.g., type of modulated current, power output, effect, duration) vary depending on the different stages of the procedure (e.g., mucosal incision, submucosal dissection, hemostasis), the type of knife utilized, and the ESG model. Furthermore, the ESG settings can also differ greatly among experts in POEM. This variability is associated with multiple factors, including operator preferences as well as patient-specific factors (e.g., fibrosis versus water content in the target tissue, etc.). In the absence of definite parameters, it is reasonable to choose initial settings based on the type of ESG available, manufacturer's guidance, and expert recommended settings.

5. Anesthesia equipment

The procedure room must be equipped with capability of preforming general anesthesia and management of critical airway. Patients with achalasia are at increased risk for aspiration at the time of endotracheal intubation. Therefore in our unit we utilize a rapid sequence intubation procedure [28].

Practical Considerations

The POEM room should be setup with taking into account the type of anesthesia used, the procedure steps involved, and possible complications that may need immediate attention.

POEM Procedure (Table 11.4)

1. *Pre-procedure preparation:* Patients are maintained on a clear liquid diet for 1–5 days prior to the procedure. Many, but not all, centers perform an EGD 1–3 days before the procedure in order to remove any solid or liquid material from the esophagus as well as to evaluate for *Candida* esophagitis or any other esophageal or gastric lesions [42]. Patients should be kept nil per os (NPO) after midnight on the day of the procedure. At this point there are no results available that confidently quantify the bacteremia rates with POEM [43]; however most operators advocate use of prophylactic antibiotics for this procedure [42]. At our institution we use intravenous antibiotics ampicillin/sulbactam or ciprofloxacin for those with penicillin allergy initiated on the day of procedure. Some centers advocate administration of antifungal agents 3–5 days prior to the procedure based on the increased incidence of esophageal candidiasis in patients with achalasia. There is no consensus of proton pump inhibitor (PPI) use pre- and post-procedure. Periprocedural anticoagulation and/or antiplatelet therapy should be managed according to the current American Society for Gastrointestinal Endoscopy (ASGE) guidelines [44]. The procedure is typically performed in supine position with general anesthesia with the patient paralyzed using positive-pressure ventilation [28].
2. *Procedure:* POEM involves four basic steps (Fig. 11.1, Table 11.4) including mucosal entry, submucosal tunnel, myotomy, and closure of mucosal entry. These were originally described by Inoue et al. [11] and have been replicated in multiple other studies with very good technical success with endoscopist and institution-based minor modifications.
   (a) *Mucosal Entry (Mucosectomy):* Any fluid or residual food is suctioned and removed from the esophageal/gastric lumen. Most institutions perform a right anterior (2 o'clock position) mucosectomy; however at some centers, a posterolateral orientation (5 o'clock position) is favored [42]. When the direction of myotomy is at 1 or 2 o'clock position, the gastric myotomy finishes at the anterior aspect of the lesser curvature, thus preserving the sling fibers and His angle and theoretically minimizing the risk of gastroesophageal reflux (GERD) post-procedure. The site of mucosal entry is approximately 12 to 15 cm above the GEJ. At our center we use 8 ml of normal saline solution admixed with indigo carmine to create a submucosal bleb, but the type of solution used for lifting may vary based on the center. The mucosal incision can be accomplished with a triangular tip (TT) knife or a Hybrid knife (HK); the latter has the advantage of being able to inject and cauterize at the same time thus obviating the need for multiple exchanges between injection needle and knife. A 10–15 mm longitudinal mucosal incision is performed until exposure of the submucosal space.
   (b) *Submucosal Tunneling:* A submucosal tunnel is then created along the length of the esophagus trough the GEJ and into the proximal cardia. The length of the submucosal tunnel is usually 8–12 cm in the esophagus and 2–3 cm in the cardia for total length from 10 to 15 cm. In type III and hypercontractile esophagus, the tunnel length is typically longer and based on the proximal extent of hypertensive contractions on the pre-procedure HRM or at the level of visible spastic contractions endoscopically. This allows the creation of a longer myotomy. The unlimited length of the myotomy that can be executed by POEM is one of the advantages over transabdominal surgical approaches such as LHM.

Table 11.4 POEM procedure steps

POEM step	Device	Length or number
Mucosectomy	Hybrid knife or TT knife	1.5 cm incision 10–15 cm above LES
Submucosal tunnel	Hybrid knife or TT knife	14–15 cm
Myotomy	Hybrid knife or TT knife	Esophageal 6–10 cm for type I and type II achalasia or longer for type III stomach 2–3 cm
Closure	Standard endoscopic clips, over-the-scope clip, suturing device metal stent	5–10 clips

To create the tunnel, the tip of the endoscope is maneuvered through the mucosal entry site and subsequently inserted into the newly created submucosal space. Submucosal dissection is achieved by using the electrocautery knife with repeated dyed saline injections; the submucosal tunnel is extended 2–3 cm caudal from the LES into the gastric cardia. This is established by the anatomical landmark changes consistent with the transition from the esophagus into the stomach. Several cues have been identified as being helpful in establishing the transition point from the esophagus to the stomach; these include insertion depth from the incisors, narrowing of the submucosal space in the area of the LES followed by widening of the space in the cardia, change in vasculature (e.g., spindle or corkscrew vessels on the muscularis propria side), and visualization of aberrant longitudinal muscle fibers at the EGJ. Two more objective methods of EGJ identification have been described, these include a double-scope method whereby an ultrathin endoscope is used to allow for exact visualization of the extent of the tunnel, and a second method described is injection of epinephrine or indocyanine green to mark the end

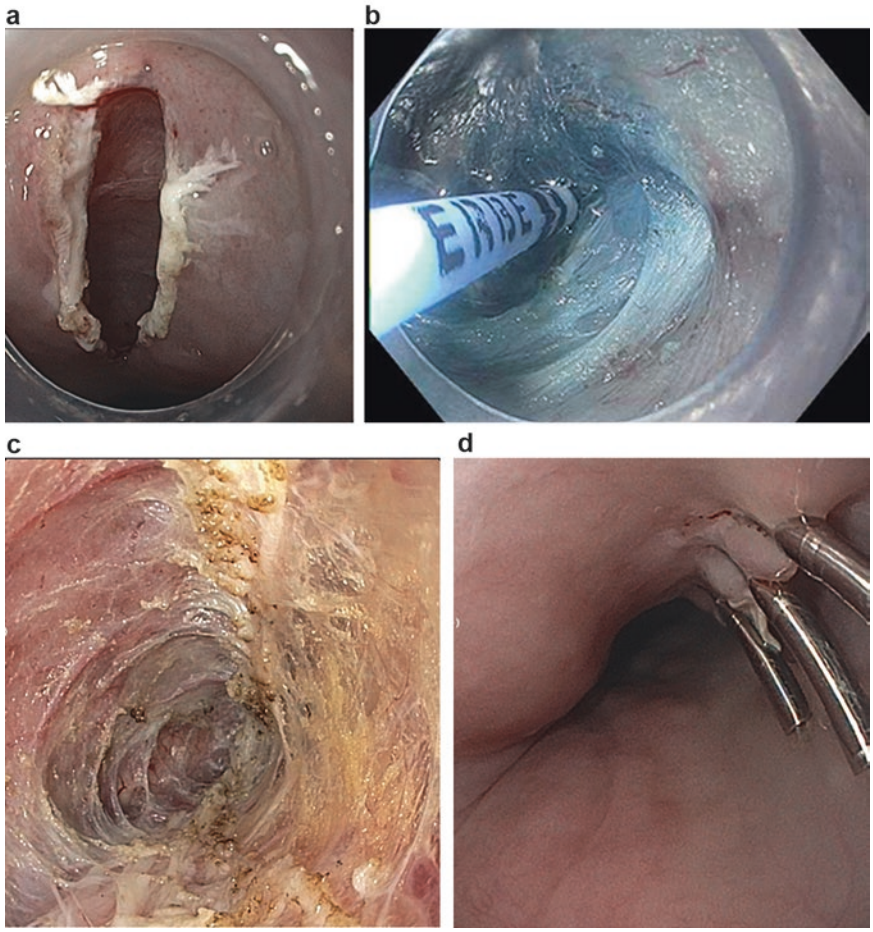

Fig. 11.1 (**a**) Mucosectomy, (**b**) submucosal tunnel, (**c**) myotomy, (**d**) mucosal entry closure with clips

of the tunnel. [45–47]. Finally fluoroscopy has been described as a way of estimating the exact extend of the submucosal tunnel [46].

(c) *Myotomy.* Myotomy is initiated with the electrocautery knife 2–3 cm distal to the mucosal entry site, proceeding proximal to distal. The myotomy is continued 2–3 cm past the LES into the gastric cardia. Adequate extension of the myotomy in the cardia by minimum of 2 cm is essential for the final success of the procedure. Selective myotomy of the circular muscle fibers or full-thickness myotomy can be performed. The type of myotomy most likely does not influence the clinical outcome [48]. In our center we favor a combined approach of doing selective myotomy in the body of the esophagus and full thickness at the LES and cardia. As such the preservation of longitudinal muscle fibers provides a useful landmark and may decrease the leakage of CO2 in the mediastinum and peritoneum. At all points of dissection, care should be taken to prophylactically coagulate with coag grasper any large blood vessel in the path of dissection to prevent any inadvertent bleeding. It is far easier and probably safer to prophylactically coagulate vessels than to inadvertently lacerate them because the resulting bleeding may be much more difficult to target with the coagulating forceps.

(d) *Closure of Mucosal Entry.* Prior to closure of the mucosotomy site, a careful examination of the true esophageal lumen, the stomach, and the submucosal tunnel should be done to look for any signs of bleeding or perforation. Closure of the mucosal entry incision site is generally achieved with standard endoscopic clips or the use of endoscopic suturing accessory, OverStitch device [49]. When closing the mucosotomy site, it is important to remember that this defect is the sole entry point where mediastinum can be contaminated upon restarting oral intake. We use 5–10 clips in a zipper fashion from distally to proximal edge of the incision sight, making sure that some of the normal tissue is captured at both ends and edges. In case of failure to close, rescue techniques have been reported with over-the-scope clip (OTSC) and covered esophageal stent [38, 50, 51].

Practical Considerations

- When performing POEM procedure, one must proceed in a stepwise approach.
- Proceeding cautiously with inject/lift-cut coag vessel observation may help in preventing and early detection of complications.

Complications (Table 11.5)

POEM when performed by experienced endoscopist is a very safe procedure with low rate of procedural and post-procedure adverse events. The technical success rate for this procedure is estimated to be 93–97%. A recent meta-analysis by Barbieri et al. [12] reported that the adverse events requiring medical/surgical intervention were 14% and these include mucosal perforation requiring endoscopic treatment with clips, pneumoperitoneum treated with needle decompression, pneumothorax requiring needle decompression, postoperative hematemesis, esophageal leak treated with clips, pneumonia requiring treatment with antibiotics and bronchial lavage, submucosal tunnel bleeding, pleural effusion, fever >38, submucosal tunnel infection, epileptic seizure, and mediastinal hematoma. The rate of need for surgical intervention post-POEM was reported as 0.2%. No POEM-related deaths have been reported. Table 11.5 shows the general approach to complications commonly seen with this procedure.

Table 11.5 Complications of POEM

Complications[a]	Treatment[b]
Mucosal perforation	Endoscopic closure after complete myotomy
Full-thickness perforation	
	Consider closure of myotomy site
Pneumoperitoneum	Veress needle decompression when physiologic compromise/symptoms
Pneumothorax	Large volume > 30% may require decompression
Pleural effusion	Large volume with symptoms treated with thoracentesis
Bleeding	Most common a GEJ, stomach side. Endoscopic treatment
Delayed perforation	Endoscopic treatment with clips, stents or surgery

[a]Common complications, not all inclusive list reported in literature
[b]May need supportive care with fluids, antibiotics, blood transfusion case by case basis

It is important to note that there are certain findings (Fig. 11.2a, b) on post-POEM imaging that are not considered complications and are simply expectant findings related to CO_2 insufflation in the submucosal space. Most common findings noted on post-POEM imaging have been pneumomediastinum, pneumoperitoneum, and subcutaneous emphysema [52–54]. Figure 11.2c shows a patient with esophageal leak on detected on post-procedure imaging.

The most common long-term complication after POEM appears to be GERD, taking into consideration the findings of erosive esophagitis on EGD; abnormal acid exposure on pH study to the estimated prevalence appears to be between 20–46% [42].

Follow-Up

The post-POEM follow-up routine at our institution is summarized in Table 11.6.

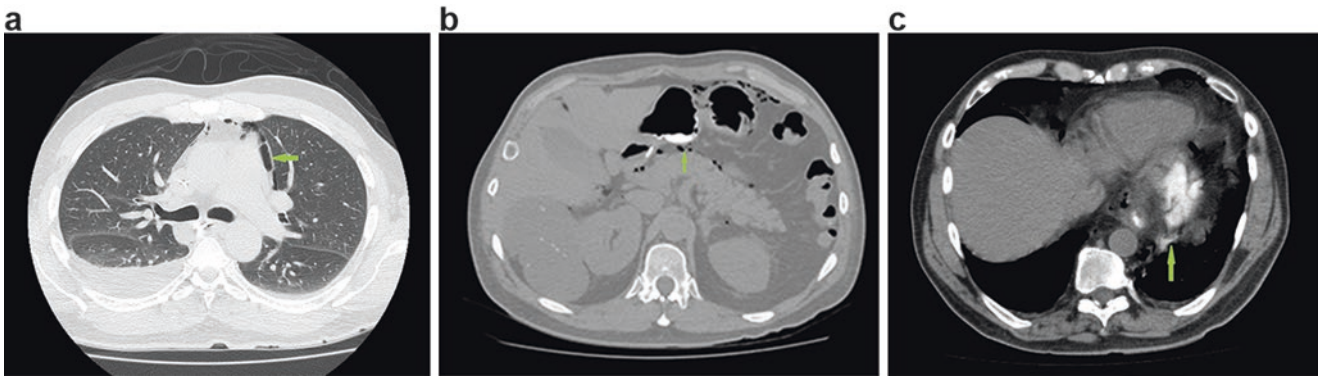

Fig. 11.2 (**a**) Post-procedure CT esophagram showing pneumomediastinum, (**b**) pneumoperitoneum, and (**c**) leak of oral contrast indicating perforation

Table 11.6 Post-POEM patient follow-up

Follow-up[a]	Assessment
1 month	Symptoms of dysphagia, GERD, additional endoscopic therapy since POEM
3–6 months	
	Symptoms as above and review results of post-procedure HRM and pH testing
12 months	
	Symptoms of dysphagia, GERD, additional endoscopic therapy since POEM, PPI use

[a]Follow-up protocol at our institution varies by institution, resource availability, and patient factors

Practical Considerations

- Know the reported complications.
- Recognize a complication when it happens.
- Have the tools needed to treat the complication.
- Know the expectant findings on post-procedure imaging.

Immediate Postoperative Care

In general, patients are hospitalized and kept NPO the night after the procedure and continued on intravenous antibiotics and PPI therapy. An esophagram is routinely obtained on postoperative day one to assure the absence of leakage of contrast into the mediastinum. Traditionally a standard fluoroscopy-based esophagram is favored by many centers. In our institution, we have developed a CT esophagram protocol which not only may be more sensitive in detecting leaks but also does not require any direct radiologist involvement thus allowing the test to be performed at any time on standard CT equipment [54]. There is no consensus on whether a "second look" EGD within 24–72 h following POEM is indicated. We do not routinely perform this procedure as it has not been shown to affect clinical management [45]. In the absence of any contraindications, a semisolid diet is initiated and maintained for 14 days prior to gradual advancement as tolerated. Antibiotics are generally stopped by time of discharge (2–3 days) and PPI therapy continued for 2 weeks postoperatively. Patients are seen in clinic 4 weeks following POEM.

Symptom Evaluation

Clinical symptoms are assessed by standardized symptom scales. An Eckardt score ≤ 3 has been used as an endpoint for clinical success following therapy for achalasia [55, 56]. However, as emphasized by Bredenoord and colleagues [7], a patient with an Eckardt score of 3 can still have daily symptoms, highlighting the intrinsic limitations of this scoring system as sole endpoint for treatment efficacy. In our institution, in addition to the Eckardt score, we use the SF-36 questionnaire as an adjunct to estimate the impact of symptoms on the patient's overall quality of life. We repeat the Eckardt score and SF-36 at each follow-up visit (1, 6, 12 months and yearly thereafter) to monitor symptom evolution.

Endoscopic Evaluation

There is no consensus regarding the role or frequency of endoscopic surveillance postoperatively. Previous clinical trials have reported variable rates (6–60%) of mild esophagitis (LA grade A and B) on routine EGD after POEM [57, 58]; albeit findings were limited by short-term follow-up. In our institution, EGD is performed on the basis of persistent or new onset of symptoms (e.g., dysphagia, regurgitation, chest pain, heartburn) and to follow-up of unexpected findings on post-procedural HRIM and/or pH study. Future long-term studies are required to define endoscopic endpoints for clinical intervention and ideally incorporate cost-effective analysis in the decision-making process.

Radiographic Evaluation

Symptom evaluation alone is an inadequate measure as a subset of patients may not endorse any in spite of objective measures demonstrating disease progression [59]. Timed barium esophagram provides both structural and functional parameters that can be monitored post-procedurally. As part of our standard post-POEM evaluation, we perform routine esophagram in all patients at 6 and 12 months after the procedure and recommend it yearly thereafter in the absence of interval changes.

High-Resolution Impedance Manometry (HRIM)

There are no concrete guidelines regarding the use of HRIM after POEM. Nonetheless, post-intervention manometric findings may have prognostic implications, as several studies have shown that an initial reduction in LES pressure to <10 mm Hg is associated with long-term efficacy following pneumatic balloon dilation [60]. HRIM may provide an objective post-procedure outcome measure. From our experience, we have encountered recovery of peristalsis on HRIM following POEM (unpublished

data); albeit the clinical implication of these findings are yet to be determined. Furthermore, recent study by Cho and colleagues [61] has suggested excellent agreement between HRIM and timed barium esophagram for assessing bolus retention. This manometric data can be correlated at the onset of recurrent symptoms and be used to determine the etiology and best course of action. We obtain HRIM at 6 and 12 months following POEM. HRIM also seems a reasonable choice in patients that have persistent symptoms after POEM.

Esophageal 24-hr pH Monitoring

Initial reports on POEM indicated a relatively low prevalence of heartburn symptoms (ranging from none to less than 10%) [11, 34, 57, 62]. However, on a study by Swänstrom and colleagues [63], objective assessment with 24-h pH probe revealed an acid-reflux prevalence of 46% (6/13 patients) 6 months after POEM. These results reiterate the often discordance between clinical symptoms and reflux disease, underscoring the importance of surveillance post-POEM. We routinely perform 24-h pH probe evaluation at 6 and 12 months and yearly thereafter. Patients with symptoms or evidence of reflux on pH studies are kept on PPI therapy once or twice daily.

Practical Considerations

- Prior to the procedure, it is important to inform the patient what the post-procedure follow-up will be.
- The long-term complications of GERD should be kept in mind when seeing these patients for follow-up.

Conclusion

POEM combines the minimally invasive endoscopic approach of pneumatic dilation with the direct vision myotomy precision of LHM. With estimated more than 5000 cases done worldwide, POEM should not be labeled anymore as experimental procedure considering the well-documented high technical and midterm clinical success rates along with excellent safety profile. While more long-term clinical outcome studies are needed, it can be safely said that this procedure is here to stay and may find additional applications for a broad category of esophageal motility disorders.

References

1. Birgisson S, Richter JE. Achalasia in Iceland, 1952–2002: an epidemiologic study. Dig Dis Sci. 2007;52(8):1855–60. PubMed PMID: 17420933. eng
2. Farrukh A, DeCaestecker J, Mayberry JF. An epidemiological study of achalasia among the South Asian population of Leicester, 1986–2005. Dysphagia. 2008;23(2):161–4. PubMed PMID: 18027026. eng
3. Sadowski DC, Ackah F, Jiang B, Svenson LW. Achalasia: incidence, prevalence and survival. A population-based study. Neurogastroenterol Motil. 2010;22(9):e256–61. PubMed PMID: 20465592. eng
4. Gennaro N, Portale G, Gallo C, Rocchietto S, Caruso V, Costantini M, et al. Esophageal achalasia in the Veneto region: epidemiology and treatment. Epidemiology and treatment of achalasia. J Gastrointest Surg. 2011;15(3):423–8. PubMed PMID: 21116729. eng
5. Nenshi R, Takata J, Stegienko S, Jacob B, Kortan P, Deitel W, et al. The cost of achalasia: quantifying the effect of symptomatic disease on patient cost burden, treatment time, and work productivity. Surg Innov. 2010;17(4):291–4. PubMed PMID: 20647236. eng
6. Pandolfino JE, Gawron AJ. Achalasia: a systematic review. JAMA. 2015;313(18):1841–52. PubMed PMID: 25965233. eng
7. Bredenoord AJ, Fox M, Kahrilas PJ, Pandolfino JE, Schwizer W, Smout AJ, et al. Chicago classification criteria of esophageal motility disorders defined in high resolution esophageal pressure topography. Neurogastroenterol Motil. 2012;24(Suppl 1):57–65. PubMed PMID: 22248109. PMCID: PMC3544361. eng
8. Campos GM, Vittinghoff E, Rabl C, Takata M, Gadenstätter M, Lin F, et al. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. Ann Surg. 2009;249(1):45–57. PubMed PMID: 19106675. eng
9. Spechler SJ. Pneumatic dilation and laparoscopic Heller's myotomy equally effective for achalasia. N Engl J Med. 2011;364(19):1868–70. PubMed PMID: 21561354. eng
10. Pasricha PJ, Hawari R, Ahmed I, Chen J, Cotton PB, Hawes RH, et al. Submucosal endoscopic esophageal myotomy: a novel experimental approach for the treatment of achalasia. Endoscopy. 2007;39(9):761–4. PubMed PMID: 17703382. eng
11. Inoue H, Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42(4):265–71. PubMed PMID: 20354937. eng
12. Barbieri LA, Hassan C, Rosati R, Romario UF, Correale L, Repici A. Systematic review and meta-analysis: efficacy and safety of POEM for achalasia. United European Gastroenterol J. 2015;3(4):325–34. PubMed PMID: 26279840. PMCID: PMC4528214. eng
13. Talukdar R, Inoue H, Nageshwar RD. Efficacy of peroral endoscopic myotomy (POEM) in the treatment of achalasia: a systematic review and meta-analysis. Surg Endosc. 2015;29(11):3030–46. PubMed PMID: 25539695. eng
14. Yang D, Draganov PV. Peroral endoscopic myotomy (POEM) for achalasia after Roux-en-Y gastric bypass. Endoscopy. 2014;46(Suppl 1):UCTN:E11-2. PubMed PMID: 24446095. eng
15. Zhou PH, Li QL, Yao LQ, Xu MD, Chen WF, Cai MY, et al. Peroral endoscopic remyotomy for failed Heller myotomy: a prospective single-center study. Endoscopy. 2013;45(3):161–6. PubMed PMID: 23389963. eng
16. Vigneswaran Y, Ujiki MB. Peroral endoscopic myotomy: an emerging minimally invasive procedure for achalasia. World J Gastrointest Endosc. 2015;7(14):1129–34. PubMed PMID: 26468336. PMCID: PMC4600178. eng
17. Onimaru M, Inoue H, Ikeda H, Yoshida A, Santi EG, Sato H, et al. Peroral endoscopic myotomy is a viable option for failed surgical esophagocardiomyotomy instead of redo surgical Heller myotomy: a single center prospective study. J Am Coll Surg. 2013;217(4):598–605. PubMed PMID: 23891071. eng

18. Hu JW, Li QL, Zhou PH, Yao LQ, Xu MD, Zhang YQ, et al. Peroral endoscopic myotomy for advanced achalasia with sigmoid-shaped esophagus: long-term outcomes from a prospective, single-center study. Surg Endosc. 2015;29(9):2841–50. PubMed PMID: 25492452. eng
19. Khashab MA, Messallam AA, Onimaru M, Teitelbaum EN, Ujiki MB, Gitelis ME, et al. International multicenter experience with peroral endoscopic myotomy for the treatment of spastic esophageal disorders refractory to medical therapy (with video). Gastrointest Endosc. 2015;81(5):1170–7. PubMed PMID: 25634487. eng
20. Chen WF, Li QL, Zhou PH, Yao LQ, Xu MD, Zhang YQ, et al. Long-term outcomes of peroral endoscopic myotomy for achalasia in pediatric patients: a prospective, single-center study. Gastrointest Endosc. 2015;81(1):91–100. PubMed PMID: 25088923. eng
21. Inoue H, Ikeda H, Hosoya T, Onimaru M, Yoshida A, Eleftheriadis N, et al. Submucosal endoscopic tumor resection for subepithelial tumors in the esophagus and cardia. Endoscopy. 2012;44(3):225–30. PubMed PMID: 22354822. eng
22. Wagh MS, Yang D, Chavalitdhamrong D, Draganov PV. Per-oral endoscopic tunneling for restoration of the esophagus (POETRE). Gastrointest Endosc. 2014;80(2):330. PubMed PMID: 24929492. eng
23. Zhou DJ, Dai ZB, Wells MM, Yu DL, Zhang J, Zhang L. Submucosal tunneling and endoscopic resection of submucosal tumors at the esophagogastric junction. World J Gastroenterol. 2015;21(2):578–83. PubMed PMID: 25593479. PMCID: PMC4294169. eng
24. Shlomovitz E, Pescarus R, Cassera MA, Sharata AM, Reavis KM, Dunst CM, et al. Early human experience with per-oral endoscopic pyloromyotomy (POP). Surg Endosc. 2015;29(3):543–51. PubMed PMID: 25106716. eng
25. Sumiyama K, Gostout CJ, Gettman MT. Status of access and closure techniques for NOTES. J Endourol. 2009;23(5):765–71. PubMed PMID: 19438293. eng
26. Inoue H, Sato H, Ikeda H, Onimaru M, Sato C, Minami H, et al. Per-Oral Endoscopic Myotomy: A Series of 500 Patients. J Am Coll Surg. 2015;221(2):256–64. PubMed PMID: 26206634. eng
27. Kurian AA, Dunst CM, Sharata A, Bhayani NH, Reavis KM, Swanström LL. Peroral endoscopic esophageal myotomy: defining the learning curve. Gastrointest Endosc. 2013;77(5):719–25. PubMed PMID: 23394838. eng
28. Yang D, Pannu D, Zhang Q, White JD, Draganov PV. Evaluation of anesthesia management, feasibility and efficacy of peroral endoscopic myotomy (POEM) for achalasia performed in the endoscopy unit. Endosc Int Open. 2015;3(4):E289–95. PubMed PMID: 26357672. PMCID: PMC4554518. eng
29. Pannu D, White JD, Draganov PV. Peroral endoscopic myotomy in the endoscopy unit: location, location, location. Gastrointest Endosc. 2016;83(1):126–8. PubMed PMID: 26706301. eng
30. Khashab MA, El Zein M, Kumbhari V, Besharati S, Ngamruengphong S, Messallam A, et al. Comprehensive analysis of efficacy and safety of peroral endoscopic myotomy performed by a gastroenterologist in the endoscopy unit: a single-center experience. Gastrointest Endosc. 2015;83:117–25. PubMed PMID: 26212369. ENG
31. Swanström LL, Soper NJ, Leonard M. Mastery of endoscopic and laparoscopic surgery. 4th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins Health; 2014. p. xv, 704.
32. Yang D, Wagh MS. Peroral endoscopic myotomy for the treatment of achalasia: an analysis. Diagn Ther Endosc. 2013;2013:389596. PubMed PMID: 24282373. PMCID: PMC3825053. eng
33. Dripps RD, Eckenhoff JE, Vandam LD, Longnecker DE, Murphy FL. Dripps/Eckenhoff/Vandam introduction to anesthesia. 9th ed. Philadelphia: Saunders; 1997. p. x, 518.
34. Costamagna G, Marchese M, Familiari P, Tringali A, Inoue H, Perri V. Peroral endoscopic myotomy (POEM) for oesophageal achalasia: preliminary results in humans. Dig Liver Dis. 2012;44(10):827–32. PubMed PMID: 22609465. eng
35. Bacani CJ, Woodward TA, Raimondo M, Al-Haddad MA, Noh KW, Pungpapong S, et al. The safety and efficacy in humans of endoscopic mucosal resection with hydroxypropyl methylcellulose as compared with normal saline. Surg Endosc. 2008;22(11):2401–6. PubMed PMID: 18622557. eng
36. Draganov PV, Gotoda T, Chavalitdhamrong D, Wallace MB. Techniques of endoscopic submucosal dissection: application for the Western endoscopist? Gastrointest Endosc. 2013;78(5):677–88. PubMed PMID: 24021491. eng
37. Cai MY, Zhou PH, Yao LQ, Xu MD, Zhong YS, Li QL, et al. Peroral endoscopic myotomy for idiopathic achalasia: randomized comparison of water-jet assisted versus conventional dissection technique. Surg Endosc. 2014;28(4):1158–65. PubMed PMID: 24232052. eng
38. Saxena P, Chavez YH, Kord Valeshabad A, Kalloo AN, Khashab MA. An alternative method for mucosal flap closure during per-oral endoscopic myotomy using an over-the-scope clipping device. Endoscopy. 2013;45(7):579–81. PubMed PMID: 23592391. eng
39. Yang D, Draganov PV. Closing the gap in POEM. Endoscopy. 2013;45(8):677. PubMed PMID: 23881808. eng
40. Kurian AA, Bhayani NH, Reavis K, Dunst C, Swanström L. Endoscopic suture repair of full-thickness esophagotomy during per-oral esophageal myotomy for achalasia. Surg Endosc. 2013;27(10):3910. PubMed PMID: 23708719. eng
41. Yang D, Zhang Q, Draganov PV. Successful placement of a fully covered esophageal stent to bridge a difficult-to-close mucosal incision during peroral endoscopic myotomy. Endoscopy. 2014;46(Suppl 1):UCTN:E467-8. PubMed PMID: 25314199. eng
42. Stavropoulos SN, Desilets DJ, Fuchs KH, Gostout CJ, Haber G, Inoue H, et al. Per-oral endoscopic myotomy white paper summary. Gastrointest Endosc. 2014;80(1):1–15. PubMed PMID: 24950639. eng
43. Khashab MA, Chithadi KV, Acosta RD, Bruining DH, Chandrasekhara V, Eloubeidi MA, et al. Antibiotic prophylaxis for GI endoscopy. Gastrointest Endosc. 2015;81(1):81–9. PubMed PMID: 25442089. eng
44. Anderson MA, Ben-Menachem T, Gan SI, Appalaneni V, Banerjee S, Cash BD, et al. Management of antithrombotic agents for endoscopic procedures. Gastrointest Endosc. 2009;70(6):1060–70. PubMed PMID: 19889407. eng
45. Stavropoulos SN, Modayil RJ, Friedel D, Savides T. The International Per Oral Endoscopic Myotomy Survey (IPOEMS): a snapshot of the global POEM experience. Surg Endosc. 2013;27(9):3322–38. PubMed PMID: 23549760. eng
46. Kumbhari V, Khashab MA. Peroral endoscopic myotomy. World J Gastrointest Endosc. 2015;7(5):496–509. PubMed PMID: 25992188. PMCID: PMC4436917. eng
47. Minami H, Inoue H, Haji A, Isomoto H, Urabe S, Hashiguchi K, et al. Per-oral endoscopic myotomy: emerging indications and evolving techniques. Dig Endosc. 2015;27(2):175–81. PubMed PMID: 25040806. eng
48. Li QL, Chen WF, Zhou PH, Yao LQ, Xu MD, Hu JW, et al. Peroral endoscopic myotomy for the treatment of achalasia: a clinical comparative study of endoscopic full-thickness and circular muscle myotomy. J Am Coll Surg. 2013;217(3):442–51. PubMed PMID: 23891074. eng
49. Stavropoulos SN, Modayil R, Friedel D. Current applications of endoscopic suturing. World J Gastrointest Endosc. 2015;7(8):777–89. PubMed PMID: 26191342. PMCID: PMC4501968. eng
50. Kumbhari V, Azola A, Saxena P, Modayil R, Kalloo AN, Stavropoulos SN, et al. Closure methods in submucosal endoscopy. Gastrointest Endosc. 2014;80(5):894–5. PubMed PMID: 24679657. eng
51. Ling T, Pei Q, Pan J, Zhang X, Lv Y, Li W, et al. Successful use of a covered, retrievable stent to seal a ruptured mucosal flap

safety valve during peroral endoscopic myotomy in a child with achalasia. Endoscopy. 2013;45(Suppl 2):UCTN:E63-4. PubMed PMID: 23526520. eng
52. Cai MY, Zhou PH, Yao LQ, Zhu BQ, Liang L, Li QL. Thoracic CT after peroral endoscopic myotomy for the treatment of achalasia. Gastrointest Endosc. 2014;80(6):1046–55. PubMed PMID: 24998467. eng
53. Yang S, Zeng MS, Zhang ZY, Zhang HL, Liang L, Zhang XW. Pneumomediastinum and pneumoperitoneum on computed tomography after peroral endoscopic myotomy (POEM): postoperative changes or complications? Acta Radiol. 2015;56(10):1216–21. PubMed PMID: 25277388. eng
54. Pannu D, Draganov PV. CT esophagram findings after POEM procedure. Gastrointest Endosc. 2015;81(6):1502. PubMed PMID: 25986121. eng
55. Boeckxstaens GE, Annese V, des Varannes SB, Chaussade S, Costantini M, Cuttitta A, et al. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. N Engl J Med. 2011;364(19):1807–16. PubMed PMID: 21561346. eng
56. Hungness ES, Teitelbaum EN, Santos BF, Arafat FO, Pandolfino JE, Kahrilas PJ, et al. Comparison of perioperative outcomes between peroral esophageal myotomy (POEM) and laparoscopic Heller myotomy. J Gastrointest Surg. 2013;17(2):228–35. PubMed PMID: 23054897. eng
57. von Renteln D, Inoue H, Minami H, Werner YB, Pace A, Kersten JF, et al. Peroral endoscopic myotomy for the treatment of achalasia: a prospective single center study. Am J Gastroenterol. 2012;107(3):411–7. PubMed PMID: 22068665. eng
58. Verlaan T, Rohof WO, Bredenoord AJ, Eberl S, Rösch T, Fockens P. Effect of peroral endoscopic myotomy on esophagogastric junction physiology in patients with achalasia. Gastrointest Endosc. 2013;78(1):39–44. PubMed PMID: 23453184. eng
59. Vaezi MF, Baker ME, Richter JE. Assessment of esophageal emptying post-pneumatic dilation: use of the timed barium esophagram. Am J Gastroenterol. 1999;94(7):1802–7. PubMed PMID: 10406238. eng
60. Hulselmans M, Vanuytsel T, Degreef T, Sifrim D, Coosemans W, Lerut T, et al. Long-term outcome of pneumatic dilation in the treatment of achalasia. Clin Gastroenterol Hepatol. 2010;8(1):30–5. PubMed PMID: 19782766. eng
61. Cho YK, Lipowska AM, Nicodème F, Teitelbaum EN, Hungness ES, Johnston ER, et al. Assessing bolus retention in achalasia using high-resolution manometry with impedance: a comparator study with timed barium esophagram. Am J Gastroenterol. 2014;109(6):829–35. PubMed PMID: 24710506. PMCID: PMC4307753. eng
62. Sharata A, Kurian AA, Dunst CM, Bhayani NH, Reavis KM, Swanström LL. Peroral endoscopic myotomy (POEM) is safe and effective in the setting of prior endoscopic intervention. J Gastrointest Surg. 2013;17(7):1188–92. PubMed PMID: 23609138. eng
63. Swanstrom LL, Kurian A, Dunst CM, Sharata A, Bhayani N, Rieder E. Long-term outcomes of an endoscopic myotomy for achalasia: the POEM procedure. Ann Surg. 2012;256(4):659–67. PubMed PMID: 22982946. eng

Endoscopic Management of Esophageal Strictures

12

Darius A. Jahann and Vanessa M. Shami

Introduction

Esophageal strictures are a problem frequently encountered by gastroenterologists. There are a multitude of endoscopic treatment modalities to select from, yet the appropriate choice of therapy is not forthright. Treatment often depends on a number of different factors related to the patient, stricture, as well as endoscopist experience.

There are various causes of esophageal strictures. Benign etiologies include peptic strictures, Schatzki's ring, anastomotic strictures, radiation-induced strictures, and eosinophilic esophagitis, among others (Fig. 12.1). Malignant causes of esophageal strictures are more commonly intrinsic from tumor growth but can also be extrinsic, such as from lymphadenopathy or lung cancer that compresses the esophagus [35].

The principle indication for endoscopic therapy in the treatment of esophageal strictures is the presence of dysphagia, whether the lesion is caused by benign or malignant etiologies. In patients with clinical complaints indicating esophageal obstruction, an initial esophagogastroduodenoscopy with therapeutic intent is less costly than a barium swallow [10]. However, imaging esophageal strictures prior to endoscopic therapy is complementary and provides crucial information regarding characteristics of the stricture to aid in formulating a therapeutic plan. Further, it can exclude alternative diagnoses that would not benefit from endoscopic therapy such abnormalities of esophageal motility.

Since the treatments of benign and malignant strictures differ to an extent, we have accordingly divided the chapter into two sections.

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Management of Benign Esophageal Strictures

When approaching a patient with a benign esophageal stricture, it is important to classify the stricture as simple or complex. Simple strictures are short (<2 cm), focal, and straight and allow passage of a normal caliber endoscope. Complex strictures are longer (>2 cm), angulated, irregular, and significantly narrowed (Fig. 12.2). Simple strictures are generally easier to manage, while complex strictures may require auxiliary tools such as fluoroscopy, smaller caliber endoscopes, repeat dilations, or, in rare cases, esophageal stenting [51].

Esophageal Dilation

Indications

The mainstay of therapy for symptomatic benign esophageal strictures is dilation with the primary intent of relieving dysphagia. Simple strictures have an adequate response to esophageal dilation with most requiring 1–3 dilations to alleviate symptoms, though recurrent strictures can occur in up to 35% of patients [40]. Peptic disease accounts for the majority of these benign simple strictures, but the incidence and recurrence rate is decreasing with the widespread use of proton pump inhibitors [16, 55]. Other etiologies of benign simple strictures amenable to dilation include Schatzki's ring or webs.

Esophageal dilation also has a role in the management of complex strictures, although this can be more challenging. Complex strictures are often refractory to dilation and frequently require fluoroscopic guidance to visualize passage of a guidewire across the stricture. Esophageal dilation is not as effective in the management of malignant strictures as a sole intervention but rather is used as an ancillary therapy to assist in endoscopic ultrasound or esophageal stent placement [41].

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Fig. 12.1 Causes of esophageal strictures

Practical Considerations

- Categorize strictures before pursuing dilation.
- Simple strictures have the best response rate to dilation.
- Wire and fluoroscopy are useful in treating complex strictures.

Indications

- Relief of dysphagia caused by esophageal strictures
- Treatment of simple esophageal strictures
- Treatment of complex esophageal strictures

Evaluation and Preparation

Pre-procedural planning is critical when approaching esophageal strictures. A thorough history and physical examination can provide cues to the underlying diagnosis in the majority of cases [4]. If available, a barium esophagram also affords key information to aid in planning: the stricture's location (proximal or distal), whether it is simple or complex, if there are alternative diagnoses, or if there is an underlying motility disorder. General anesthesia with endotracheal intubation should be considered in cases of proximal strictures in order to protect the patient's airway or if a prolonged procedure is anticipated to maintain patient comfort. Additionally, fluoroscopic assistance is worthwhile when approaching complex strictures or guidewire placement. Prior to starting the procedure, familiarity with the operating equipment is also paramount to be able to troubleshoot in the event of a malfunction.

Instruments and Accessories

The use of esophageal dilation was described as early as the seventeenth century when a piece of carved whalebone with a sponge attached to the distal end was used in patients with achalasia [56]. In current practice, there are three dilator types currently being utilized: bougies (Maloney or Hurst), wire-guided polyvinyl dilators (Savary-Gilliard or American), and through-the-scope (TTS) balloon dilators (Fig. 12.3). Bougies and wire-guided polyvinyl dilators are considered mechanical dilators. Mechanical and balloon dilators have different mechanisms of action. Mechanical dilators exert both a radial and longitudinal force upon the stricture, whereas TTS balloon dilators only apply a radial force. Despite this difference in expansile forces, there is no data establishing the superiority of one dilator type over another [6, 45, 49, 61].

Maloney dilators have a tapered tip and are normally used without fluoroscopic guidance though they can be passed under fluoroscopy if desired. When passed blindly they confer a higher risk of perforation thus should be reserved for patients with simple strictures with a minimal diameter of 12–14 mm [17].

A guidewire distal to the stricture, preferably in the gastric antrum, is necessary for use of Savary or American dilators. The dilator is then advanced over the wire.

TTS balloon dilators are available in single or multiple sizes and can be used with or without a guidewire. Neither the Savary nor the TTS balloon dilators require fluoroscopy for use, but it is advantageous in confirming guidewire placement and stricture characterization.

Practical Considerations

- The type of dilator is usually selected based upon endoscopist experience/preference.
- There is no superiority of one dilator type over another.
- Fluoroscopy is useful in confirming guidewire placement and characterizing strictures.

Instruments and Accessories

- Upper endoscope
- Bougie or wire-guided polyvinyl or TTS balloon dilator
- Guidewire
- Iodine-based contrast media

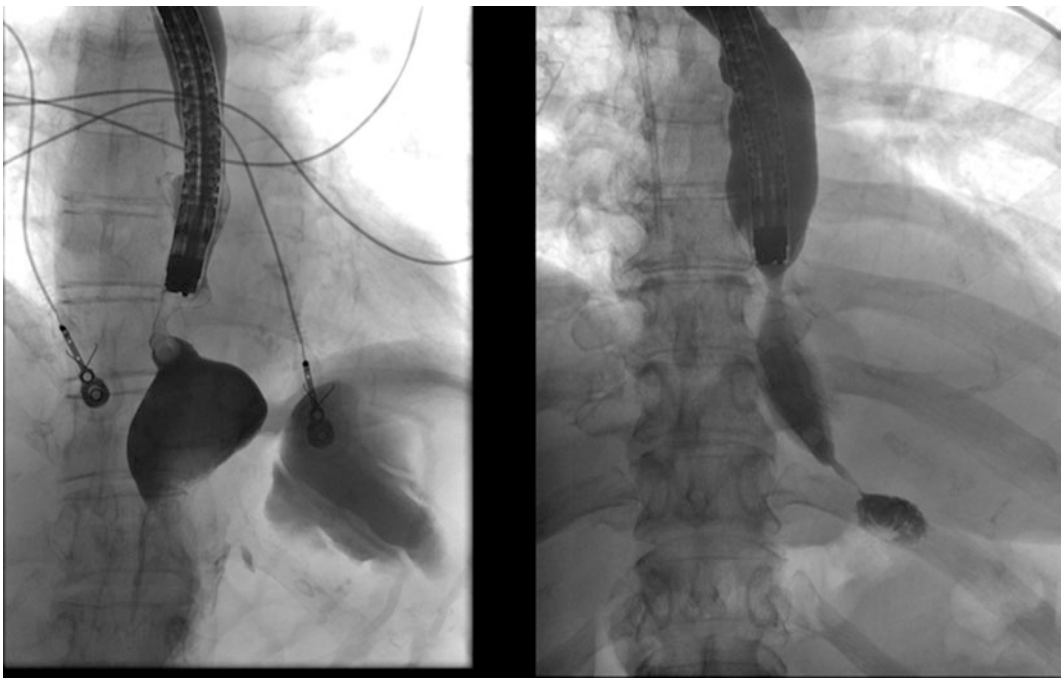

Fig. 12.2 These are fluoroscopic images of a simple stricture (*left*) just above the gastroesophageal junction and a high grade, complex (*right*) stricture

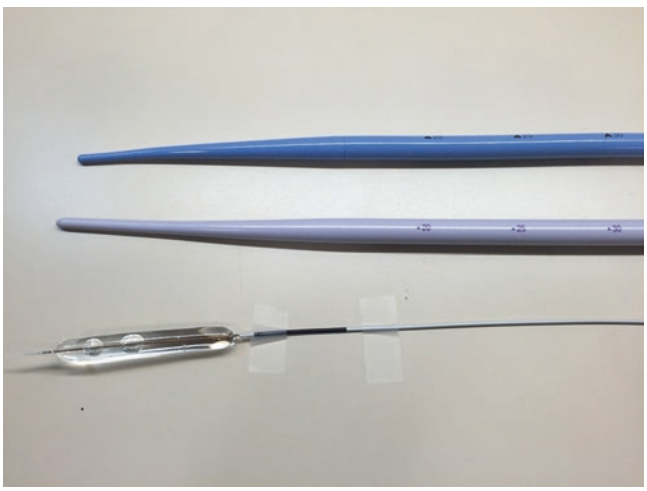

Fig. 12.3 Pictured (*bottom* to *top*) are the distal portions of a bougie, savary, and TTS balloon dilator

Technique: Mechanical and TTS Balloon Dilators

The "rule of three" is a widely accepted principle describing the extent to which dilation should be performed in one session [33]. It dictates that no more than three dilators of progressively increasing diameter should be used during one procedure, thereby minimizing the risk of complications.

The procedure begins with passage of the upper endoscope and visualization of the stricture while calculating an estimated diameter of the lesion. If mechanical dilation is the preferred method, the first dilator chosen is based on the diameter of the stricture. A gauge to use in calculating the diameter of the stricture is the width of the distal portion of the diagnostic gastroscope, most of which range from 8 to 9 mm. If a guidewire is not used, the endoscope is then removed. To ease passage of the dilator through the upper esophageal sphincter, lubricant is applied to the tapered portion of the dilator, and the patient's head is slightly extended. The dilator is then blindly passed. While doing this, assess for resistance to passage of the dilator and the presence of blood on the device after removal. If moderate resistance is encountered, this suggests appropriate dilator size, and two subsequently larger dilations in 1 mm increments can safely be performed during that session.

If the mechanical dilator is being passed over a guidewire, the guidewire is passed through the accessory channel of the endoscope past the stricture and ideally into the stomach. If the scope cannot traverse the stricture, then fluoroscopy should be used to confirm wire placement. Subsequently, the endoscope is withdrawn carefully while simultaneously feeding the wire to maintain its position. As the distal portion of the endoscope is removed, the wire is grasped at the patient's mouth, and the dilator is loaded onto the back of the wire. The dilator is then passed while holding the guidewire in place. It is removed in similar fashion to the endoscope while maintaining wire position so subsequent dilations can be performed. After completion, the dilator and guidewire are concurrently removed.

Unlike mechanical dilation, TTS balloon dilation is performed through the endoscope. The endoscope is positioned just proximal to the stricture in order to stabilize the balloon

during inflation. The dilator is then passed through the working channel of the endoscope into the stricture. This can be done with direct vision, or in cases of complex or challenging strictures, this can be accomplished with a guidewire and/or fluoroscopic guidance. Ideal balloon placement is in the middle of the stricture, and prior to inflation the balloon sheath should be held tightly with the operator's fingers for additional stability. The technician then inflates the balloon to the pressure which corresponds to the chosen diameter. There are no established criteria for the length of time the balloon should be inflated to achieve optimal dilation, but 30–60 s is likely adequate. The "rule of three" was meant to be applied to bougie-type dilators, but an equivalent principle can be applied to balloon dilation where data supports incremental dilator of sizes greater than 2 mm or a single large dilator (≥15 mm) in one session when treating a simple esophageal stricture (Fig. 12.4) [32].

Practical Considerations

- Follow the "rule of three."
- The feel of the operator in gauging the resistance of the stricture is necessary in mechanical dilation.
- Using the width of your gastroscope is helpful in estimating stricture diameter.

Mechanical Dilation with Guidewire

- Visualize stricture and calculate diameter using endoscope ± fluoroscopy.
- Pass guidewire through the working channel past the stricture.
- Slowly remove endoscope while feeding guidewire and maintaining its position.
- As endoscope is completely removed, grasp guidewire at the patient's mouth.
- Apply lubricant to the tapered portion and backload the dilator onto the guidewire.
- Slightly extend patient neck and pass the dilator while holding the guidewire in place.
- Assess for resistance while passing the stricture; remove dilator (maintain guidewire position) and evaluate for presence of blood.
- If moderate resistance and/or presence of blood, then repeat steps with two subsequently large dilator sizes.

Mechanical Dilation Without Guidewire

- Visualize stricture and calculate diameter using endoscope ± fluoroscopy.
- Remove endoscope and lubricate tapered portion of first dilator.
- Slightly extend patient neck and blindly insert dilator.
- Assess for resistance while passing the stricture; remove dilator and evaluate for presence of blood.
- If moderate resistance and/or presence of blood, then repeat steps with two subsequently large dilator sizes.

Through-the-Scope Balloon Dilation

- Visualize stricture and calculate diameter using endoscope ± fluoroscopy.
- If using a guidewire, then pass it through the working channel past the stricture.
- Pass the balloon dilator through the working channel and confirm its placement by visualization and/or fluoroscopy.
- Technician should inflate the balloon to the pressure that correlates to the chosen diameter, maintaining it for 30–60 s.

Complications and Contraindications

An in-depth discussion with patients regarding the risks of esophageal dilation is advisable. The most concerning complication of esophageal dilation is perforation, with a risk of 0.1–0.4% [17, 26, 36, 54]. The features of strictures with a higher risk of perforation during dilation include angulations, irregularities, longer length, or high-grade strictures by which a normal caliber endoscope cannot pass [17]. Radiation-induced and caustic strictures also portend a higher risk [5, 42]. Endoscopist experience may have an impact on perforation rate, with data suggesting that the rate of perforation is four times greater when the performing physician has less than 500 diagnostic upper endoscopies [43]. Clinical symptoms suggestive of a perforation include persistent pain, fever, shortness of breath, or tachycardia; physical examination may reveal subcutaneous crepitus of the chest. If suspected, a chest radiograph may be the initial test of choice, but a negative x-ray does not exclude the diagnosis.

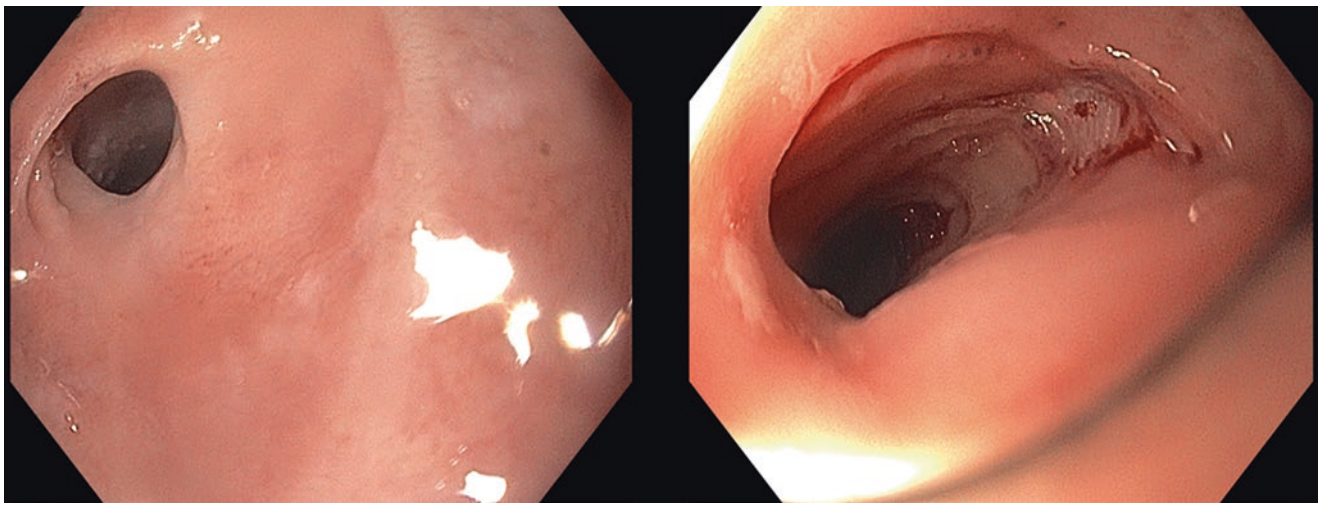

Fig. 12.4 These are before and after endoscopic photos of a TTS balloon dilation of a simple stricture to 12 mm

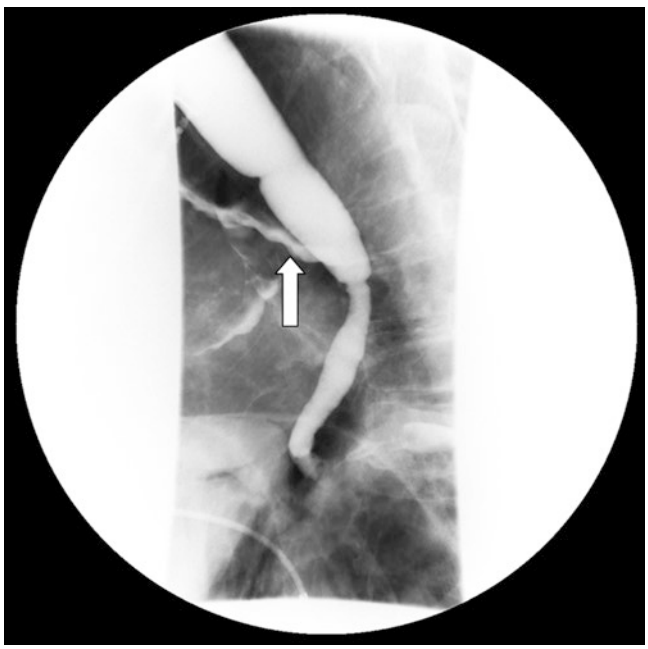

Fig. 12.5 This barium swallow illustrates a perforation in the mid esophagus following esophageal dilation

Practical Considerations

- Complex strictures have a higher risk of perforation.
- Anastomotic strictures are particularly difficult to treat and may require repeat dilation.
- Any alarm symptoms should prompt urgent imaging to identify procedural complications.

Complications

- Perforation
- Bleeding
- Bacteremia
- Aspiration
- Death

Contraindications

- Recent esophageal perforation
- Bleeding diathesis (if not correctable prior to dilation)

A water-soluble esophagram or contrast chest computed tomogram may be ultimately required to identify this complication (Fig. 12.5) [57]. A working relationship with a thoracic surgeon is vital in the event of a perforation.

Other major complications include hemorrhage, bacteremia, and aspiration. While the rate of serious hemorrhage is 0.4% [54], it can occur to a milder extent after successful dilation [49]. An acute or recently healed esophageal perforation is a contraindication to esophageal dilation. Caution should also be exercised when considering patients with severe cardiac disease, compromised pulmonary function, or a propensity for bleeding.

Refractory Esophageal Strictures

Although dilation is usually successful in relieving dysphagia caused by benign esophageal strictures, recurrent and

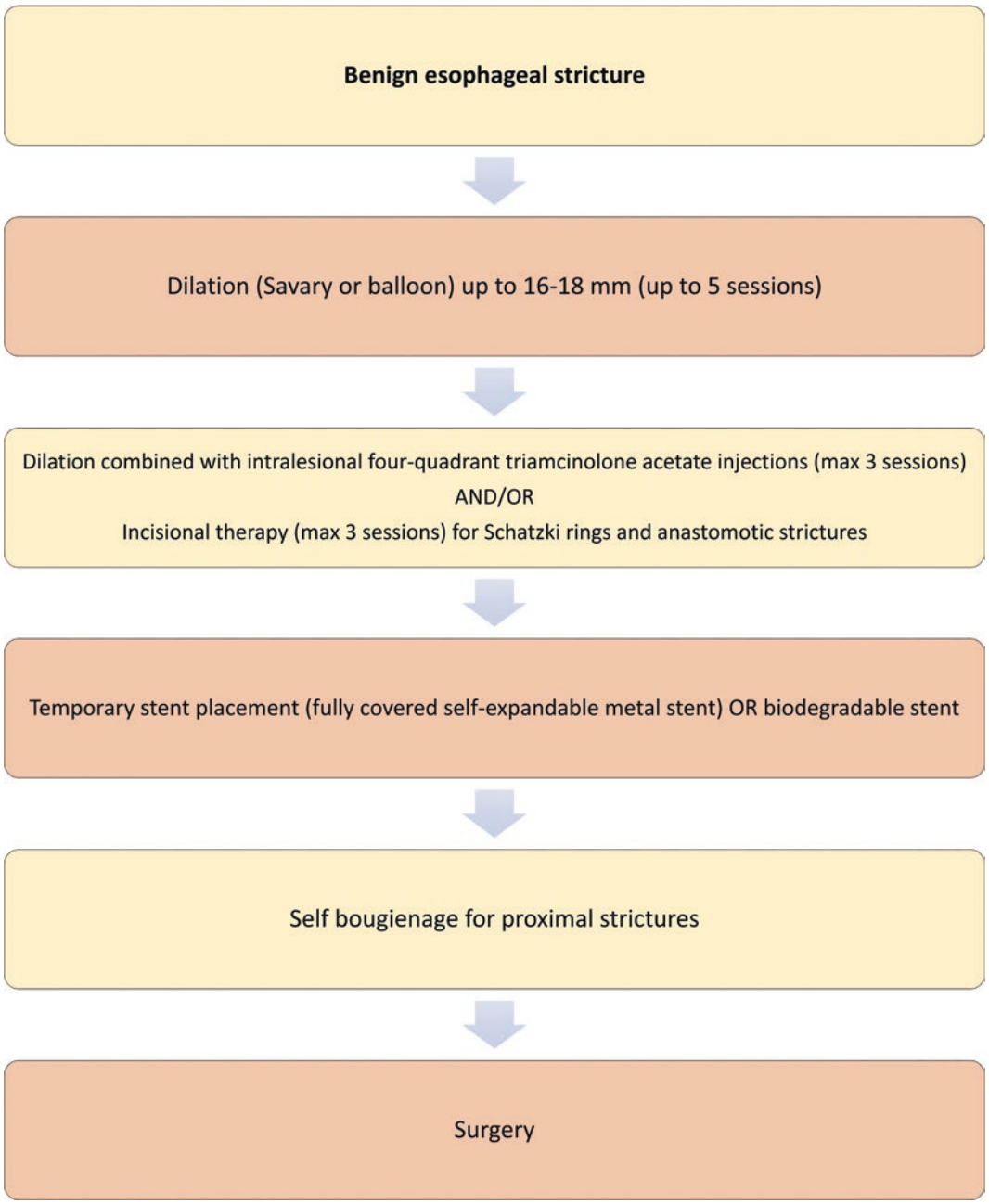

Fig. 12.6 A proposed treatment algorithm for refractory benign esophageal strictures [8]

refractory strictures pose a treatment challenge. A recurrent esophageal stricture is defined by when a target esophageal diameter of 14 mm has been achieved by dilation, and the stricture subsequently returns. Refractory strictures are those that are not even able to be dilated to 14 mm over five sessions at 2-week intervals. These definitions are not meant to include patients with an inflammatory stricture or those with impairment in underlying neuromuscular dysfunction [31]. Approaching these strictures may require dilation combined with adjunct therapy such as corticosteroid injections, esophageal stenting, incisional therapy, self-dilation, or surgery [53]. Anastomotic strictures, radiation therapy, caustic ingestion, and photodynamic therapy are common culprits of refractory strictures [35]. Figure 12.6 illustrates an algorithm proposed by Wijkerslooth et al. for approaching refractory esophageal strictures.

Corticosteroid Injections

Steroid injection for the treatment of scars and keloids is a therapy that dates back to 1966 with the use of triamcinolone

acetonide [14, 27]. The formation of benign esophageal strictures is via a similar mechanism as scars – the deposition of collagen and fibrous tissue. Thus, intralesional steroids were applied to esophageal strictures, but the results have been inconsistent over the decades. Early data demonstrated promising results in patients with peptic strictures, but many of these studies were small and uncontrolled [21, 29, 30]. However, more recent data in peptic strictures suggests a decrease in the need for repeat dilation and the average time to repeat dilation in patients that received intralesional steroids when compared to placebo [44].

Intralesional steroid injections have not demonstrated as promising results in benign strictures of other etiologies. When administered to patients with caustic strictures, steroid injection did not impact dilation frequency or recurrent dysphagia when compared to placebo [2]. Similarly, intralesional triamcinolone did not provide a decrease in the frequency of repeat dilations or prolongation of the dysphagia-free period in patients with benign anastomotic esophagogastric strictures following esophagectomy [19]. The lack of efficacy of intralesional steroids in anastomotic strictures compared to peptic strictures is likely due to the pathogenesis of stricture formation. Anastomotic strictures are a result of ischemic, whereas peptic strictures develop from inflammation and ulceration from acid reflux [22]. This is a somewhat foreseeable outcome given that steroids are presumed to inhibit the inflammatory response.

There are no standardized recommendations regarding dose or drug concentration. Steroids are administered prior to dilation with mechanical or balloon dilators. Triamcinolone acetonide is injected via a sclerotherapy needle in four quadrants of 0.5 mL per injection at concentrations of 20–40 mg/mL [29, 44].

Esophageal Stent Placement

Esophageal prosthesis placement has been increasingly utilized for treatment of refractory benign esophageal strictures. Options include partially and fully covered self-expandable metal stents (SEMS), self-expandable plastic stents (SEPS), and biodegradable stents.

Uncovered SEMS were the first to be utilized for the treatment of refractory benign esophageal strictures; however they were associated with major complications. Early data suggested ingrowth of granulation tissue through the mesh occurred as early as 2–6 weeks after stent placement and resulted in recurrent obstruction in up to 40% of patients [7, 11]. Further, this risk of tissue ingrowth increases over time. Other common complications from esophageal stents include stent migration, pain, gastroesophageal reflux if the stent is across the gastroesophageal junction, and fistula formation [20]. To address the issue of tissue ingrowth and removability, more recently, partially covered and fully covered SEMS are the most commonly employed types. While this decreases the problem of ingrowth, these covered stents are more prone to migration.

While excessive tissue ingrowth can cause recurrent symptoms and obstruction, minor ingrowth may reduce the risk of stent migration by embedding into the mucosa [37]. This accounts for the widely reported higher migration rates of fully covered stents. If encountered, excessive tissue ingrowth can be treated with stent-in-stent placement of a fully covered stent with a size equal to or slightly larger than the originally placed partially covered stent [18].

Data on the use of fully covered SEMS for benign esophageal strictures is limited. There have been a few small studies with varying results. Eloubeidi et al. reported a clinical success rate of 29% in 31 patients over a 16-month period [9]. A retrospective study in seven patients with refractory stricture reported that none of these patients were adequately treated and half experienced stent migration [1]. Evaluation of the fully covered Wallflex (Boston Scientific) in 15 patients with refractory benign esophageal strictures also demonstrated lackluster results with a migration rate of 35% and recurrence of dysphagia after a median of 15 days after stent removal.

SEPS has been considered as an alternative to SEMS to minimize recurrence from ingrowth of granulation tissue. It is thus easily removable and FDA approved for the treatment of benign esophageal strictures. The available SEPS is the Polyflex stent (Boston Scientific), a fully covered stent composed of silicone and polyester. A systemic review of 172 patients with benign esophageal stricture who underwent SEPS placement describes a technical success rate of 98%, clinical success rate of 45%, and early stent migration rate of 31%, necessitating frequent reintervention [15]. The disadvantages to this stent are that the deployment system is labor intensive, requires assembly, and is quite bulky.

Given these less favorable outcomes with SEPS, biodegradable stents were developed as an alternative. Currently available ones include ELLA BD stent (ELLA CS) which is composed of polydioxanone, a material used to make surgical sutures, and (PLLA)-BD stent (Marui Textile Machinery), consisting of knitted poly-L-lactic acid monofilaments. These stents are not approved by the Food and Drug Administration for use in the United States. The advantage over the SEPS stent is that it does not require removal, even when migrated. These stents are degraded by hydrolysis after about 4–5 weeks and dissolve by about 2–3 months. The low pH gastric environment accelerates the process of hydrolysis [58]. Results of the (PLLA)-BD stent demonstrated a 70% migration rate within 10–21 days after insertion [46, 47, 59]. In contrast, the ELLA-BD stent has more promising results. It has an uncovered design and can thus embed in the mucosa much like the SEMS. Nine studies of the ELLA-BD stent report a clinical success rate of 47% and a migration rate of 21% [15].

There are no studies that establish superiority of SEPS and biodegradable stents over SEMS, yet each stent has their own merits. Factors to consider when choosing a stent for this indication include cost, availability, endoscopist experience, patient preference, and stricture characteristics. Larger prospective studies comparing biodegradable stents with SEMS are needed.

Incisional Therapy

Refractory anastomotic strictures can occur commonly following gastrointestinal surgery, with an incidence of 2–30% [22, 25, 48]. Incisional therapy offers an alternative to repeat dilations. Used as an adjunct to dilation, this can be performed with a needle knife or with a polypectomy snare with additional argon plasma coagulation. It has demonstrated safety and efficacy in simple, short (<10 mm) anastomotic strictures that were refractory to dilation [23]. It was also effective in patients who were dilation naïve. In a study of 24 patients with anastomotic strictures who had not undergone previous dilation, 87.5% of patients remained free of dysphagia after one treatment [34]. When incisional therapy was compared directly to Savary dilation, no significant difference was detected in success rates [24]. Thus in cases of short, fibrotic strictures, such as those at an anastomotic site, incisional therapy is a safe alternative to dilation.

Management of Malignant Esophageal Strictures

Malignant esophageal strictures can be from extrinsic or intrinsic causes, the latter of which is more common (Fig. 12.7). The goal of endoscopic therapy in malignant esophageal strictures is palliation, namely, the relief of dysphagia. This goal is most commonly pursued via esophageal stent placement, though other options exist including brachytherapy, photodynamic therapy, dilation, and chemical injection therapy, among others. As previously mentioned, dilation of malignant strictures generally serves as an adjunct to perform endoscopic ultrasound for staging, as a temporary palliative therapy prior to surgery, to assist in the placement of SEMS or in laser photoablation [35].

SEPS were initially used more commonly for malignant strictures, but due to their high complication rate, including perforation and device migration, there has been a trend toward usage of metal stents [28]. Specifically, partially and fully covered SEMS offer better long-term palliation than uncovered SEMS because of decreased rates of tumor ingrowth and subsequent necessity for reintervention [60]. However, fully covered stents avoid tumor ingrowth at the expense of a higher migration rate since the stent does not embed in the mucosa. A retrospective comparison of partially covered SEMS and fully covered SEMS demonstrated equal efficacy at relieving dysphagia but a significantly higher migration rate in the fully covered stents (37.5% vs. 9.1%) and a higher rate of tissue ingrowth in the partially covered group (53.4% vs. 29.1%) [50]. Fully covered SEMS have also been examined in the neoadjuvant setting. In a prospective study of 55 patients with locally advanced esophageal cancer undergoing neoadjuvant therapy, fully covered SEMS improves dysphagia and allows for oral nutrition. Though the migration rate was 31%, this actually represented a positive response to neoadjuvant therapy, and only 1 of 17 patients experienced recurrent dysphagia.

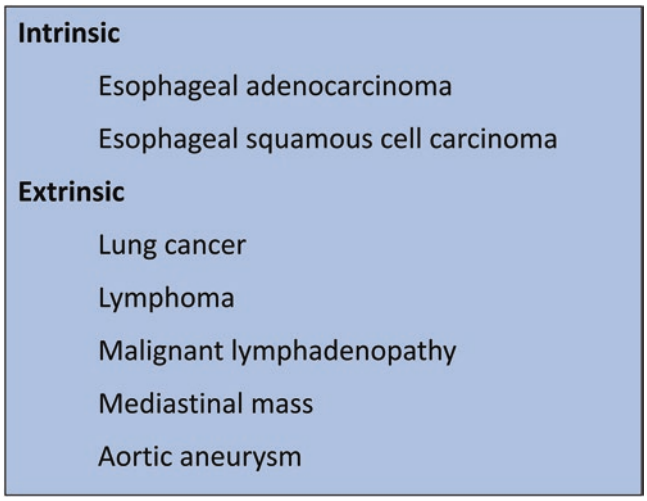

Fig. 12.7 Causes of malignant esophageal stricture

Photodynamic Therapy

Another palliative modality for treatment of malignant esophageal strictures is photodynamic therapy (PDT). This is a two-part treatment that initially requires intravenous infusion of a photosensitizing agent, a hematoporphyrin derivative, followed by upper endoscopy with exposure of the malignant cells to produce free radicals and subsequently cause tissue necrosis of the exposed area.

PDT has uses in multiple clinical scenarios. For patients with advanced esophageal carcinoma, it is an effective palliative measure with a mean survival of 9.2 months after therapy [38]. Patients with early-stage disease, both adenocarcinoma and squamous cell carcinoma, who are not operative candidates also benefit from PDT with a complete response rate of 87% when PDT was used in conjunction with another modality or as sole therapy; the 5-year disease-specific survival rate was 74% [52]. It can also aid in addressing tumor regrowth through a previously placed esophageal stent. Further, in patients with squamous cell carcinoma who failed prior chemotherapy, PDT provided a clinical response in 76% of patients and a 48-month progression-free survival of 40% [62].

Subsequent to therapy, patients are required to avoid exposure to sunlight for at least 4–6 weeks to minimize potential for skin photosensitivity, which occurs in up to 20% of patients [39]. Common side effects include dysphagia and chest pain, which gradually resolve, or esophageal stricture formation. Rare complications include bleeding or perforation.

Final Words

- A detailed history and physical examination is paramount in the evaluation of a patient with a suspected esophageal stricture.
- Be familiar with the various types of dilators and utilize all the tools at your disposal, such as fluoroscopy and a guidewire.
- Complex strictures may require more advanced techniques and tools.
- Know your personal limitations when pursuing more complex strictures, and refer to a tertiary care center if necessary.

Cryotherapy

Cryotherapy is one of the newer palliative options for malignant esophageal strictures, first described in 2007 in squamous cell carcinoma [3]. This uses liquid nitrogen distributed on mucosa through a low-pressure device significantly reducing temperatures down to −196 °C, inducing apoptosis and causing cryonecrosis of targeted tissue [12]. In a retrospective cohort of 79 patients with esophageal carcinoma who had either failed or were ineligible for conventional therapy, a complete intraluminal response was seen in 63% of patients who completed therapy. Formation of benign esophageal strictures was noted in ten patients, though all of these had undergone previous endoscopic therapy. The most common side effect of this therapy is post-procedural pain requiring analgesia [13].

Conclusion

Approaching esophageal strictures is a deliberate endeavor. It commences with a detailed history and physical examination followed by complementary imaging to determine the underlying cause and characterize the lesion. The most common modality used is esophageal dilation, either by mechanical or balloon devices, but more complex strictures may require the use of fluoroscopy or a guidewire. Refractory or recurrent strictures are more challenging entities and may necessitate repeat dilations, corticosteroid injection, incisional therapy, or esophageal stenting, which is the palliative intervention of choice for malignant esophageal strictures.

References

1. Bakken JC, Wong Kee Song LM, de Groen PC, Baron TH. Use of a fully covered self-expandable metal stent for the treatment of benign esophageal diseases. Gastrointest Endosc. 2010;72:712–20. doi:10.1016/j.gie.2010.06.028.
2. Camargo MA, Lopes LR, Grangeia Tde A, et al. Use of corticosteroids after esophageal dilations on patients with corrosive stenosis: prospective, randomized and double-blind study. Rev Assoc Méd Bras. 2003;49:286–92. doi:10.1590/S0104-42302003000300033.
3. Cash BD, Johnston LR, Johnston MH. Cryospray ablation (CSA) in the palliative treatment of squamous cell carcinoma of the esophagus. World J Surg Oncol. 2007;5:34. doi:10.1186/1477-7819-5-34.
4. Castell DO, Donner MW. Evaluation of dysphagia: a careful history is crucial. Dysphagia. 1987;2:65–71.
5. Clouse RE. Complications of endoscopic gastrointestinal dilation techniques. Gastrointest Endosc Clin N Am. 1996;6:323–41.
6. Cox JG, Winter RK, Maslin SC, et al. Balloon or bougie for dilatation of benign esophageal stricture? Dig Dis Sci. 1994;39:776–81.
7. Cwikiel W, Willén R, Stridbeck H, et al. Self-expanding stent in the treatment of benign esophageal strictures: experimental study in pigs and presentation of clinical cases. Radiology. 1993;187:667–71. doi:10.1148/radiology.187.3.8497612.
8. de Wijkerslooth LRH, Vleggaar FP, Siersema PD. Endoscopic management of difficult or recurrent esophageal strictures. Am J Gastroenterol. 2011;106:2080–2091.; quiz 2092. doi:10.1038/ajg.2011.348.
9. Eloubeidi MA, Lopes TL. Novel removable internally fully covered self-expanding metal esophageal stent: feasibility, technique of removal, and tissue response in humans. Am J Gastroenterol. 2009;104:1374–81. doi:10.1038/ajg.2009.133.
10. Esfandyari T, Potter JW, Vaezi MF. Dysphagia: a cost analysis of the diagnostic approach. Am J Gastroenterol. 2002;97:2733–7. doi:10.1111/j.1572-0241.2002.07061.x.
11. Fiorini A, Fleischer D, Valero J, et al. Self-expandable metal coil stents in the treatment of benign esophageal strictures refractory to conventional therapy: a case series. Gastrointest Endosc. 2000;52:259–62. doi:10.1067/mge.2000.107709.
12. Graña L, Ablin RJ, Goldman S, Milhouse E. Freezing of the esophagus: histological changes and immunological response. Int Surg. 1981;66:295–301.
13. Greenwald BD, Dumot JA, Abrams JA, et al. Endoscopic spray cryotherapy for esophageal cancer: safety and efficacy. Gastrointest Endosc. 2010;71:686–93. doi:10.1016/j.gie.2010.01.042.
14. Griffith BH. The treatment of keloids with triamcinolone acetonide. Plast Reconstr Surg. 1966;38:202–8.
15. Ham YH, Kim GH. Plastic and biodegradable stents for complex and refractory benign esophageal strictures. Clin Endosc. 2014;47:295–300. doi:10.5946/ce.2014.47.4.295.
16. Hands LJ, Papavramidis S, Bishop H, et al. The natural history of peptic oesophageal strictures treated by dilatation and antireflux therapy alone. Ann R Coll Surg Engl. 1989;71:306–10.
17. Hernandez LJ, Jacobson JW, Harris MS. Comparison among the perforation rates of Maloney, balloon, and savary dilation of esophageal strictures. Gastrointest Endosc. 2000;51:460–2. doi:10.1016/S0016-5107(00)70448-2.
18. Hirdes MMC, Siersema PD, Houben MHMG, et al. Stent-in-stent technique for removal of embedded esophageal self-expanding

metal stents. Am J Gastroenterol. 2011;106:286–93. doi:10.1038/ajg.2010.394.
19. Hirdes MMC, van Hooft JE, Koornstra JJ, et al. Endoscopic corticosteroid injections do not reduce dysphagia after endoscopic dilation therapy in patients with benign esophagogastric anastomotic strictures. Clin Gastroenterol Hepatol. 2013;11:795–801.e1. doi:10.1016/j.cgh.2013.01.016.
20. Hirdes MMC, Vleggaar FP, Siersema PD. Stent placement for esophageal strictures: an update. Expert Rev Med Devices. 2011;8:733–55. doi:10.1586/erd.11.44.
21. Holder TM, Ashcraft KW, Leape L. The treatment of patients with esophageal strictures by local steroid injections. J Pediatr Surg. 1969;4:646–53.
22. Honkoop P, Siersema PD, Tilanus HW, et al. Benign anastomotic strictures after transhiatal esophagectomy and cervical esophagogastrostomy: risk factors and management. J Thorac Cardiovasc Surg. 1996;111:1141–6; discussion 1147–1148
23. Hordijk ML, Siersema PD, Tilanus HW, Kuipers EJ. Electrocautery therapy for refractory anastomotic strictures of the esophagus. Gastrointest Endosc. 2006;63:157–63. doi:10.1016/j.gie.2005.06.016.
24. Hordijk ML, van Hooft JE, Hansen BE, et al. A randomized comparison of electrocautery incision with Savary bougienage for relief of anastomotic gastroesophageal strictures. Gastrointest Endosc. 2009;70:849–55. doi:10.1016/j.gie.2009.02.023.
25. Johansson J, Zilling T, von Holstein CS, et al. Anastomotic diameters and strictures following esophagectomy and total gastrectomy in 256 patients. World J Surg. 2000;24:78–84. discussion 84–85
26. Karnak I, Tanyel FC, Büyükpamukçu N, Hiçsönmez A. Esophageal perforations encountered during the dilation of caustic esophageal strictures. J Cardiovasc Surg. 1998;39:373–7.
27. Ketchum LD, Smith J, Robinson DW, Masters FW. The treatment of hypertrophic scar, keloid and scar contracture by triamcinolone acetonide. Plast Reconstr Surg. 1966;38:209–18.
28. Knyrim K, Wagner H-J, Bethge N, et al. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. N Engl J Med. 1993;329:1302–7. doi:10.1056/NEJM199310283291803.
29. Kochhar R, Makharia GK. Usefulness of intralesional triamcinolone in treatment of benign esophageal strictures. Gastrointest Endosc. 2002;56:829–34. doi:10.1067/mge.2002.129871.
30. Kochhar R, Ray JD, Sriram PV, et al. Intralesional steroids augment the effects of endoscopic dilation in corrosive esophageal strictures. Gastrointest Endosc. 1999;49:509–13.
31. Kochman ML, McClave SA, Boyce HW. The refractory and the recurrent esophageal stricture: a definition. Gastrointest Endosc. 2005;62:474–5. doi:10.1016/j.gie.2005.04.050.
32. Kozarek RA, Patterson DJ, Ball TJ, et al. Esophageal dilation can be done safely using selective fluoroscopy and single dilating sessions. J Clin Gastroenterol. 1995;20:184–8.
33. Langdon DF. The rule of three in esophageal dilation. Gastrointest Endosc. 1997;45:111.
34. Lee TH, Lee S-H, Park J-Y, et al. Primary incisional therapy with a modified method for patients with benign anastomotic esophageal stricture. Gastrointest Endosc. 2009;69:1029–33. doi:10.1016/j.gie.2008.07.018.
35. Lew RJ, Kochman ML. A review of endoscopic methods of esophageal dilation. J Clin Gastroenterol. 2002;35:117–26.
36. Mandelstam P, Sugawa C, Silvis SE, et al. Complications associated with esophagogastroduodenoscopy and with esophageal dilation. Gastrointest Endosc. 1976;23:16–9.
37. Mayoral W, Fleischer D, Salcedo J, et al. Nonmalignant obstruction is a common problem with metal stents in the treatment of esophageal cancer. Gastrointest Endosc. 2000;51:556–9.
38. McCaughan JS, Ellison EC, Guy JT, et al. Photodynamic therapy for esophageal malignancy: a prospective twelve-year study. Ann Thorac Surg. 1996;62:1005–1009.; discussion 1009–1010. doi:10.1016/0003-4975(96)00563-2.
39. Moghissi K, Dixon K. Photodynamic therapy (PDT) in esophageal cancer: a surgical view of its indications based on 14 years experience. Technol Cancer Res Treat. 2003;2:319–26.
40. Pereira-Lima JC, Ramires RP, Zamin I, et al. Endoscopic dilation of benign esophageal strictures: report on 1043 procedures. Am J Gastroenterol. 1999;94:1497–501. doi:10.1111/j.1572-0241.1999.01061.x.
41. Pfau PR, Ginsberg GG, Lew RJ, et al. Esophageal dilation for endosonographic evaluation of malignant esophageal strictures is safe and effective. Am J Gastroenterol. 2000;95:2813–5. doi:10.1111/j.1572-0241.2000.02309.x.
42. Poley J-W, Steyerberg EW, Kuipers EJ, et al. Ingestion of acid and alkaline agents: outcome and prognostic value of early upper endoscopy. Gastrointest Endosc. 2004;60:372–7.
43. Quine MA, Bell GD, McCloy RF, Matthews HR. Prospective audit of perforation rates following upper gastrointestinal endoscopy in two regions of England. Br J Surg. 1995;82:530–3.
44. Ramage JI, Rumalla A, Baron TH, et al. A prospective, randomized, double-blind, placebo-controlled trial of endoscopic steroid injection therapy for recalcitrant esophageal peptic strictures. Am J Gastroenterol. 2005;100:2419–25. doi:10.1111/j.1572-0241.2005.00331.x.
45. Saeed ZA, Winchester CB, Ferro PS, et al. Prospective randomized comparison of polyvinyl bougies and through-the-scope balloons for dilation of peptic strictures of the esophagus. Gastrointest Endosc. 1995;41:189–95.
46. Saito Y, Tanaka T, Andoh A, et al. Usefulness of biodegradable stents constructed of poly-l-lactic acid monofilaments in patients with benign esophageal stenosis. World J Gastroenterol. 2007;13:3977–80. doi:10.3748/wjg.v13.i29.3977.
47. Saito Y, Tanaka T, Andoh A, et al. Novel biodegradable stents for benign esophageal strictures following endoscopic submucosal dissection. Dig Dis Sci. 2008;53:330–3. doi:10.1007/s10620-007-9873-6.
48. Schlegel RD, Dehni N, Parc R, et al. Results of reoperations in colorectal anastomotic strictures. Dis Colon Rectum. 2001;44:1464–8.
49. Scolapio JS, Pasha TM, Gostout CJ, et al. A randomized prospective study comparing rigid to balloon dilators for benign esophageal strictures and rings. Gastrointest Endosc. 1999;50:13–7.
50. Seven G, Irani S, Ross AS, et al. Partially versus fully covered self-expanding metal stents for benign and malignant esophageal conditions: a single center experience. Surg Endosc. 2013;27:2185–92. doi:10.1007/s00464-012-2738-x.
51. Shami VM. Endoscopic management of esophageal strictures. Gastroenterol Hepatol. 2014;10:389–91.
52. Sibille A, Lambert R, Souquet JC, et al. Long-term survival after photodynamic therapy for esophageal cancer. Gastroenterology. 1995;108:337–44.
53. Siersema PD. Treatment options for esophageal strictures. Nat Clin Pract Gastroenterol Hepatol. 2008;5:142–52. doi:10.1038/ncpgasthep1053.
54. Silvis SE, Nebel O, Rogers G, et al. Endoscopic complications. Results of the 1974 American Society for Gastrointestinal Endoscopy Survey. JAMA. 1976;235:928–30.
55. Smith PM, Kerr GD, Cockel R, et al. A comparison of omeprazole and ranitidine in the prevention of recurrence of benign esophageal stricture. Restore Investigator Group. Gastroenterology. 1994;107:1312–8.
56. Spiess AE, Kahrilas PJ. Treating achalasia: from whalebone to laparoscope. JAMA. 1998;280:638–42. doi:10.1001/jama.280.7.638.
57. Standards of Practice Committee, Egan JV, Baron TH, et al. Esophageal dilation. Gastrointest Endosc. 2006;63:755–60. doi:10.1016/j.gie.2006.02.031.
58. Stivaros SM, Williams LR, Senger C, et al. Woven polydioxanone biodegradable stents: a new treatment option for benign and

malignant oesophageal strictures. Eur Radiol. 2010;20:1069–72. doi:10.1007/s00330-009-1662-5.
59. Tanaka T, Takahashi M, Nitta N, et al. Newly developed biodegradable stents for benign gastrointestinal tract stenoses: a preliminary clinical trial. Digestion. 2006;74:199–205. doi:10.1159/000100504.
60. Vakil N, Morris AI, Marcon N, et al. A prospective, randomized, controlled trial of covered expandable metal stents in the palliation of malignant esophageal obstruction at the gastroesophageal junction. Am J Gastroenterol. 2001;96:1791–6. doi:10.1111/j.1572-0241.2001.03923.x.
61. Yamamoto H, Hughes RW, Schroeder KW, et al. Treatment of benign esophageal stricture by Eder-Puestow or balloon dilators: a comparison between randomized and prospective nonrandomized trials. Mayo Clin Proc. 1992;67:228–36.
62. Yano T, Muto M, Minashi K, et al. Photodynamic therapy as salvage treatment for local failure after chemoradiotherapy in patients with esophageal squamous cell carcinoma: a phase II study. Int J Cancer. 2012;131:1228–34. doi:10.1002/ijc.27320.

Argon Plasma Coagulation in Gastroenterology

13

Theodore Rokkas

Introduction

Interventional procedures are a milestone in the evolution of digestive tract endoscopy. Argon plasma coagulation (APC) is a well-established technique included in the endoscopic armamentarium. This device is intended for thermal coagulation of tissues and originally APC developed as an alternative to laser in open and laparoscopic surgery [1]. Soon, APC was adapted for use in flexible endoscopy in the early 1990s [2]. Argon gas reaches the target tissue, in a nonconduct mode, using a flexible catheter which passes through the endoscopic biopsy channel. APC has revealed a remarkable spectrum of clinical applications, raising questions as to whether it could replace laser in clinical practice. The following advantages, among many, should be stressed: effective and safe coagulation, non-contact mode of action, marked desiccation, no destruction of metal stents, reduced smoke and vapor, and less expensive than laser. Most importantly, the ease in device handling makes it friendly to gastroenterologists, whereas no extended safety precautions are required. This chapter will mainly discuss the basic physical principles, equipment, and technique and the main applications of APC in gastroenterology.

Physical Principles

Basically, APC applies high-frequency (HF) current to tissue in a non-contact mode. This method entails substituting argon gas for the usual electric current used in other modalities, i.e., electrocautery. The entire device comprises an argon source, an HF current source, and the suitable applying catheter (Fig. 13.1a, b, and c). The APC catheter contains an electrode. As soon as sufficient HF voltage is generated between the first electrode and the tissue, argon gas flows out of the catheter and becomes ionized in the high-voltage electric field that has been created. Thus, argon gas is transformed to plasma beams, and HF current completes the electrical circuit via the second neutral electrode patch. The heat which is generated devitalizes, coagulates, desiccates, and ultimately shrinks the tissue (Fig. 13.1d). A desiccated tissue loses electric conductivity because of its higher electrical resistance [3, 4]. Hence the APC beam goes on to the next viable area. In this way, the whole area is uniformly desiccated and, most importantly, at the same depth. The depth is limited to 3 mm at most, depending upon the application time [1].The automatically limited depth, as well as the absence of tissue vaporization, is a safety guard against thin wall perforation. As a result, APC can barely remove large tumor masses.

Practical Considerations

- Despite other thermal coagulation methods, APC applies high-frequency (HF) current to tissue in a non-contact mode.
- The depth is limited to 3 mm at most, depending upon the application time.
- The automatically limited depth, as well as the absence of tissue vaporization, is a safety guard against thin wall perforation.

Equipment

The equipment consists of an APC unit, an electrosurgical generator, and APC instruments. There are three APC systems available on the market, i.e., the ERBE (Erbe Elektromedizin GmbH, Tübingen, and Erbe USA, Marietta, Ga), ConMed Electrosurgery (Englewood, Colo), and

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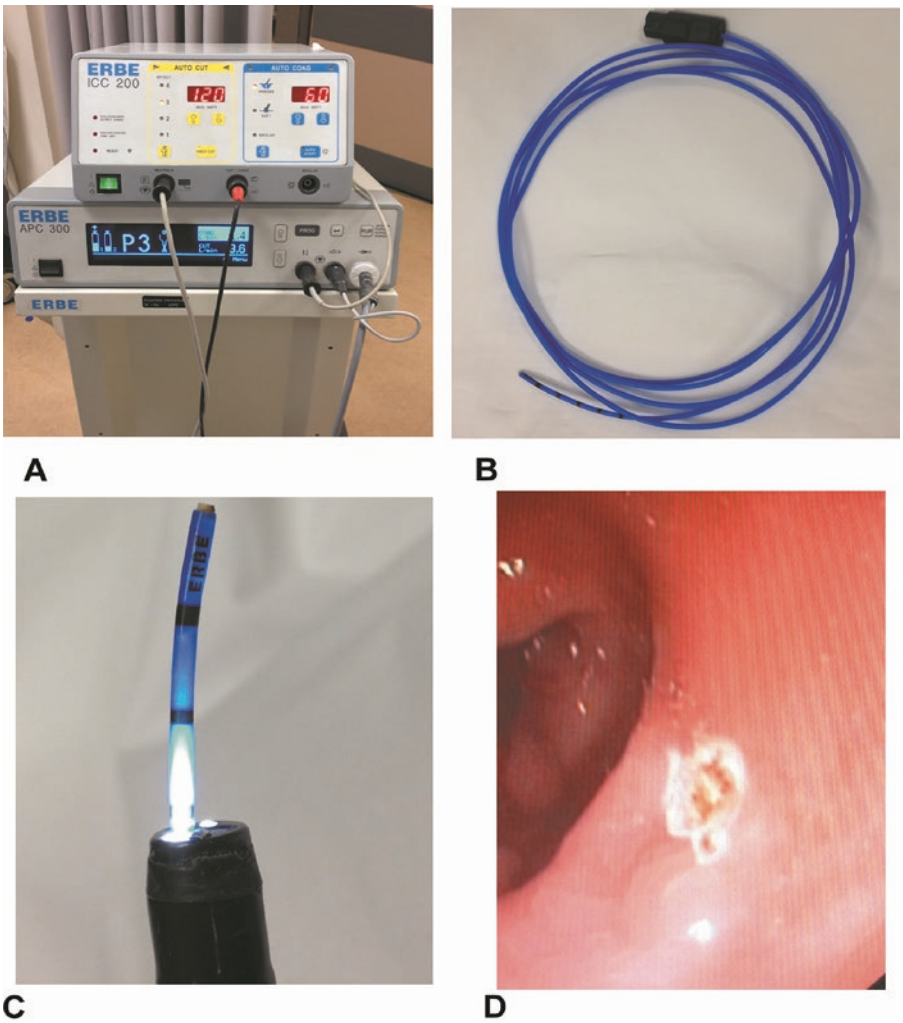

Fig. 13.1 (**a**) APC unit and electrosurgical generator. (**b**) Front firing flexible probe catheter. (**c**) Probe passing through endoscope. (**d**) APC application on colonic mucosa (effect on bleeding angiodysplasia)

Canady Technology (Pittsburgh, Pa). The most commonly used APC device and endoscopic catheters (front firing, side firing, and circumferential tips) are manufactured by ERBE. The whole APC apparatus is accompanied by a foot switch to activate both HF current source and gas. The catheters are disposable and covered with Teflon. Two sizes are available: 2.3 mm diameter and 2.2 m length and 3.2 mm diameter and 2.2 m length. The ERBE argon flow varies from 0.1 to 9 L/min, according to the manufacturer's manual.

Procedure

The appropriate device settings vary between manufacturers, indications, and protocols. Power and flow settings are intensified according to indications; hence, vascular lesions are treated with settings of 40–50 W and argon flow usually 0.8 L/min. Tissue ablation is achieved with settings of up to 70–90 W and argon flow 1 L/min [5]. Higher settings cause gaseous distention and discomfort for the patient. APC is a non-contact

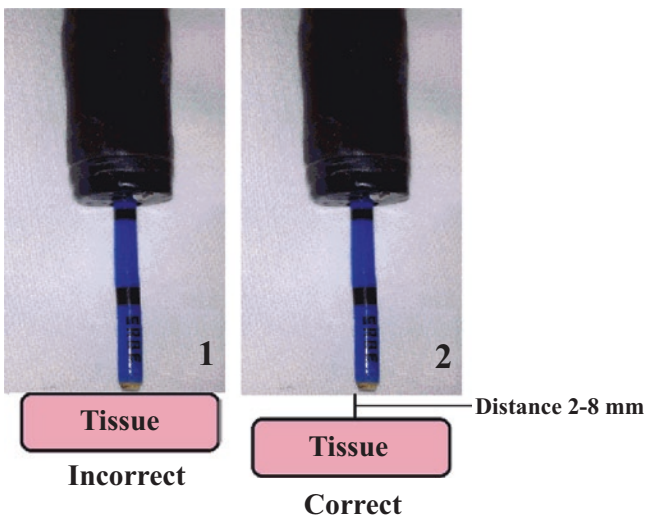

Fig. 13.2 (*1*) The probe is too close to the tissue, which may result in an undesirable thermal effect and/or submucosal emphysema; (*2*) The distance of the probe is sufficient, leading to a more even distribution of current

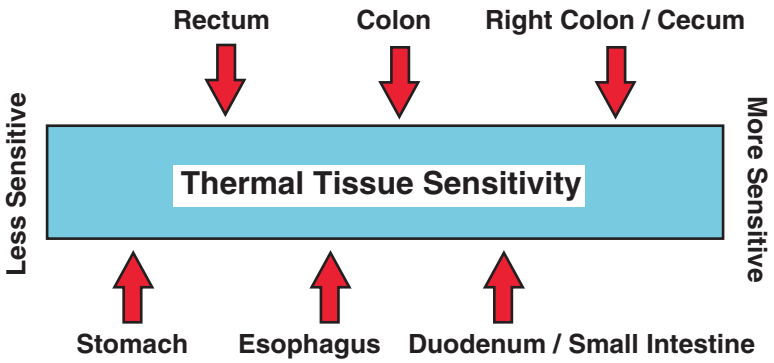

Fig. 13.3 Thermal tissue sensitivity

Table 13.1 Power limit and single-shot duration in various APC applications

Application	Power limit (Watts)	Single-shot duration (seconds)
Esophagus	60–80	1–3
Stomach	70–99	1–3
Small intestine	60–80	1–3
Right colon	40–50	0.5–1
Remaining colon	40–60	1–2
Rectum	60–80	1–3
Small tumors	60	0.5–5
Medium size tumors (0.5–1.5 cm)	80	3–5
Large tumors (>1.5 cm)	99	3–10
Stent ingrowth or overgrowth	60	1–3

technique providing an operative distance from probe to tissue from 2 to 8 mm [6] (Fig. 13.2). So, the endoscopist must not hold the probe too far from the tissue as the argon plasma beam will be nonexistent at low power settings. Conversely, tissue contact with the probe leads to tissue-probe sticking and thermal injury. Deep thermal injury results in argon gas flowing into the submucosa and thus producing pneumatosis and extraintestinal gas. Consequently, care should be taken to avoid tissue contact with the probe. There must be no intermediate liquid (included blood) between the argon probe and the tissue surface; otherwise, a coagulation film develops and the underlying tissue surface remains inadequately treated. Thus, surface fluids should be rinsed or sucked out as indicated [7]. Depending on the indication, apart from spot application, the probe tip can be applied on extended confluent or linear areas in a paintbrush-like manner. Direct vision of the probe tip is essential throughout the application. Misdirection of the plasma beam to the endoscope tip may result in video chip damage [7]. Frequent suctions are needed to decompress the intraluminal argon gas and clear the smoke from the visual field. Settings should be adapted to various parts of the GI tract, since thermal tissue sensitivity varies from less sensitive (e.g., stomach) to more sensitive (e.g., cecum) (Fig. 13.3). In addition settings should be lowered in the treatment of tissue in contact with metal implants, such as stents. Reported complication rates, on average, vary from 0% to 24% [7] and include gaseous distension, pneumatosis intestinalis, pneumomediastinum and pneumoperitoneum, subcutaneous emphysema, pain, chronic ulceration, stricture, bleeding, transmural burn syndrome, perforation, and death. It is therefore highly recommended that APC applications should follow instructions for the power limit and single-shot duration as shown in Table 13.1 (derived from ref. 8). Finally, when a combustible gas, such as methane, is suspected, it is imperative that the colon should be carefully cleansed before the APC session, as danger of explosion exists. Therefore dilation with bougienage or ballooning should be performed in stenotic areas of the colon so as to evacuate possible explosive gases which may be entrapped [8].

Practical Considerations

- APC is a non-contact technique providing an operative distance from the probe to tissue from 2 to 8 mm.
- The endoscopist must not hold the probe too far from the tissue as the argon plasma beam will be nonexistent at low power settings.
- Tissue contact with the probe leads to tissue-probe sticking and thermal injury.
- Thermal tissue sensitivity varies from less sensitive (e.g., stomach) to more sensitive (e.g., cecum).
- When a combustible gas, such as methane, is suspected, it is imperative that the colon should be carefully cleansed before the APC session, as danger of explosion exists.

Indications

There are two main axes of APC use in clinical practice, i.e., hemostasis and ablation. Thus APC has been used in the following main indications: treatment of vascular ectasias,

postradiation enteropathy or proctopathy, bleeding ulcers and bleeding varices, eradication of Barrett's esophagus, disruption of polyps and remnant adenomatous tissue after polypectomy, and malignant tumor debulking. In addition APC has been used for the treatment of some miscellaneous pathologies as judged by published small series or case reports.

Vascular Ectasias

Vascular ectasia (VE) is a general term involving lesions located in the upper or lower gastrointestinal tract. Vascular ectasia, including gastric antral vascular ectasia (GAVE), formerly known as watermelon stomach and angiodysplasia, is increasingly recognized as an important source of gastrointestinal bleeding. APC has been used successfully in the endoscopic treatment of GAVE, sporadic or inherited angiodysplasia, and hemorrhagic telangiectasia [4, 9–13]. More specifically GAVE can successfully be eliminated by APC [14]. However, GAVE patients might have a higher recurrent bleeding rate and may require multiple treatment sessions for sustained hemostasis. Thus, in one early study [15], 17 patients were treated with this technique requiring one to four sessions. After a 30.4-month follow-up period, GAVE relapsed and needed further treatment in only five patients (29%) [15]. Disappearance of bleeding and improvement on endoscopy were noted from the first session in another study [16]. In the case of angiodysplasia, the adequate number of patients and follow-up period after treatment with APC lead us to conclude that APC is a safe method of treatment compared to other modalities, such as laser [4, 9, 14–18]. In early studies, although perforation is rare, it occurred in about 0.31% of cases [19]. Other reported side effects include submucosal emphysema (usually mild) [19], inflammatory polyps [20], and gas explosion [21]. However, a more recent study [22] showed that endoscopic hemostasis with APC is a safe treatment modality for both angiodysplasia and GAVE bleeding. In addition this study showed that the efficacy of APC treatment is greater for angiodysplasia than for GAVE bleeding.

Postradiation Proctopathy

Many studies suggest that APC is an efficient endoscopic treatment modality in patients with postradiation proctopathy [11, 23–28]. In these studies, clinical success rates varied from 90% to 94%, while complete disappearance of bleeding varied from 81% to 86%. One to two sessions of APC were sufficient for patients with mild proctitis, whereas patients with a moderate to severe form required a statistically significantly higher number of APC sessions [28]. Side effects were relatively common during treatment for postradiation proctopathy, rising to 14% [26], and this seems to be associated with the power setting of the device. Thus a setting of less than 45 W must be employed so as to avoid injury to a fragile, thinned rectal wall previously irradiated. Reported side effects include symptom-free stenosis, as well as pain which can be treated with the usual analgesics. Only one perforation and one extensive necrosis were reported [26].

Bleeding Ulcers

In the literature, there are studies which suggest that APC is efficient in stopping bleeding in peptic ulcers [2, 29, 30]. In these studies the distance between the APC probe and the tissue varied from 2 to 8 mm and the power setting from 40 to 70 W. According to one study [30], APC was comparable to the heater probe as the two hemostatic approaches gave similar results, although APC provided faster hemostasis. It must be noted that this study was a small randomized trial with limited statistical power. However, it should be taken into account that there has been concern that in bleeding ulcers, APC may be inadequate if blood interferes between the APC beam and the tissue, especially in spurting bleeding ulcers. Additionally, care must be taken to avoid submucosal accumulation of the gas, which may lead to delayed perforation. However, no major complications have been observed during APC application in bleeding ulcers except for transient pain and tachycardia due to gut over inflation [29]. A recent meta-analysis showed that among other endoscopic methods, epinephrine injection plus APC is superior to epinephrine injection alone in high-risk bleeding ulcers [31]. APC has also been used in diffuse bleeding from a large area, coagulation disorders, and tumor bleeding [17, 32]. Finally, APC has successfully been involved in the treatment of active bleeding due to Dieulafoy's lesion [8, 33].

Bleeding Varices

Randomized controlled studies indicate that APC application in the distal esophageal mucosa, after banding ligation of esophageal varices, is safe and effective in reducing the rate of variceal recurrence [6, 34]. According to these studies, the mean power output was 60 W, while the number of sessions per patient ranged from 1 to 3. During the procedure, circumferential coagulation of the entire esophageal mucosa was performed, starting from the Z line to 5 cm proximally. Immediate complications were transient, with fever, dysphagia, and retrosternal pain or discomfort being the most common. All these complications resolved spontaneously within 24 h. The patients were followed up for a mean period of 16 months (range 9–28 months), and variceal recurrence was significantly less frequent in the APC groups.

Barrett's Esophagus

Early studies reported the results of APC in ablating Barrett's esophagus, including patients in whom histology varied from low-grade dysplasia to adenocarcinoma in situ [35–43]. Best results were obtained in short-segment non-circumferential Barrett's esophagus [37]. Most patients were under concurrent high-dose proton pump inhibitor therapy. Additionally, some other patients had undergone anti-reflux surgery. Although the data in the above studies present a great variability, successful ablation of Barrett esophagus was achieved in 68% of patients, after a mean of 2.5 sessions per patient and a follow-up of 6–36 months [35, 37, 39, 40]. In a more recent randomized control trial [44], APC plus acid suppression proved to be as effective as multipolar electrocoagulation (MPEC) in achieving complete reversal of Barrett's esophagus, which could be maintained in approximately 70% of patients. In recent evidence-based studies, i.e., meta-analyses and cost-effective analyses, APC proved to be as effective as other ablation therapies in use, i.e., laser therapy, photodynamic therapy (PDT), multipolar electrocoagulation (MPEC), and radiofrequency (RFA) [45, 46]. RFA (HALO) is nowadays considered the treatment of choice for Barrett's esophagus, and in a very recent consensus statement by the American Gastroenterological Association [47], this notion has received more than 80% consensus agreement. Post-ablation complications varied from mild to serious and included chest pain and odynophagia (within 3–10 days), high fever and pleural effusions, severe esophagitis (requiring transfusion), esophageal strictures, pneumomediastinum, and subcutaneous emphysema [37, 40, 44]. A true perforation with consequent death was reported in one patient [42]. It must be noted that after Barrett's tissue ablation, buried metaplastic glands or true adenocarcinoma might hide under new squamous epithelium in otherwise normal-appearing mucosa [37, 48, 49]. A recent study [50] estimated the persistence of restored squamous epithelium and the risk of cancer in Barrett's tissue, without high-grade dysplasia, ablated by APC 16 years after its application. Long-term reepithelialization was observed in the majority of patients who previously had complete eradication of Barrett's esophagus. However, this did not provide protection against cancer development, as the incidence of cancers arising from buried glands or from residual Barrett's esophagus was similar to that observed in patients undergoing no specific treatment. This should always be kept in mind, stressing the importance of endoscopic surveillance in Barrett's patients after ablation. It also stresses the need for long-term posttreatment surveillance follow-up data before ablation can be used in routine clinical care.

Polyps and Remnant Adenomatous Tissue After Polypectomy

The usefulness of APC as a complimentary step following piecemeal snare polypectomy has been reported in various studies [51, 52]. In one of these studies [52], 50% of patients had complete elimination of the residual adenomatous tissue after one session of APC, whereas the remainder required two sessions. APC has been used as a first-step therapy for the ablation of intestinal polyps in some studies [8, 9]. In this context, multiple small polyps seen in familial adenomatous polyposis syndrome have easily been fulgurated by APC [53]. However, long-term results are necessary.

Malignant Tumor Debulking

APC has been used for tumor debulking. Hence, in a large study [54], APC was applied as palliative therapy in 83 patients with esophageal and gastric cardia tumors. Recanalization was achieved in 58% which allowed food passage and dysphagia relief even after one session. Twenty-six percent needed two sessions, whereas the remaining 12% reported dysphagia score improvement of at least one grade. In 8.3% of patients, perforation occurred which was treated conservatively in all but one. Other reports have confirmed the previous findings of successful treatment for dysphagia [55–57]. APC has also been used in association with other treatments, such as dilatation, radiotherapy, and chemotherapy [54, 55], or just before stenting [4, 54]. In addition APC has been used in small series to treat tumors of the ampulla of Vater and colon tumors [4, 9]. Another study [58] reported patients with either esophageal, stomach, or rectal cancer, staged by EUS and histology as T1, who were treated by APC. In this study, local response was achieved in 9 out of 10 patients (90%), over a 9.5-month follow-up period.

Miscellaneous

Other miscellaneous applications using APC include ablation of heterotopic gastric dysplastic mucosa, elimination of tumor ingrowth or overgrowth in metal stents, and elimination of cutoff displaced metal stents [2, 59–62]. In addition post-interventional hemostasis when required, i.e., after polypectomy, mucosectomy, or bougienage, and septotomy in Zenker's diverticulum can be achieved by APC [63]. In all the above studies, APC proved to be an effective and safe tool, offering patients an alternative therapy to open surgery. Finally, fistulas prior to the use of fibrin glue are an extra indication for APC application. This situation requires a superficial destruction of the epithelium around the opening

and within the fistula, which enhances adhesion of the glue for fistula closing [2].

APC Main Indications

- There are two main axes of APC use in clinical practice, i.e., hemostasis and ablation.
- APC has been used successfully in the endoscopic treatment of angiodysplasias and GAVE.
- APC is an efficient endoscopic treatment modality in patients with postradiation proctopathy.
- APC is efficient in stopping bleeding in peptic ulcers.
- APC has successfully been involved in the treatment of active bleeding due to Dieulafoy's lesion.
- APC has been used in ablating Barrett's esophagus.
- APC has been used for tumor debulking.

Safety and Complications

Reported APC complication rates range from 0% to 24% [36, 39–42, 64–67]. Among them are pneumoperitoneum, pneumomediastinum, perforation, subcutaneous emphysema, transmural burn syndrome, pain at the site of application, chronic ulceration, luminal distension with argon gas, and stricture. It seems that the power setting, the distance of the probe tip from the target, and the duration of application influence the complication rate. Thus, the largest study of APC in the colon reported a complication rate of 1.7%, with one transient fever and one pneumoperitoneum, without evidence of perforation, and this was managed conservatively [68]. Colonic explosion during APC treatment, in a poorly prepared colon, has been described [21, 69, 70], which stresses the fact that when APC is used to treat radiation proctitis, a complete bowel preparation, rather than an enema preparation, should be used.

Complications

- Reported APC complication rates range from 0% to 24%.
- Many are transient, such as fever, and can be managed conservatively.
- Colonic explosion during APC treatment, in a poorly prepared colon, has been described. Therefore, complete bowel preparation, rather than an enema preparation, should be used.

Table 13.2 Comparison of alternative endoscopic procedures in use for hemostasis and ablation

Procedure	Use and effectiveness
Argon plasma coagulation (APC)	Effective and safe coagulation, non-contact mode of action, ease in device handling, no extended safety precautions
Thermal coagulation with heater probes	In use for hemostasis, but not as commonly in cancer ablation due to higher recurrence rates
Multipolar electrocautery (MPEC)	Useful for hemostasis and sometimes for ablation. Suitable for patients with implanted pacemakers
Nd/YAG laser, KTP (potassium titanyl phosphate) laser, and argon lasers	Used for tumor ablation and for treating vascular lesions. KTP with a wavelength better absorbed by hemoglobin is more helpful in hemostasis, while Nd/YAG helps to ablate deeper tissue. All of these require the use of bulky expensive equipment, and some require special certification for use
Cryotherapy	Widely used in various skin and mucosal cancers. Never been fully adopted to use with endoscopy
Photodynamic therapy (PDT)	Used in Barrett's esophagus as an alternative to APC with similar efficacy and complication rates
Radiofrequency ablation (RFA)	RFA (HALO) is now considered the treatment of choice for Barrett's esophagus

Alternative Endoscopic Procedures

Apart from APC, endoscopic procedures available today include thermal coagulation with heater probes, bipolar electrocautery, Nd/YAG laser, KTP (potassium titanyl phosphate) laser and argon lasers, cryotherapy, photodynamic therapy, and radiofrequency ablation (RFA) [71, 72]. The efficacy of these alternative endoscopic procedures for hemostasis and ablation (with pros and cons) is shown in Table 13.2 (derived from Ref. 7, 71, and 72).

Cost Considerations

APC cost varies from country to country. Although in the literature cost data are unavailable for most countries, in the USA [71], the cost of an APC apparatus is $ 16,750 (ERBE), $24,500 (Canady), and $27,783 (ConMed). The probe cost is $1995/box of 10 (ERBE), $1555/box of 10 (Canady), and 2748, 90/box of 10 (ConMed). Details on the costs and billing codes are given in an American Society for Gastrointestinal Endoscopy (ASGE) technical report on mucosal ablation devices [71]. Concerning cost-effectiveness of various ablation techniques, a cost-utility analysis of ablative therapy for Barrett's esophagus was published in 2009 [45].

Conclusions

Argon plasma coagulation is a widely available efficacious method of treating a variety of bleeding and neoplastic lesions. Its use has been expanded and is expected to continue. However, although this prospect is welcome, more studies are necessary to further evaluate results and technical details of the procedure.

Overall Practical Considerations

- Do not confuse APC with argon laser. They are completely different in physics, application, and effect.
- Always check argon gas flow as well as plasma beam outside the endoscope before inserting the probe into the working channel.
- Advance the APC probe far enough, so that the first black ring is clearly visible in the endoscopic field.
- Always perform APC under continuous visual control.
- Be sure that the APC probe neither touches the target tissue nor is too far away during performance.
- Never press the activated probe against the organ wall or into tissue for this may result in emphysema or wall damage or perforation.
- Do not touch metal stents directly with the APC probe; keep the appropriate distance.
- Avoid over inflation by checking for abdominal distention; deflate repeatedly as indicated.
- Set the power limit of the electrosurgical unit and the duration of the APC supply as indicated by the affected organ (e.g., upper limit of 50 W in the right colon or cecum but higher for tumor ablation).
- Many short duration applications are more effective than a few long-duration ones. Control the penetration depth by altering the duration rather than lowering the settings.

References

1. Farin G, Grund KE. Technology of argon plasma coagulation with particular regard to endoscopic applications. Endosc Surg Allied Technol. 1994;2:71–7.
2. Grund KE, Storek D, Farin G. Endoscopic argon plasma coagulation (APC). First clinical experiences in flexible endoscopy. Endosc Surg Allied Technol. 1994;2:42–6.
3. Johanns W, Luis W, Janssen J, Kahl S, Greiner L. Argon plasma coagulation (APC) in gastroenterology: experimental and clinical experiences. Eur J Gastroenterol Hepatol. 1997;9:581–7.
4. Watson JP, Bennett MK, Griffin SM, Mattewson K. The tissue effect of argon plasma coagulation on esophageal and gastric mucosa. Gastrointest Endosc. 2000;52:342–5.
5. Waye J. How I use the argon plasma coagulator. Clin Perspect Gastroenterol. 1999;2:249–52.
6. Nakamura S, Mitsunaga A, Murata Y, Suzuki S, Hayashi N. Endoscopic induction of mucosal fibrosis by argon plasma coagulation (APC) for esophageal varices: a prospective randomized trial of ligation plus APC vs. ligation alone. Endoscopy. 2001;33:210–5.
7. Ginsberg GG, Barkun AN, Bosco JJ, et al. American Society for Gastrointestinal Endoscopy. The argon plasma coagulator: review. Gastrointest Endosc. 2002;55:807–10.
8. Grund KE, Farin G. Clinical application of argon plasma coagulation in flexible endoscopy. In: Practice of therapeutic endoscopy. London: W.B. Saunders Ed; 2001. p. 87–99.
9. Wahab PJ, Mudler CJJ, Den Hartog G, Thies JE. Argon plasma coagulation in flexible gastrointestinal endoscopy: pilot experiences. Endoscopy. 1997;29:176–81.
10. Shudo R, Yazaki Y, Sakurai S, et al. Diffuse antral vascular ectasia: EUS after argon plasma coagulation. Gastrointest Endosc. 2001;54:636–42.
11. Rolachon A, Papillon E, Fournet J. Is argon plasma coagulation an efficient treatment for digestive system vascular malformation and radiation proctitis? Gastroenterol Clin Biol. 2000;24:1205–10.
12. Smith S, Wallner K, Dominitz JA, et al. Argon plasma coagulation for rectal bleeding after prostate brachytherapy. Int J Radiat Oncol Biol Phys. 2001;51:636–42.
13. Kitamura T, Tanabe S, Koizumi W, et al. Rendu-Osler-Weber disease successfully treated by argon plasma coagulation. Gastrointest Endosc. 2001;39:447–52.
14. Abedi M, Haber GB. Watermelon stomach. Gastroenterologist. 1997;5:179–84.
15. Probst A, Scheubel R, Wienbeck M. Treatment of watermelon stomach (GAVE syndrome) by means of endoscopic argon plasma coagulation (APC): long-term outcome. Z Gastroenterol. 2001;39:447–52.
16. Canard JM, Vedrenne B. Clinical application of argon plasma coagulation in gastrointestinal endoscopy: has the time come to replace the laser? Endoscopy. 2001;33:353–7.
17. Waye JD, Grund KE, Farin G. Argon plasma coagulation (APC). Clinical usefulness in inflexible endoscopy. Gastrointest Endosc. 1996;43:306.
18. Cohen J, Abebi M, Haber G, et al. Argon plasma coagulation: a new effective technique of non-contact thermal coagulation. Experience in 44 cases of GI angiomata. Gastrointest Endosc. 1996;43:293.
19. Hoyer N, Thouet R, Zellweger U. Massive pneumoperitoneum after argon plasma coagulation. Endoscopy. 1998;30:S44–5.
20. Schmeck-Lindenau HJ, Kurtz W, Heine M. Inflammatory polyps: an unreported side effect of argon plasma coagulation. Endoscopy. 1998;30:S93–4.
21. Zinsser E, Will U, Gottschalk P, Bosseckert H. Bowel gas explosion during argon plasma coagulation. Endoscopy. 1999;31:S26.
22. Chiu YC, Lu LS, Wu KL, et al. Comparison of argon plasma coagulation in management of upper gastrointestinal angiodysplasia and gastric antral vascular ectasia hemorrhage. BMC Gastroenterol. 2012;12:67.
23. Silva RA, Correia AJ, Dias LM, Viana HL, Viana RL. Argon plasma coagulation therapy for hemorhagic radiation proctosigmoiditis. Gastrointest Endosc. 1999;50:221–4.
24. Fantin AC, Binek J, Suter WR, Meyenberger C. Argon beam coagulation for treatment of symptomatic radiation proctitis. Gastrointest Endosc. 1999;49:515–8.
25. Kaasis M, Oberti E, Burtin P, Boyer J. Argon plasma coagulation therapy for the treatment of hemorhagic radiation proctitis. Endoscopy. 2000;32:673–6.
26. Tam W, Moore J, Schoeman M. Treatment of radiation proctitis with argon plasma coagulation. Endoscopy. 2000;32:667–72.
27. Canard JM, Védrenne B, Bors G, Claude P, Bader R, Sondag D. Long term results of treatment of hemorrhagic radiation

proctitis by argon plasma coagulation. Gastroenterol Clin Biol. 2003;27:455–9.
28. Karamanolis G, Psatha P, Triantafyllou K. Endoscopic treatments for chronic radiation proctitis. World J Gastrointest Endosc. 2013;5:308–12.
29. Grund KE, Straub T, Farin G. New hemostatic techniques: argon plasma coagulation. Baillieres Best Pract Res Clin Gastroenterol. 1999;13:67–84.
30. Cipolletta L, Bianco MA, Rotondano G, et al. Prospective comparison of argon plasma coagulation and heater probe in the endoscopic treatment of major peptic ulcer. Gastrointest Endosc. 1998;48:191–5.
31. Vergara M, Bennett C, Calvet X, Gisbert JP. Epinephrine injection versus epinephrine injection and a second endoscopic method in high-risk bleeding ulcers. Cochrane Database Syst Rev. 2014;10:CD005584.
32. Thosani N, Rao B, Ghouri Y, et al. Role of argon plasma coagulation in management of bleeding GI tumors: evaluating outcomes and survival. Turk J Gastroenterol. 2014;25(Suppl 1):38–42.
33. Nojkov B, Cappell MS. Gastrointestinal bleeding from Dieulafoy's lesion: clinical presentation, endoscopic findings, and endoscopic therapy. World J Gastrointest Endosc. 2015;7:295–307.
34. Cipolletta L, Bianco MA, Rotondano G, et al. Argon plasma coagulation prevents variceal reccurence after band ligation of esophageal varices: preliminary results of a prospective randomized trial. Gastrointest Endosc. 2002;56:467–71.
35. Dumoulin FL, Terjung B, Neubrand M, et al. Treatment of Barrett.s oesophagus by endoscopic argon plasma coagulation. Endoscopy. 1997;29:751–3.
36. Mork H, Barth T, Kreipe H-H, et al. Reconstitution of squamous epithelium in Barrett.s oesophagus with endoscopic argon plasma coagulation: a prospective study. Scand J Gastroenterol. 1998;33:1130–4.
37. Van Laethem JL, Cremer M, Peny MO, Delhaye M, Deviere J. Eradicaton of Barrett's mucosa with endoscopic argon plasma coagulation and acid suppression: immediate and midterm results. Gut. 1998;43:747–51.
38. Tigges H, Fuchs KH, Maroske J, et al. Combination of and antireflux surgery for treatment of Barrett.s oesophagus. J Gastrointest Surg. 2001;5:251–9.
39. Van Laethem JL, Jagodzinski R, Peny MO, Cremer M, Deviere J. Argon plasma coagulation in the treatment of Barrett.s high-grade dysplasia and adenocarcinoma. Endoscopy. 2001;33:257–61.
40. Pereira-Lima JC, Busnello JV, Saul C, et al. High power setting argon plasma coagulation for the eradication of Barrett.s oesophagus. Am J Gastroenterol. 2000;95:1661–8.
41. Schultz H, Miehlke S, Antos D, et al. Ablation of Barrett's epithelium by endoscopic argon plasma coagulation in combination with high dose omeprazole. Gastrointest Endosc. 2000;51:659–63.
42. Byrne JP, Armstrong GR, Attwood SE. Restoration of the normal squamous lining in Barrett's oesophagus by argon beam plasma coagulation. Am J Gastroenterol. 1998;93:1810–5.
43. Morris CD, Byrne JP, Armostrong GR, Attwood SE. Prevention of the neoplastic progression of Barrett's oesophagus by endoscopic argon beam plasma ablation. Br J Surg. 2001;88:1357–62.
44. Sharma P, Wani S, Weston AP, et al. A randomised controlled trial of ablation of Barrett's oesophagus with multipolar electrocoagulation versus argon plasma coagulation in combination with acid suppression: long term results. Gut. 2006;55:1233–9.
45. Inadomi JM, Somsouk M, Madanick RD, Thomas JP, Shaheen N. A cost-utility analysis of ablative therapy for Barrett's esophagus. Gastroenterology. 2009;136:2101–14.
46. De Souza TF, Artifon EL, Mestieri LH, et al. Systematic review and meta-analysis of endoscopic ablative treatment of Barrett's esophagus. Rev Gastroenterol Peru. 2014;34:217–24.
47. Sharma P, Katska DA, Gupta N, et al. Quality indicators for the management of Barrett's esophagus, dysplasia and esophageal adenocarcinoma: international consensus recommendations from the American Gastroenterological Association. Gastroenterology. 2015;149:1599–606.
48. Van Laethem JL, Peny MO, Salmon I, Cremer M, Deviere J. Intramucosal adenocarcinoma arising under squamous reepithelialisation of Barrett.s oesophagus. Gut. 2000;46:574–7.
49. Hornick JL, Blount PL, Sanchez CA, et al. Biologic properties of columnar epithelium underneath reepithelialized squamous mucosa in Barrett's esophagus. Am J Surg Pathol. 2005;29:372–80.
50. Milashka M, Calomme A, Van Laethem JL, et al. Sixteen-year follow-up of Barrett's esophagus, endoscopically treated with argon plasma coagulation. United European Gastroenterol J. 2014;2:367–73.
51. Regula J, Wronska E, Polkowski M, et al. Argon plasma coagulation (APC) after piecemeal polypectomy for colorectal adenomas. Endoscopy. 1996;28:S61.
52. Zlatanic J, Waye JD, Kim PS, Baiocco PJ, Gleim GW. Large sessile colonic adenomas: use of argon plasma coagulator to supplement piecemeal snare polypectomy. Gastrointest Endosc. 1999;49:731–5.
53. Beveridge IG, Swain DJW, Saunders BP, et al. Evaluation of argon plasma coagulation for the fulguration of rectal polyps in familial adenomatous polyposis. DDW, Orlando, Florida. 1999:A809.
54. Hiendorff H, Wojdemann M, Bisgaard T, Svendsen LB. Endoscopic palliation of inoperable cancer of the oesophagus or cardia by argon electrocoagulation. Scand J Gastroenterol. 1998;33:21–3.
55. Niezychowski W, Regula J, Fijuth J, et al. Argon plasma coagulation in palliative treatment of malignant dysphagia. Gut. 1996;39(Suppl. 3):A5.
56. Robertson GSM, Thomas M, Jamieson J, et al. Palliation of oesophageal carcinoma using the argon plasma coagulator. Br J Surg. 1996;83:1769–71.
57. Watson JP, Jowett S, Oppong K, et al. Endoscopic argon plasma coagulation: a better treatment for malignant dysphagia than laser therapy? Endoscopy. 1997;29:E32–3.
58. Sessler MJ, Becker H-D, Flesch I, Grund KE. Therapeutic effect of argon plasma coagulation on small malignant gastrointestinal tumours. J Cancer Res Clin Oncol. 1995;121:235–8.
59. Sauve G, Groue A, Denez B, Boyer J. High-grade dysplasia in heterotopic gastric mucosa in the upper esophagus after radiotherapy: successful eradication 2 years after endoscopic treatment by argon plasma coagulation. Endoscopy. 2001;33:732.
60. Klaase JM, Lemaire LC, Rauws EA, Offerhaus GJ, Van Lanschot JJ. Heterotopic gastric mucosa of the cervical esophagus: a case of high-grade dysplasia treated with argon plasma coagulation and a case of adenocarcinoma. Gastrointest Endosc. 2001;53:101–4.
61. Demarquay JF, Dumas R, Peten EP, Rampal P. Argon plasma endoscopic section of biliary metallic prostheses. Endoscopy. 2001;33:289–90.
62. Rajendran N, Haqqani MT, Crumplin MK, Krasner N. Management of stent overgrowth in a patient with Crohn's oesophagitis by argon plasma coagulation. Endoscopy. 2000;32:S44.
63. Mulder CJJ. Zapping Zenker's diverticulum: gastroscopic treatment. Can J Gastroenterol. 1999;13:405–7.
64. Morino M, Rebecchi F, Giaccone C, et al. Endoscopic ablation of Barrett's esophagus using argon plasma coagulation (APC) following surgical laparoscopic fundoplication. Surg Endosc. 2003;17:539–42.
65. Grade AJ, Shah IA, Medlin SM, et al. The efficacy and safety of argon plasma coagulation therapy in Barrett's esophagus. Gastrointest Endosc. 1999;50:18–22.
66. Basu K, Pick B, Bale R, et al. Efficacy and one year follow-up of argon plasma coagulation therapy for ablation of Barrett's oesophagus: factors determining persistence and recurrence of Barrett's epithelium. Gut. 2002;51:776–80.

67. May A, Gossner L, Gunter E, et al. Local treatment of early cancer in short Barrett's esophagus by means of argon plasma coagulation: initial experience. Endoscopy. 1999;31:497–500.
68. Olmos JA, Marcolongo M, Pogorelsky V, et al. Long term outcome of argon plasma ablation therapy for bleeding in 100 consecutive patients with colonic angiodysplasia. Dis Colon Rectum. 2006;49:1507–16.
69. Soussan EB, Mathieu N, Roque I, et al. Bowel explosion with colonic perforation during argon plasma coagulation for hemorrhagic radiation- induced proctitis. Gastrointest Endosc. 2003;57:412–3.
70. Soussan EB. Argon plasma coagulation in the treatment of hemorrhagic radiation proctitis is efficient but requires a perfect colonic cleansing to be safe. Eur J Gastroenterol Hepatol. 2004;16:1315–8.
71. Rodriguez SA, Adler DG, Chand B, et al. American Society for Gastrointestinal Endoscopy technology status evaluation report: mucosal ablation devices. Gastrointest Endosc. 2008;68:1031–42.
72. Shaheen NJ, Sharma P, Overholt BF. Radiofrequency ablation in Barrett's esophagus with dysplasia. N Engl J Med. 2009;360:2277–88.

Endoscopic Management of Esophageal Varices and Variceal Hemorrhage

14

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Introduction

A varix (pl. varices) is an abnormally dilated vessel with a tortuous course. Esophageal varices are portosystemic collaterals. They form as a consequence of portal hypertension (a progressive complication of cirrhosis), preferentially in the submucosa of the lower esophagus. Acute variceal hemorrhage is a medical emergency. Approximately 40% of patients with cirrhosis are found to have esophageal varices on endoscopic evaluation [7], and approximately one-third of patients will experience variceal hemorrhage [37]. Historically, mortality after index hemorrhage in patient with cirrhosis has been reported up to 50%, with a 30% mortality rate associated with subsequent bleeding episodes [44]. More recent data suggest improvement in mortality with improvement in management, however still associated with 20% mortality risk at 6 weeks [8]. The risk of variceal hemorrhage is increased in large varices and in those that demonstrate stigmata of bleeding (Table 14.2 and Fig. 14.4), as well as in patients with high Child–Pugh scores, high variceal pressure, and previous episodes of variceal hemorrhage and in patients who continue to ingest alcohol [44]. The size of the varix is the single most important predictor of bleeding risk. Primary prophylaxis of varices should be considered in varices larger than 5 mm [19]. Esophageal varices are graded according to size and appearance (Table 14.1 and 14.2 and Figs. 14.1, 14.2, 14.3 and 14.4). Grade 1 (F1) varices are small, are straight, and flatten with distention of the esophagus (Fig. 14.1). Grade 2 (F2) varices are tortuous, comprise less than one-third of the lumen, and do not disappear with distention (Fig. 14.2). Grade 3 (F3) varices are tortuous and comprise greater than one-third of the lumen (Figs. 14.3 and 14.4; Table 14.2).

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Risk Assessment of Patients

Assessing the risk of variceal hemorrhage is essential to the proper treatment of esophageal varices. The treatment of varices should be considered in terms of preprimary prophylaxis, primary prophylaxis, secondary prophylaxis, and treatment of acute hemorrhage.

Preprimary Prophylaxis

The objective of preprimary prophylaxis is to prevent the development of varices in patients with portal hypertension who are yet to develop varices. Although treatment with nonselective beta-blocker is not recommended, the treatment of underlying liver disease may help to lower the development of varices [18, 30]. Additionally, in order to detect the development of varices, routine surveillance endoscopy should be performed every 2–3 years or annually in the setting of decompensated liver disease [25].

Primary Prophylaxis

The primary prophylaxis refers to prevention of first variceal hemorrhage in a patient with varices. Ideally, the risk

Practical Considerations

- Size of the varix is the single most important predictor of bleeding risk.
- Risk of hemorrhage increase with size, presence of stigmata, high Child–Pugh score, high variceal pressure, and previous history of bleeding.

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Table 14.1 Endoscopic grading of esophageal varices

F1	Small, straight varices
F2	Enlarged, tortuous varices that occupy less than one-third of the lumen
F3	Large, coil-shaped varices that occupy more than one-third of the lumen

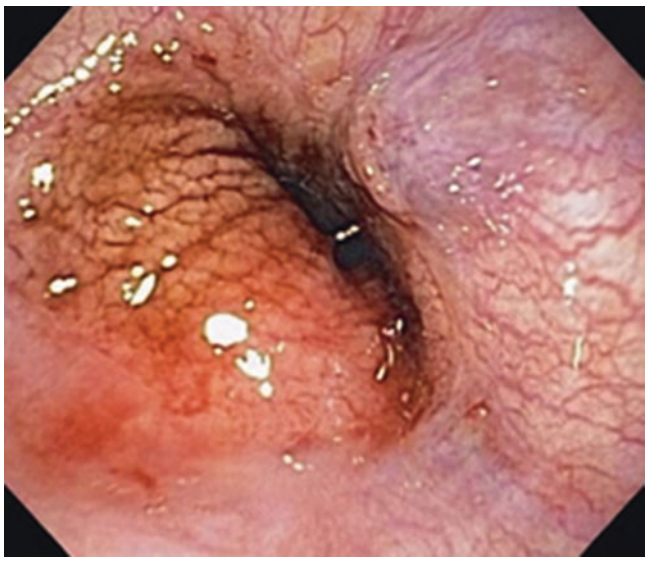

Fig. 14.1 An endoscopic view of grade 1 (F1) esophageal varices

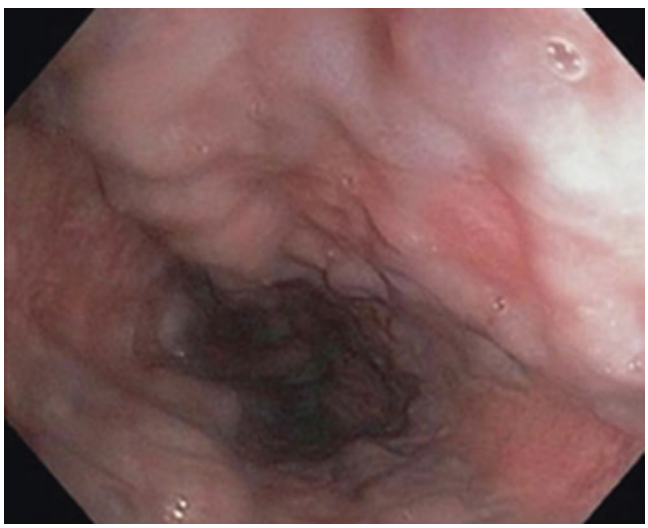

Fig. 14.2 An endoscopic view of grade 2 (F2) esophageal varices

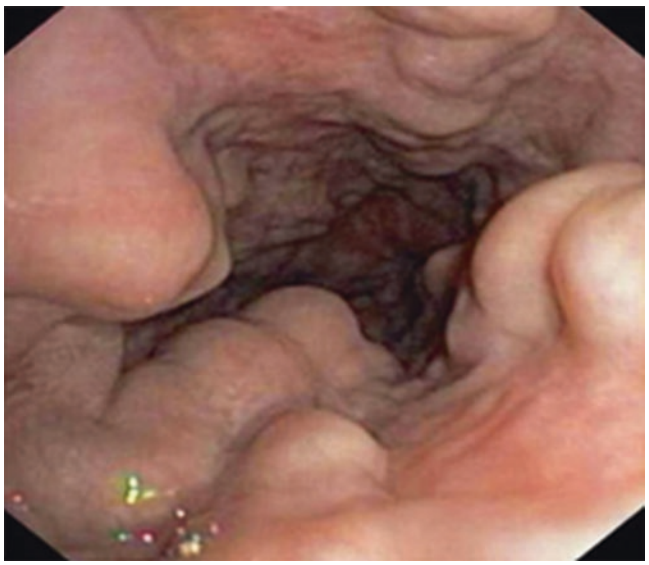

Fig. 14.3 An endoscopic view of grade 3 (F3) esophageal varices without stigmata of recent bleeding

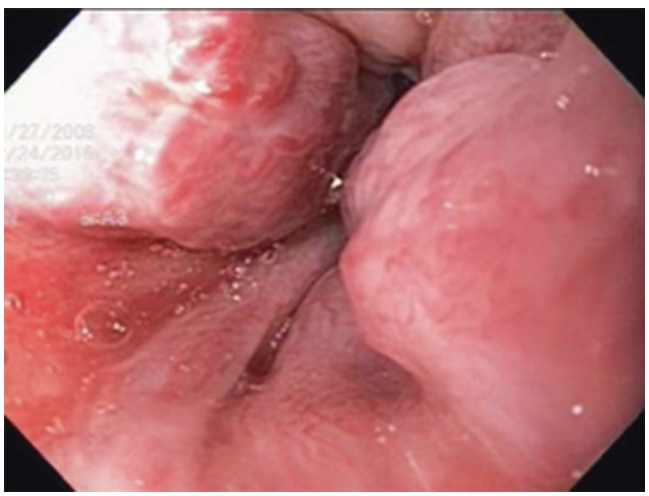

Fig. 14.4 An endoscopic view of grade 3 (F3) esophageal varices with stigmata of recent bleeding

Table 14.2 Endoscopic findings associated with an increased risk of hemorrhage

Longitudinal red streaks on the varices (red wale marks)
Cherry-colored spots that are flat and overlie varices
Raised, discrete red spots (hematocystic spots)

of hemorrhage in a patient with cirrhosis could be established by calculating the hepatic venous pressure gradient (HVPG, pressure difference in free and wedged hepatic vein), as bleeding is unlikely to occur at a pressure gradient less than 12 mm Hg. However, this procedure is invasive, costly, and not routinely performed. Clinical parameters such as platelet count and Child–Pugh score can be used to predict which patients will have large varices [11, 56]. However, it is generally recommended that all patients with cirrhosis undergo screening endoscopy. Patients should have a recent laboratory evaluation including hemoglobin, platelet count, and prothrombin time prior to endoscopic evaluation. Adequate intravenous access should be established, and the procedure should be performed by an

endoscopist experienced in assessment and ligation of varices. The size of the varices along with the presence of stigmata dictates the need for intervention. Varices <5 mm can be monitored with surveillance endoscopy, while those >5 mm are at higher risk of hemorrhage, and should be considered for ligation and/or medical management. Stigmata such as red wales or pigmented spots should also be considered to be signs of high risk for hemorrhage, and ligation should be performed.

A reduction of the HVPG by >20% or to <12 mm Hg can significantly reduce the incidence of an initial variceal hemorrhage [15]. More importantly, a reduction by >20% also reduces mortality in patients with esophageal varices [15, 29]. Nonselective beta-blockers such as propranolol and nadolol (nadolol has fewer systemic side effects than propranolol) lower HVPG and are the primary therapeutic interventions used for this purpose. These medications act by reducing splanchnic blood flow and portal pressure. They may also decrease the risk of developing ascites or spontaneous bacterial peritonitis, possibly by reducing portal pressure and decreasing bacterial translocation [32, 57]. Beta-blockers are initiated at a low dose and then slowly titrated to increasing doses in order to achieve a 25% reduction in resting heart rate. The vast majority of patients will experience some level of portal venous pressure reduction, but only 35% will attain the desired reduction of >20% [23]. Primary prophylaxis with nonselective beta-blockers results in a reduction in the risk of bleeding by approximately 40% [16, 45].

High-risk esophageal varices, such as those >5 mm in diameter or those demonstrating stigmata, should be considered for band ligation during endoscopy. This technique involves the use of a banding device, which attaches to the tip of an upper endoscope, and works by aspirating the varix into the banding chamber, where a rubber band is deployed around the vessel. This results in ligation or thrombosis of the vessel. Some studies have shown that band ligation is superior to beta-blockers in the prevention of hemorrhage [53, 60]. However, a more recent meta-analysis, which only used trials with adequate bias control, showed no difference in bleeding rates or mortality between those groups that underwent band ligation versus those treated with beta-blockers [27]. Band ligation often requires multiple endoscopic therapy sessions as patients must return every 2–4 weeks for repeat banding until the varices have been completely ligated. Thereafter, the patients will require continued surveillance as their varices frequently recur. Benefit from adding beta-blockers in patients who have undergone band ligation has not been well studied. One randomized study has shown combination therapy was not more effective than band ligation alone in preventing hemorrhage or death but less likely to cause recurrence [54].

Sclerotherapy utilizing agents such as ethanol, sodium morrhuate, ethanolamine oleate, or sodium tetradecyl sulfate, a previously preferred endoscopic technique for variceal ablation, have been supplanted by band ligation because ligation has a better safety profile and result in less long-term bleeding episodes. The overall benefit of sclerotherapy for treatment of esophageal varices has not been clearly demonstrated [59]. In fact, although sclerotherapy lowers subsequent bleeding episodes, it has been shown to increase mortality (the Veterans Affairs Cooperative Variceal Sclerotherapy) [31]. Thus, the band ligation should be favored over sclerotherapy for primary prophylaxis.

Surveillance endoscopy should be performed annually in patients with ongoing liver injury the setting of decompensated liver disease, whereas compensated liver disease with no varices should have repeat surveillance every 2 years [18].

Secondary Prophylaxis

Secondary prophylaxis refers to treatment of varices following an episode of hemorrhage.

Treatment in this group of patients is essential, as two-thirds will have a second episode of hemorrhage within 1 year [14]. As mentioned previously, large varix size, the presence of stigmata of recent bleeding, high variceal pressure, and severity of liver disease all increase rebleeding risk. A reduction of the HVPG by >20% results in a significant reduction in the recurrence of bleeding. Nonselective beta-blockers have been shown to decrease recurrent bleeding and improve survival at 2 years when used for secondary prophylaxis [3]. Similar to primary prophylaxis, the heart rate should be reduced by 25% or to a resting rate of 55. Long-acting nitrates may be added to beta-blocker therapy as they can further decrease portal venous pressure. However, these agents have not been shown to reduce mortality when used as monotherapy and can add to the side effect profile of medical management causing reduced patient compliance. One study showed a reduced incidence of rebleeding when medical management was compared to band ligation performed every 2–3 weeks, especially for those patients who had achieved >20% reduction in HVPG [9, 62]. The risk of complications for medical management remains lower than that of endoscopic management. However, other studies have found differing results when comparing endoscopic versus medical management, especially when treating patients with noncirrhosis-related portal hypertension [55]. More importantly, the combination of endoscopic ligation with medical management has recently been shown to decrease rebleeding rates when compared to single modality therapy [20, 28]. Sclerotherapy with sodium morrhuate or ethanolamine has been shown to be as effective as band ligation in controlling the initial bleeding episode. But, these agents were not shown to be as effective at preventing rebleeding episodes and had a much higher risk of complications [38]. Therefore, sclerotherapy should be avoided for secondary prophylaxis of hemorrhage. Variceal band ligation is performed every

2–3 weeks until obliteration of the varices is complete. This usually requires three to four sessions with subsequent surveillance endoscopy for the recurrence of varices, which commonly occurs.

Practical Considerations

- Most patients with cirrhosis should undergo diagnostic endoscopy to determine the presence and risk of bleeding.
- Patients with small varices should be treated with beta-blocker, medium-size varices should be treated with either beta-blocker or band ligation, and larger varices should be treated with band ligation.
- Variceal band ligation is performed every 2–3 weeks until obliteration of the varices is complete and usually requires three or four sessions.

Initial Management of Acute Variceal Hemorrhage

Presentation of variceal hemorrhage is seldom subtle, as patients often present with massive hematemesis with resulting tachycardia and hypotension (Fig. 14.5). Patients may also demonstrate signs of hepatic encephalopathy on presentation. Initial management should involve stabilization of the patient including preserving hemodynamic stability and airway patency. Adequate intravenous access should be established, and resuscitation with intravenous fluids and blood products should be initiated. Coagulation studies and platelet count must be obtained as soon as possible. Fresh frozen plasma transfusion may be considered for patients with elevated prothrombin times. Central venous pressure monitoring may assist in the management of fluid administration. Overenthusiastic fluid administration should be avoided, especially with normal saline as this may raise portal pressure and increase the risk of subsequent bleeding. Patients should be managed in an intensive care setting if possible. Endotracheal intubation should be strongly considered for airway protection as patients are at risk for aspiration in the setting of large volume bleeding, agitation, and the risk of the ensuing endoscopy. Pharmacologic therapy is integral for the cessation of hemorrhage. Somatostatin analogues such as octreotide reduce portal pressure by inhibiting release of glucagon and inducing splanchnic vasoconstriction.

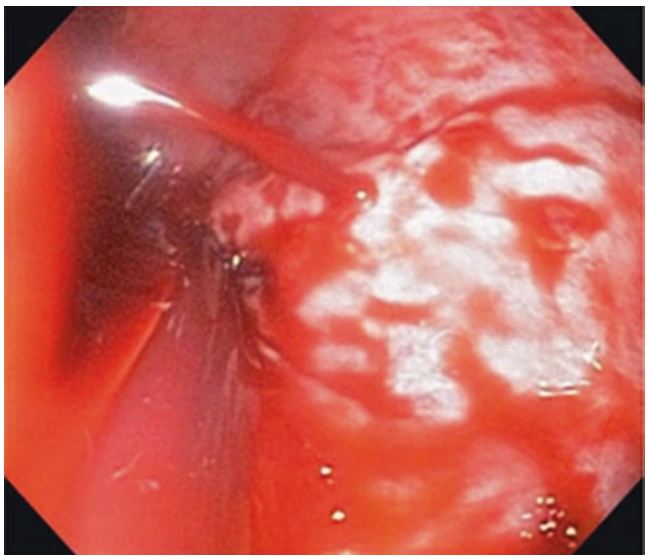

Fig. 14.5 An endoscopic view of active variceal hemorrhage in the esophagus

Pharmacologic therapy should be initiated in the emergency department. These agents control bleeding in up to 85% of patients and may be equivalent to endoscopic therapy for this purpose [17, 35, 58]. Therapy with octreotide can be continued for several days. However, the majority of the benefit is obtained within the first 24 h of treatment. Terlipressin, a vasopressin analogue with fewer systemic side effects than vasopressin, has been shown to be as effective as the somatostatin analogues in the control of active variceal hemorrhage [34]. Unfortunately, terlipressin is not available in the USA. Intravenous administration of a proton pump inhibitor is often utilized in order to raise the intragastric and intraesophageal pH and optimize coagulation capability. Antibiotic use (fluoroquinolone or third-generation cephalosporin) should be initiated on admission as this intervention has been shown to decrease infection risk, including the risk of spontaneous bacterial peritonitis as well as urinary tract infections and pneumonia, and reduce mortality [2, 6]. Early antibiotic use has also been shown to decrease the risk of future rebleeding [36].

Following interventions to achieve hemodynamic stabilization and management with octreotide, proton pump inhibitor, and antibiotics, more definitive therapy should be initiated with endoscopy, especially in those patients that continue to demonstrate evidence of continued bleeding. Endoscopy should be performed by an endoscopist experienced in management of variceal bleeding and in a controlled setting such as the intensive care unit. The patient must have adequate IV access prior to the procedure. Endoscopic therapy is effective in hemorrhage control in approximately 90% of cases. Variceal band ligation and sclerotherapy are equally efficacious in controlling variceal hemorrhage. However, band ligation is preferred as it causes fewer complications and has a lower incidence of rebleeding [41]. Unfortunately, the banding mechanism can interfere with visualization of an actively spurting vessel, necessitating the use of sclerotherapy, which allows the operator a full field of vision.

In some situations, medical management and endoscopic techniques are unsuccessful in controlling variceal hemorrhage. This situation generally necessitates the placement of a

Table 14.3 Items to be present for balloon tamponade placement

A tamponade tube kit (with the tube and clamps)
A manometer
Large-volume syringes
A traction/pulley system to maintain constant tension on the tube
Adequate suction

Sengstaken–Blakemore or Minnesota tube to control bleeding while a more definitive approach is pursued (Table 14.3). The Sengstaken–Blakemore tube has two balloons, one that inflates in the stomach and another that inflates in the esophagus. It has four lumens, one each for inflating the esophageal and gastric balloons, one for aspirating the stomach, and one for suctioning secretions in the esophagus. Prior to placement of a tamponade balloon, the patient should undergo endotracheal intubation if that has not already been performed. The physician managing the bleeding patient must confirm functioning balloons and suction ports prior to insertion. Following intubation, the tube is inserted, and the position is confirmed by auscultation, while air is insufflated into the gastric port. The position can also be established via endoscopic visualization. The gastric balloon is then inflated with 50–100 mL of air, and the position of the balloon is then confirmed radiographically. Once confirmation has been obtained, the balloon is then inflated with a total of 300–350 mL of air, and the apparatus is pulled upward and may be placed in traction. It is this external, upward traction that tamponades the bleeding varices. The position of the tube exiting the nostril (our preferred method) or the mouth should be marked for future reference. If bleeding is not controlled with this intervention, then the esophageal balloon should be inflated to approximately 25–35 mm Hg. Both the gastric and the esophageal balloons must be periodically deflated to avoid pressure necrosis of the mucosa. Balloon tamponade is very effective in hemorrhage control. But, unfortunately, it can cause severe complications, including ulceration, esophageal or gastric perforation, and aspiration. The tube should be considered only as a bridge to more definitive treatment and should be removed within 12–24 h of placement.

The transjugular intrahepatic portosystemic shunt (TIPS) procedure should be considered in the remaining 10% of patients in whom endoscopic control of variceal hemorrhage is not possible. In this procedure, a shunt is created by an interventional radiologist between the hepatic and portal vein with an expandable metal stent through the liver parenchyma, under fluoroscopic guidance. TIPS is effective in controlling hemorrhage from both esophageal and gastric varices. It has a lower short-term mortality rate than surgical shunts and provides equally efficacious portal decompression. Unfortunately, approximately one quarter of patients develop hepatic encephalopathy following placement of TIPS. The procedure also markedly increases the 30-day mortality of patients with elevated Child–Pugh scores or advanced MELD (Model for End-Stage Liver Disease) scores [10]. Surgical shunts are also a consideration in situations where TIPS is not feasible or not available. Surgical shunting should also be considered when definitive therapy is sought for treatment of varices not amenable to endoscopic therapy in patients who are not liver transplant candidates. Emergency shunt surgery is extremely effective in arresting hemorrhage and preventing rebleeding. However, it is associated with up to 50% mortality rate [49, 64]. Unfortunately, most of the patients die of liver failure and complications of surgery, despite achievement of hemostasis.

In patients who are not candidates for TIPS (Child–Pugh score > 14) or in centers where TIPS is not readily available, use of self-expandable metal stents (SEMS) is gaining rapid attention. The SEMS can be used without endoscopic or radiological assistance, can achieve rapid hemostasis, and can carry low side effect profile. In 2006, Hubmann and colleagues reported a study of 20 patients with refractory esophageal variceal bleeding (not responding to initial endoscopic therapy). Hemostasis was achieved in 100% of the patients [33]. A recent meta-analyses of five studies reported high success rate to achieve hemostasis and low adverse events associated with use of SEMS [51]. In a most recent randomized control trial [22], efficacy of balloon tamponade was compared with the SEMS in 28 patients with refractory esophageal variceal bleeding. The control of bleeding was higher (85% vs. 47%) and transfusion requirements (2 vs. 6 units of packed red cells) and adverse events were lower (15% vs. 47%) in the esophageal stent group compared to the balloon tamponade group. Thus, SEMs could be a viable and perhaps a better alternative in patients with refractory variceal bleeding.

Practical Considerations

Initial management of acute variceal hemorrhage should include:

- Initial resuscitation of bleeding patient.
- Correction of coagulation and platelet count.
- Avoid overenthusiastic fluid administration.
- Management in the intensive care unit.
- IV octreotide, proton pump inhibitor, antibiotics.
- Low threshold for intubation and ventilation.
- Upper endoscopy should be performed for diagnosis and treatment within 12 h of presentation.
- The use of balloon tamponade is decreasing due to risk of rebleeding and major complications. It should be considered as a temporary measure only until more definitive treatment is available.
- A transjugular intrahepatic portosystemic shunt (TIPSS) is a good alternative when endoscopic treatment and pharmacotherapy fail.

Several endoscopic therapies are available for the management of acute variceal hemorrhage: endoscopic variceal band ligation (EVL), injection sclerotherapy, argon plasma coagulation, detachable endoloops, and snares.

Endoscopic Variceal Band Ligation

The basic principle of ligation of varices is that elastic bands are used to strangulate a varix, causing thrombosis, inflammation, and necrosis and finally sloughing of the overlying mucosa. There are some drawbacks to this technique. The endoscope has to be withdrawn and loaded with a banding cylinder, which obviously takes several minutes, and can be costly in the setting of acute hemorrhage. Second, although the cylinder is transparent, it can reduce the viewing field, which makes visualization of the bleeding site difficult, especially with a vigorously bleeding vessel. Therefore, it is important to survey the upper gastrointestinal tract thoroughly initially for the presence and the grade of varices, exclude any other cause for bleeding (Fig. 14.6), and measure the distance of the varices in relation to gastroesophageal junction and incisors prior to attaching the cylinder to the endoscope. There are no absolute restrictions on coagulation parameters that precludе performing variceal ligation, although in patients with active bleeding, attempts should be made to improve the coagulation status [61]. When the decision has been made to pursue EVL, the endoscope is withdrawn and the banding device is affixed to the end of the endoscope before reintubation of the endoscope.

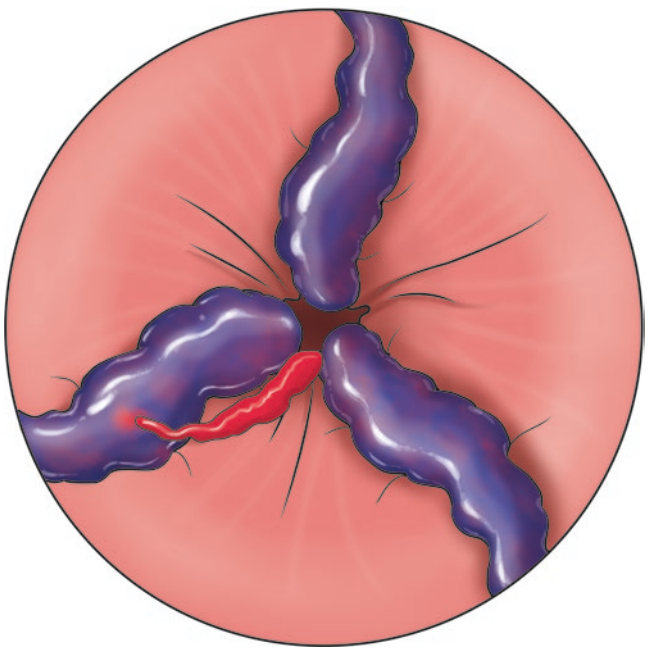

Fig. 14.6 An artist's depiction of a bleeding esophageal varix

Endoscopic variceal band ligation is more effective than sclerotherapy with greater control of hemorrhage, lower rebleeding, and lower adverse events but without differences in mortality [63].

Technique

The banding device consists of a transparent cylinder preloaded with elastic bands, which can be attached to the tip of the endoscope. Trigger threads traverse through the biopsy channel and wind around the trigger wheel. The endoscope is advanced and positioned in such a way that the tip of the endoscope faces tangentially to the varix, as close to the gastroesophageal junction or the most distal point of the variceal column as possible.

It is better to treat the varix below (a location in the esophagus distal) to the bleeding point. The suction should be turned to "maximum or high." The varix is then suctioned into the banding chamber, which gives rise to "complete red out or blue out" (caused by close approximation of the mucosa overlying the varix within the ligating chamber to the lens on the tip of the endoscope), indicating that an adequate amount of tissue has been captured by the device (Fig. 14.7). Once the varix has completely filled the chamber during suctioning (Fig. 14.8), a single band (or possibly two) is fired using the trigger wheel. Successful deployment of the band on to the varix causes a knuckle in the varix (Fig. 14.9). The band, left in this location (Fig. 14.10), will then cause thrombosis and ligation of the vessel. The endoscopist should proceed with banding of other varices in a circumferential pattern spiraling gradually up.

With regard to prophylactic banding, one study demonstrated that applying more than six bands per session

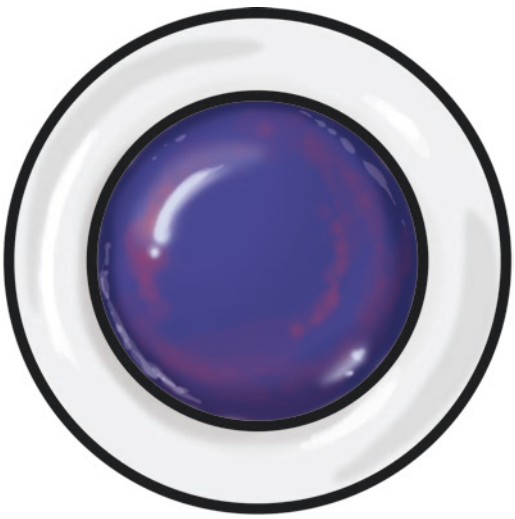

Fig. 14.7 "Blue-out" during band ligation of an esophageal varix

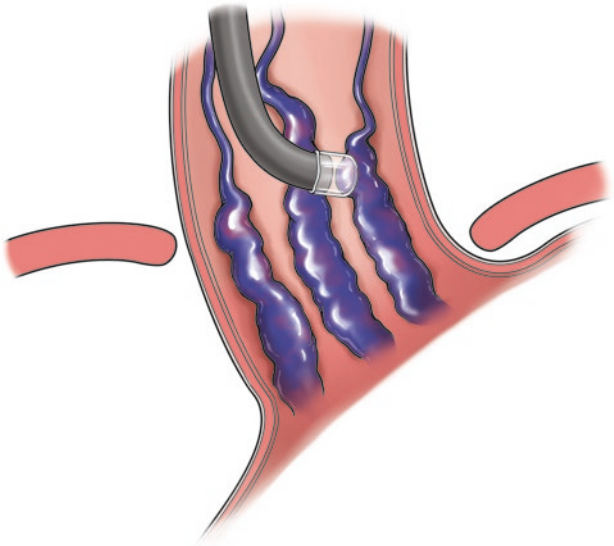

Fig. 14.8 An artist's depiction of suction of an esophageal varix into the cap of a band ligator

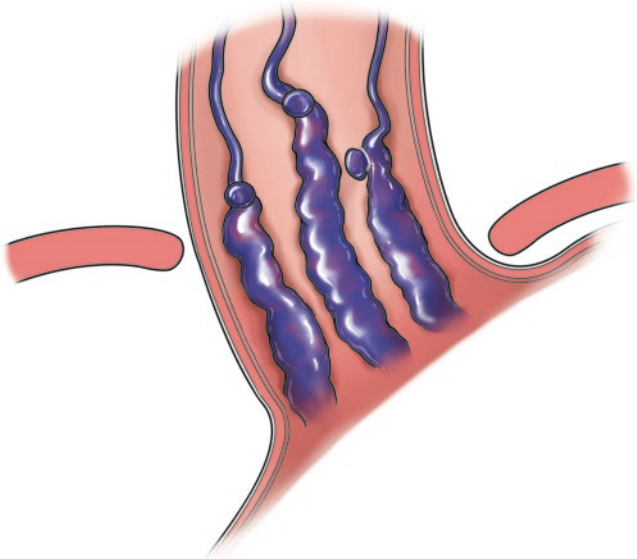

Fig. 14.9 An artist's depiction of a successful banding of esophageal varices

prolonged endoscopy time and did not reduce the total number of sessions required to obliterate visible varices [48]. Thus, prophylactic banding should generally be limited to six or fewer band ligations per session. The complications associated with band ligation include ulceration and stricture formation (Table 14.4). The banding kits come with different numbers of bands currently ranging from four to ten. The choice of which to use depends on the situation; more bands are required for acutely bleeding patients than for those undergoing elective re-banding [13].

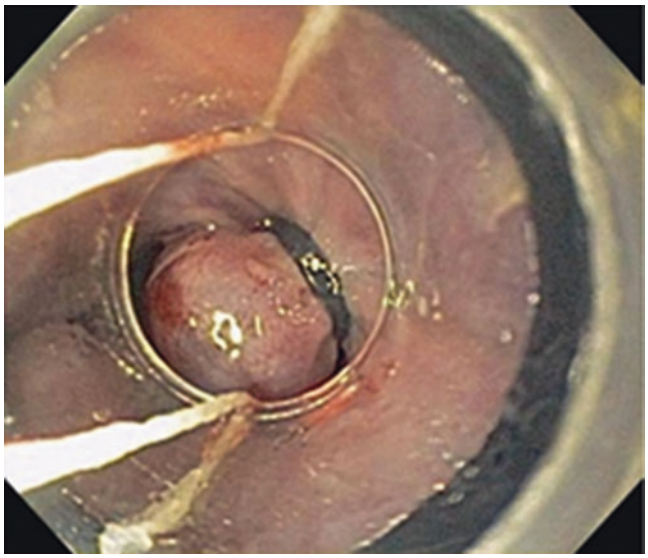

Fig. 14.10 An endoscopic view of band just placed on an esophageal varix using a band ligator

Table 14.4 Items to be present for endoscopic banding

Banding kit
Transparent cylinder loads with four, six, or ten bands
Trigger cord
Loading wheel
Loading catheter
Irrigation adapter
Suction should be turned to maximum or high prior to suctioning the varix into the cylinder

Injection Therapy

We describe this technique if one has to perform in emergency (the technique is going out of current practice). The sclerosants of choice are generally either 5% ethanolamine oleate or 5% sodium morrhuate. It is always advisable to keep a tamponade balloon readily available (Sengstaken–Blakemore) during sclerotherapy.

Technique

All injection devices consist of a fine needle with a beveled edge at the tip of a plastic tube, the proximal end of which has a luer lock (Table 14.5). It may help to orientate oneself within the esophagus and to grade the varices before therapy. It is advisable to inject the most distal varices first so that bleeding will not obscure the field of view of more proximal uninjected varices.

With the patient lying in the left lateral position, a drop of water or sclerosant from the tip of the needle or the catheter protruding from the biopsy channel will fall "down" to the left.

Table 14.5 Items to be present for endoscopic injection

Injector
Sclerosant
Syringes
Goggles
Experienced nurse
Sengstaken–Blakemore tube

If this point is considered to be 6 o' clock on a clockface, then the varices can be recorded around the clock. Similarly, a small pool of secretions may also serve the same purpose. We generally record the varices and their grades just above the gastroesophageal junction and approximately 5 cm proximally. The lower 5 cm is the most common site of bleeding, and, therefore, it is here that the injections should be placed. This area is also rich in large perforating vessels, which feed the varices from the periesophageal plexus of veins [42]. "Red blebs" are very thin areas, which are prone to bleeding and, therefore, should not be injected directly. No attempt should be made to inject ulcers and thrombosed varices on follow-up endoscopy as further ulceration and bleeding may occur.

Various techniques for injection have been endorsed throughout the literature. While some investigators advocate intravariceal injection, others advocate paravariceal injection, in order to cause fibrosis around the vessel and avoid systemic complications from the sclerosant. Others advocate a combination approach. It is difficult to determine which approach is most effective as many "intravariceal" injections may result in paravariceal injections.

Intravariceal Injection

Large varices are easier to inject, and, therefore, it is reasonable to choose the largest varix nearest to the 6 o'clock position, just above the gastroesophageal junction. The injector with its needle properly retracted is advanced through the biopsy channel and is advanced into the field of view. The needle is then pushed out and positioned between 30° and 45°. This is achieved by manipulating the tip of the endoscope. The injector is then inserted into the varix, and the sclerosant is injected (Fig. 14.11). Bulging and blanching are the signs of extravasation, which should be avoided. An experienced nurse can detect an intravariceal injection from the lower resistance felt on compressing the syringe plunger. In spite of taking extreme caution, extravasation may still go undetected, and, therefore, it is advisable that no more than 2 mL of sclerosant be injected at any one site. On withdrawal of the needle, a little bleeding may occur. Our practice is to insert the needle into the variceal column followed by injection of the sclerosant. After the injection, we maintain sufficient pressure on the varix for at least 15 s and then gradually withdraw the needle while maintaining pressure with the catheter tip for at least another 15 s. The catheter is gradually released watching for any evidence of bleeding (Fig. 14.12). If any signs of bleeding appear, the catheter is firmly applied to the varix and it is reinjected. If the varices are large, further, more distal injections within a 5 cm zone may be required. The needle is carefully withdrawn into the sheath before removing the injection catheter from the biopsy channel.

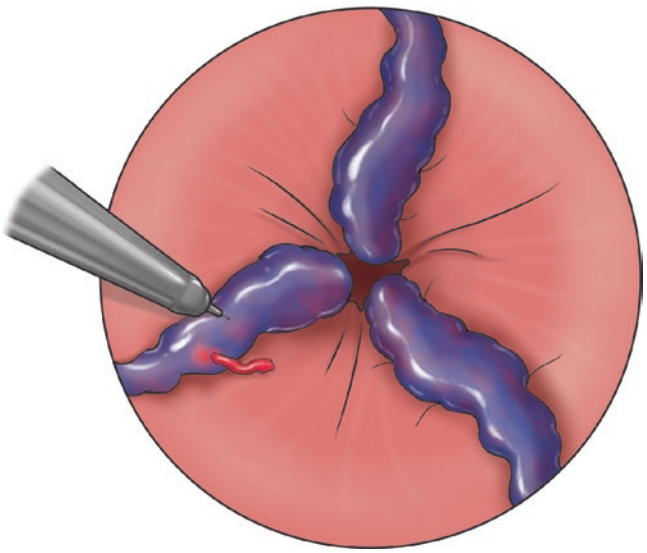

Fig. 14.11 An artist's depiction of intravariceal injection of sclerosant into an esophageal varix

Paravariceal Injection

Paravariceal injections of sclerosants produce fibrosis without ulceration or thrombosis of the varices. Small volumes of sclerosants are injected superficially adjacent to the variceal columns (Fig. 14.13). The injections are done more obliquely and superficially than for variceal thrombosis. Injections should begin just above the gastroesophageal junction and proceed in a spiral manner, up the esophagus, causing a uniform edematous sheath surrounding the variceal columns in the distal part of the esophagus (Fig. 14.14). Some endoscopists inject into the varices to cause thrombosis and make injections adjacent to and over the surface of the varices for added effect.

Endoscopic sessions are repeated every 1–3 weeks, and it may require six to eight sessions before obliteration of the varices is complete. Sclerotherapy has been associated with ulceration, esophageal perforation, esophageal stricture, portal vein thrombosis, and pulmonary embolism.

Practical Considerations

- Endoscopic variceal ligation works by capturing all or part of a varix within a band, resulting in occlusion from thrombosis.
- Cumulative data from a number of studies suggest that band ligation is preferred over sclerotherapy primarily due to greater control of hemorrhage, lower rebleeding, and lower adverse events.

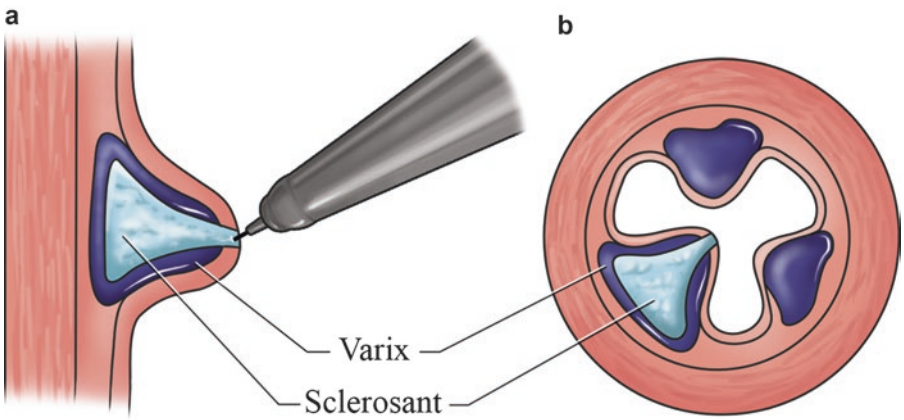

Fig. 14.12 An artist's depiction of an esophageal varix after intravariceal injection of a sclerosant (**a**) Linear view; (**b**) Sectional view

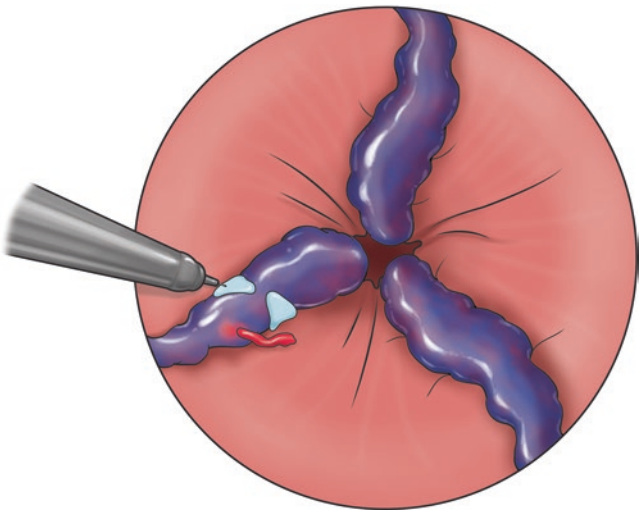

Fig. 14.13 An artist's depiction of an esophageal varix for paravariceal injection of a sclerosant

Combination of Band Ligation and Sclerotherapy

Combination treatment may hasten variceal eradication. Some endoscopists inject smaller volumes of sclerotherapy agents immediately after banding just proximal to the band ligation sites. Venous stasis above the banded site may enhance the effect of therapy. Others prefer injecting the sclerosant between the banded sites. It should be remembered that these approaches may not be superior to band ligation alone [21, 26, 39, 50]. Moreover, complications and mortality with combination therapy have been found to be higher than with band ligation or sclerotherapy alone [5, 40, 50].

Argon Plasma Coagulation

Argon plasma coagulation (APC) utilizes argon gas to conduct a high-frequency electrical current to produce coagulation that is only a few millimeters deep, without tissue contact by the probe. Several studies have demonstrated that APC may reduce the rebleeding rate of esophageal varices following effective band ligation therapy [24, 43]. Further studies should be performed before this procedure is performed in routine practice.

Gastric Varices

Gastric varices are found with advanced portal hypertension and are the source of hemorrhage in approximately 10% of patients with variceal bleeding. Gastric varices (GOV) are classified according to location and continuity with esophageal varices. GOV1 extend from the esophagus a short distance past the GE junction. GOV2 are in continuity with esophageal varices and extend into the fundus. IGV1 are isolated varices in the fundus, and IGV2 are isolated varices that occur in the body or antrum of the stomach. Gastric fundal varices are less likely to bleed than those found in other locations, but the magnitude of blood loss is comparatively more severe to esophageal variceal hemorrhage (Table 14.6, Figs. 14.15 and 14.16) [52].

The initial management of gastric variceal bleeding is similar to that of esophageal variceal bleeding and should include hemodynamic stabilization, adequate IV access, central venous pressure monitoring, consideration of endotracheal intubation, and intravenous administration of octreotide, a proton pump inhibitor, and antibiotics (either a fluoroquinolone or a third-generation cephalosporin). Unfortunately, large randomized controlled trials pertaining to endoscopic management of gastric varices do not exist. Band ligation in the stomach can be complicated by large ulcerations because of the mucosa overlying the vessel being banded. Sclerotherapy utilizing ethanolamine oleate or sodium morrhuate for gastric varices is often ineffective and, because it requires larger amounts of sclerosants than esophageal sclerotherapy, can often lead to complications. Treatment with cyanoacrylate has been shown to effectively control bleeding.

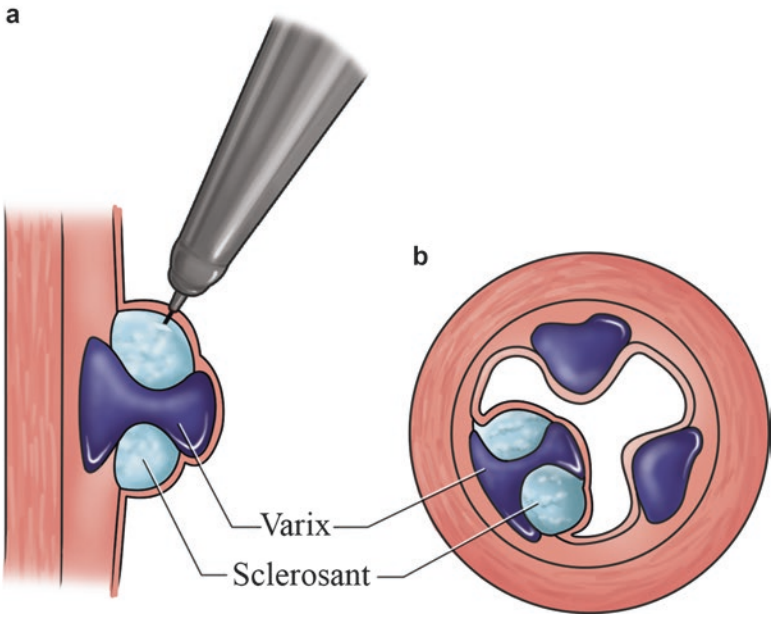

Fig. 14.14 An artist's depiction of a cross-sectional view of an esophageal varix for paravariceal injection of a sclerosant (**a**) Linear view; (**b**) Sectional view

Table 14.6 Endoscopic grading of gastric varices

GOV1	Gastroesophageal varices along the lesser curvature of the stomach
GOV2	Gastroesophageal varices along the greater curvature of the stomach
IGV1	Isolated gastric varices in the fundus
IGV2	Isolated gastric varices at other loci in the stomach

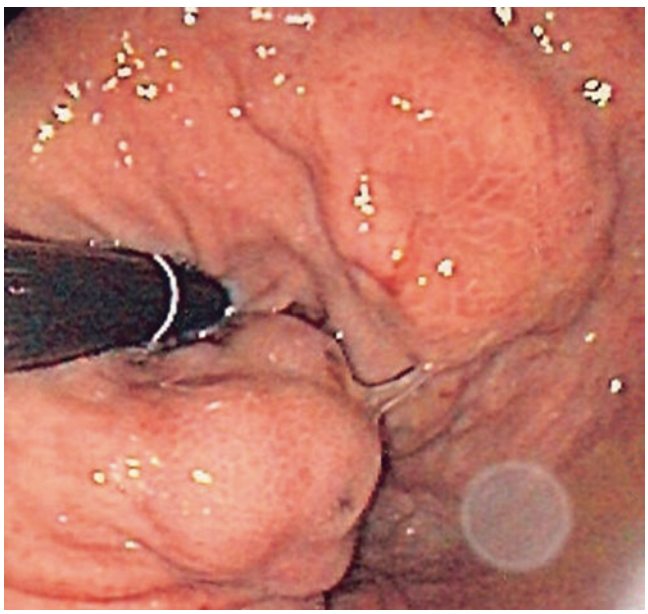

Fig. 14.15 An endoscopic view of gastric varices

However, this treatment has been shown to cause ulceration, bacteremia, and embolic disease. Cyanoacrylate is not currently approved for treatment in the USA and, therefore, is

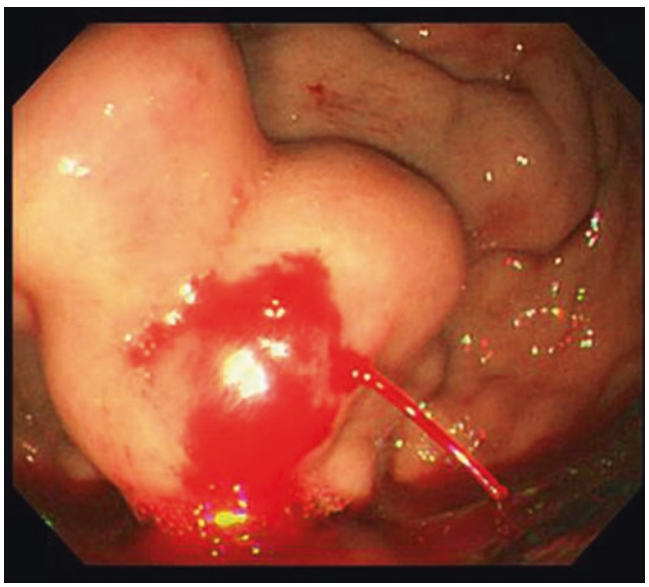

Fig. 14.16 An endoscopic view of an actively bleeding gastric varix

not discussed in detail here. Thrombin injections (approximately 1000 IU) have also been shown in small trials to effectively control bleeding from gastric varices in up to 90% of patients and decrease rebleeding rates to 20% at 6-week follow-up, without any reported adverse effects [46, 47, 65]. Several sessions of therapy are generally required. The use of a detachable snare with simultaneous sclerotherapy and O-ring ligation was recently reported in the literature to achieve hemostasis of gastric variceal hemorrhage in eight out of eight patients with a 97% resolution of gastric varices in 35 patients for whom it was used for primary or secondary prophylaxis of bleeding [66]. A Linton–Nachlas tube can

temporarily halt bleeding, while a more definitive treatment is pursued in those patients who continue to bleed. The Linton–Nachlas tube has a larger gastric balloon than the Sengstaken–Blakemore tube and, thus, causes more effective tamponade of gastric variceal bleeding. Endoscopic ultrasound-guided coiling and cyanoacrylate injection are in the experimental phase. These techniques are reported to achieve >90% obliteration of the gastric fundal varices [4]. However, it is a high-risk procedure, which is only available at selected centers and requires special skills. Balloon-occluded retrograde transvenous obliteration (BRTO) has been used for bleeding gastric varices. It involves occluding blood flow by inflation of a balloon catheter within a draining vessel, followed by instillation of a sclerosant proximal to the site of balloon occlusion. BRTO has shown good long-term bleeding control. However, technical failure occurs in approximately 10% of cases and may increase portal pressure leading to the development or worsening of esophageal varices, ascites, and systemic venous thrombosis [1, 12]. TIPS or surgical shunting are highly effective in controlling gastric variceal bleeding. Devascularization, as described by Sugiura and Futagawa, is a final option for the control of bleeding varices. Similar to esophageal varices, nonselective beta-blockers should be considered for primary and secondary prophylaxis in order to decrease the HVPG (Fig. 14.17).

Follow-Up

Following endoscopic therapy, patients will require close follow-up as complications are a well-known aspect of current therapy. Patients undergoing sclerotherapy are at risk for ulceration, bleeding, chest pain, and perforation. Band ligation can induce ulcers, bleeding, and strictures. Patients who undergo obliteration of varices for primary or secondary prophylaxis will need endoscopic sessions every 2–3 weeks, until obliteration is complete, and then subsequent surveillance endoscopies to monitor for recurrence of disease. Patients who are initiated on nonselective beta-blockers will need to gradually increase their dose every 5 days in order to achieve a 25% reduction from baseline heart rate or a resting heart rate of 55/min. Patients will need to be monitored for bradycardia and hypotension and should be counseled on compliance, as these agents can cause unpleasant side effects such as fatigue, wheezing, gastrointestinal symptoms, and impotence.

It is beyond the scope of this chapter to discuss the relative costs of various treatment modalities; however, with increasing cost constraints, physicians dealing with variceal hemorrhage should be aware of the cost-effectiveness of different treatments with consideration of their level of expertise and the availability of different therapeutic options.

Practical Considerations

- Endoscopic treatment of bleeding gastric varices with injection of the tissue adhesive cyanoacrylate (if available) is more effective and less invasive than TIPS procedure.
- TIPS placement is an alternative in areas where cyanoacrylate is not available.

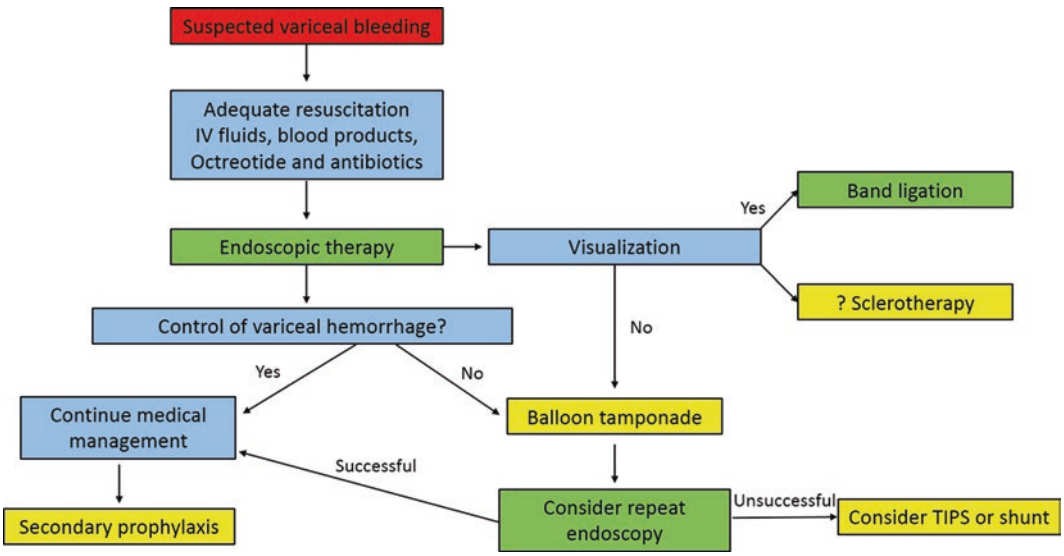

Fig. 14.17 An algorithm for the management of variceal hemorrhage

Conclusions

- The management of varices can be categorized into prepprimary prophylaxis, primary prophylaxis, secondary prophylaxis, and management of acute hemorrhage.
- Current therapeutic endoscopic modalities now offer outcomes superior to previous treatment methods, and new options for prophylaxis and management of acute hemorrhage appear imminent.
- Regardless of technological advances, the foundation of hemorrhage management remains rooted in the medical stabilization of the patient prior to the endoscopic therapy.

References

1. Akahoshi T, Hashizume M, Tomikawa M, Kawanaka H, Yamaguchi S, Konishi K, Kinjo N, Maehara Y. Long-term results of balloon-occluded retrograde transvenous obliteration for gastric variceal bleeding and risky gastric varices: a 10-year experience. J Gastroenterol Hepatol. 2008;23:1702–9.
2. Bernard B, Grange JD, Khac EN, Amiot X, Opolon P, Poynard T. Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: a meta-analysis. Hepatology. 1999;29:1655–61.
3. Bernard B, Lebrec D, Mathurin P, Opolon P, Poynard T. Beta-adrenergic antagonists in the prevention of gastrointestinal rebleeding in patients with cirrhosis: a meta-analysis. Hepatology. 1997;25:63–70.
4. Bhat YM, Weilert F, Fredrick RT, Kane SD, Shah JN, Hamerski CM, Binmoeller KF. EUS-guided treatment of gastric fundal varices with combined injection of coils and cyanoacrylate glue: a large U.S. experience over 6 years (with video). Gastrointest Endosc. 2016;83(6):1164–72.
5. Bhargava DK, Pokharna R. Endoscopic variceal ligation versus endoscopic variceal ligation and endoscopic sclerotherapy: a prospective randomized study. Am J Gastroenterol. 1997;92:950–3.
6. Blaise M, Pateron D, Trinchet JC, Levacher S, Beaugrand M, Pourriat JL. Systemic antibiotic therapy prevents bacterial infection in cirrhotic patients with gastrointestinal hemorrhage. Hepatology. 1994;20:34–8.
7. Bosch J, Abraldes JG, Groszmann R. Current management of portal hypertension. J Hepatol. 2003;38(Suppl 1):S54–68.
8. Carbonell N, Pauwels A, Serfaty L, Fourdan O, Levy VG, Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. Hepatology. 2004;40:652–9.
9. Chalasani N, Boyer TD. Primary prophylaxis against variceal bleeding: beta-blockers, endoscopic ligation, or both? Am J Gastroenterol. 2005;100:805–7.
10. Chalasani N, Clark WS, Martin LG, Kamean J, Khan MA, Patel NH, Boyer TD. Determinants of mortality in patients with advanced cirrhosis after transjugular intrahepatic portosystemic shunting. Gastroenterology. 2000;118:138–44.
11. Chalasani N, Imperiale TF, Ismail A, Sood G, Carey M, Wilcox CM, Madichetty H, Kwo PY, Boyer TD. Predictors of large esophageal varices in patients with cirrhosis. Am J Gastroenterol. 1999;94:3285–91.
12. Cho SK, Shin SW, Lee IH, Do YS, Choo SW, Park KB, Yoo BC. Balloon-occluded retrograde transvenous obliteration of gastric varices: outcomes and complications in 49 patients. AJR Am J Roentgenol. 2007;189:W365–72.
13. Committee AT, Liu J, Petersen BT, Tierney WM, Chuttani R, Disario JA, Coffie JM, Mishkin DS, Shah RJ, Somogyi L, Song LM. Endoscopic banding devices. Gastrointest Endosc. 2008;68:217–21.
14. D'amico G. Esophageal varices: from appearance to rupture; natural history and prognostic indicators. Portal hypertension in the 21st century. 2004.
15. D'amico G, Garcia-Pagan JC, Luca A, Bosch J. Hepatic vein pressure gradient reduction and prevention of variceal bleeding in cirrhosis: a systematic review. Gastroenterology. 2006;131:1611–24.
16. D'amico G, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. Semin Liver Dis. 1999;19:475–505.
17. D'amico G, Pietrosi G, Tarantino I, Pagliaro L. Emergency sclerotherapy versus vasoactive drugs for variceal bleeding in cirrhosis: a Cochrane meta-analysis. Gastroenterology. 2003;124:1277–91.
18. De Franchis R, Baveno VIF. Expanding consensus in portal hypertension: report of the Baveno VI consensus workshop: stratifying risk and individualizing care for portal hypertension. J Hepatol. 2015;63:743–52.
19. De Franchis R, Primignani M. Natural history of portal hypertension in patients with cirrhosis. Clin Liver Dis. 2001;5:645–63.
20. De La Pena J, Brullet E, Sanchez-Hernandez E, Rivero M, Vergara M, Martin-Lorente JL, Garcia suarez C. Variceal ligation plus nadolol compared with ligation for prophylaxis of variceal rebleeding: a multicenter trial. Hepatology. 2005;41:572–8.
21. Djurdjevic D, Janosevic S, Dapcevic B, Vukcevic V, Djordjevic D, Svorcan P, Grgov S. Combined ligation and sclerotherapy versus ligation alone for eradication of bleeding esophageal varices: a randomized and prospective trial. Endoscopy. 1999;31:286–90.
22. Escorsell À, Pavel O, Cárdenas A, Morillas R, Llop E, Villanueva C, Garcia-Pagán JC, Bosch J, Variceal BLEEDING STUDY GROUP. Esophageal balloon tamponade versus esophageal stent in controlling acute refractory variceal bleeding: a multicenter randomized, controlled trial. Hepatology. 2016;63(6):1957–67.
23. Feu F, Garcia-Pagan JC, Bosch J, Luca A, Teres J, Escorsell A, Rodes J. Relation between portal pressure response to pharmacotherapy and risk of recurrent variceal haemorrhage in patients with cirrhosis. Lancet. 1995;346:1056–9.
24. Furukawa K, Aoyagi Y, Harada T, Enomoto H. The usefulness of prevention consolidation therapy of esophageal varices using an argon plasma coagulation technique. Hepatol Res. 2002;23:220–5.
25. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W, Practice Guidelines Committee of the American Association for the Study of Liver Diseases, Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology. 2007;46:922–38.
26. Garg PK, Joshi YK, Tandon RK. Comparison of endoscopic variceal sclerotherapy with sequential endoscopic band ligation plus low-dose sclerotherapy for secondary prophylaxis of variceal hemorrhage: a prospective randomized study. Gastrointest Endosc. 1999;50:369–73.
27. Gluud LL, Klingenberg S, Nikolova D, Gluud C. Banding ligation versus beta-blockers as primary prophylaxis in esophageal varices: systematic review of randomized trials. Am J Gastroenterol. 2007;102:2842–8. quiz 2841, 2849
28. Gonzalez R, Zamora J, Gomez-Camarero J, Molinero LM, Banares R, Albillos A. Meta-analysis: combination endoscopic and drug therapy to prevent variceal rebleeding in cirrhosis. Ann Intern Med. 2008;149:109–22.
29. Groszmann RJ, Bosch J, Grace ND, Conn HO, Garcia-Tsao G, Navasa M, Alberts J, Rodes J, Fischer R, Bermann M, et al. Hemodynamic events in a prospective randomized trial of proprano-

lol versus placebo in the prevention of a first variceal hemorrhage. Gastroenterology. 1990;99:1401–7.
30. Groszmann RJ, Garcia-Tsao G, Bosch J, Grace ND, Burroughs AK, Planas R, Escorsell A, Garcia-Pagan JC, Patch D, Matloff DS, Gao H, Makuch R, PORTAL HYPERTENSION COLLABORATIVE, G. Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. N Engl J Med. 2005;353:2254–61.
31. GROUP, T. V. A. C. V. S. Prophylactic sclerotherapy for esophageal varices in men with alcoholic liver disease. A randomized, single-blind, multicenter clinical trial. The veterans affairs cooperative variceal sclerotherapy Group. N Engl J Med. 1991;324:1779–84.
32. Hernandez-Gea V, Aracil C, Colomo A, Garupera I, Poca M, Torras X, Minana J, Guarner C, Villanueva C. Development of ascites in compensated cirrhosis with severe portal hypertension treated with beta-blockers. Am J Gastroenterol. 2012;107:418–27.
33. Hubmann R, Bodlaj G, Czompo M, Benkö L, Pichler P, Al-Kathib S. The use of self-expanding metal stents to treat acute esophageal variceal bleeding. Endoscopy. 2006;38:896–901.
34. Ioannou G, Doust J, Rockey DC. Terlipressin for acute esophageal variceal hemorrhage. Cochrane Database Syst Rev. 2003: (vol.1) CD002147.
35. Jenkins SA, Shields R, Davies M, Elias E, Turnbull AJ, Bassendine MF, James OF, Iredale JP, Vyas SK, Arthur MJ, Kingsnorth AN, Sutton R. A multicentre randomised trial comparing octreotide and injection sclerotherapy in the management and outcome of acute variceal haemorrhage. Gut. 1997;41:526–33.
36. Jun CH, Park CH, Lee WS, Joo YE, Kim HS, Choi SK, Rew JS, Kim SJ, Kim YD. Antibiotic prophylaxis using third generation cephalosporins can reduce the risk of early rebleeding in the first acute gastroesophageal variceal hemorrhage: a prospective randomized study. J Korean Med Sci. 2006;21:883–90.
37. Kleber G, Sauerbruch T, Ansari H, Paumgartner G. Prediction of variceal hemorrhage in cirrhosis: a prospective follow-up study. Gastroenterology. 1991;100:1332–7.
38. Laine L, El-Newihi HM, Migikovsky B, Sloane R, Garcia F. Endoscopic ligation compared with sclerotherapy for the treatment of bleeding esophageal varices. Ann Intern Med. 1993;119:1–7.
39. Laine L, Estrada R, Trujillo M, Fukanaga K, Neil G. Randomized comparison of differing periods of twice-a-day triple therapy for the eradication of helicobacter pylori. Aliment Pharmacol Ther. 1996a;10:1029–33.
40. Laine L, Stein C, Sharma V. Randomized comparison of ligation versus ligation plus sclerotherapy in patients with bleeding esophageal varices. Gastroenterology. 1996b;110:529–33.
41. Lo GH, Lai KH, Cheng JS, Lin CK, Huang JS, Hsu PI, Chiang HT. Emergency banding ligation versus sclerotherapy for the control of active bleeding from esophageal varices. Hepatology. 1997;25:1101–4.
42. Mccormack TT, Rose JD, Smith PM, Johnson AG. Perforating veins and blood flow in oesophageal varices. Lancet. 1983;2:1442–4.
43. Nakamura S, Mitsunaga A, Murata Y, Suzuki S, Hayashi N. Endoscopic induction of mucosal fibrosis by argon plasma coagulation (APC) for esophageal varices: a prospective randomized trial of ligation plus APC vs. ligation alone. Endoscopy. 2001;33:210–5.
44. North Italian Endoscopic Club for the, S. & Treatment of Esophageal, V. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. N Engl J Med. 1988;319:983–9.
45. Pagliaro L, D'amico G, Sorensen TI, Lebrec D, Burroughs AK, Morabito A, Tine F, Politi F, Traina M. Prevention of first bleeding in cirrhosis. A meta-analysis of randomized trials of nonsurgical treatment. Ann Intern Med. 1992;117:59–70.
46. Przemioslo RT, Mcnair A, Williams R. Thrombin is effective in arresting bleeding from gastric variceal hemorrhage. Dig Dis Sci. 1999;44:778–81.
47. Ramesh J, Limdi JK, Sharma V, Makin AJ. The use of thrombin injections in the management of bleeding gastric varices: a single-center experience. Gastrointest Endosc. 2008;68:877–82.
48. Ramirez FC, Colon VJ, Landan D, Grade AJ, Evanich E. The effects of the number of rubber bands placed at each endoscopic session upon variceal outcomes: a prospective, randomized study. Am J Gastroenterol. 2007;102:1372–6.
49. Rikkers LF, Jin G. Emergency shunt. Role in the present management of variceal bleeding. Arch Surg. 1995;130:472–7.
50. Saeed ZA, Stiegmann GV, Ramirez FC, Reveille RM, Goff JS, Hepps KS, Cole RA. Endoscopic variceal ligation is superior to combined ligation and sclerotherapy for esophageal varices: a multicenter prospective randomized trial. Hepatology. 1997;25:71–4.
51. Shao XD, Qi XS, Guo XD. Esophageal stent for refractory Variceal bleeding: a systemic review and meta-analysis. Biomed Res Int. Vol. 2016: Article ID 4054513.
52. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology. 1992;16:1343–9.
53. Sarin SK, Lamba GS, Kumar M, Misra A, Murthy NS. Comparison of endoscopic ligation and propranolol for the primary prevention of variceal bleeding. N Engl J Med. 1999;340:988–93.
54. Sarin SK, Wadhawan M, Agarwal SR, Tyagi P, Sharma BC. Endoscopic variceal ligation plus propranolol versus endoscopic variceal ligation alone in primary prophylaxis of variceal bleeding. Am J Gastroenterol. 2005a;100:797–804.
55. Sarin SK, wadhawan M, Gupta R, Shahi H. Evaluation of endoscopic variceal ligation (EVL) versus propanolol plus isosorbide mononitrate/nadolol (ISMN) in the prevention of variceal rebleeding: comparison of cirrhotic and noncirrhotic patients. Dig Dis Sci. 2005b;50:1538–47.
56. Schepis F, Camma C, Niceforo D, Magnano A, Pallio S, Cinquegrani M, D'amico G, Pasta L, Craxi A, Saitta A, Raimondo G. Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection? Hepatology. 2001;33:333–8.
57. Senzolo M, Cholongitas E, Burra P, Leandro G, Thalheimer U, Patch D, Burroughs AK. Beta-blockers protect against spontaneous bacterial peritonitis in cirrhotic patients: a meta-analysis. Liver Int. 2009;29:1189–93.
58. Sung JJ, Chung SC, Lai CW, Chan FK, Leung JW, Yung MY, Kassianides C, Li AK. Octreotide infusion or emergency sclerotherapy for variceal haemorrhage. Lancet. 1993;342:637–41.
59. Teres J, Bosch J, Bordas JM, Garcia Pagan JC, Feu F, Cirera I, Rodes J. Propranolol versus sclerotherapy in preventing variceal rebleeding: a randomized controlled trial. Gastroenterology. 1993;105:1508–14.
60. Triantos C, Vlachogiannakos J, Manolakopoulos S, Burroughs A, Avgerinos A. Is banding ligation for primary prevention of variceal bleeding as effective as beta-blockers, and is it safe? Hepatology. 2006;43:196–7. discussion 197-8
61. Vieira DA, Rocha EC, D'amico EA, Caldwell SH, Flores DA, Rocha TR, Soares ESCS, Dos Santos Bomfim V, Felga G, Barbosa WF, Kassab F, Polli DA, Carrilho FJ, Farias AQ. A prospective study of conventional and expanded coagulation indices in predicting ulcer bleeding after variceal band ligation. Clin Gastroenterol Hepatol. 2009;7:988–93.
62. Villanueva C, Minana J, Ortiz J, Gallego A, Soriano G, Torras X, Sainz S, boadas J, Cusso X, Guarner C, Balanzo J. Endoscopic ligation compared with combined treatment with nadolol and

isosorbide mononitrate to prevent recurrent variceal bleeding. N Engl J Med. 2001;345:647–55.
63. Villanueva C, Piqueras M, Aracil C, Gomez C, Lopez-Balaguer JM, Gonzalez B, Gallego A, Torras X, Soriano G, Sainz S, Benito S, Balanzo J. A randomized controlled trial comparing ligation and sclerotherapy as emergency endoscopic treatment added to somatostatin in acute variceal bleeding. J Hepatol. 2006;45:560–7.
64. Villeneuve JP, Pomier-Layrargues G, Duguay L, Lapointe R, Tanguay S, Marleau D, Willems B, Huet PM, Infante-Rivard C, Lavoie P. Emergency portacaval shunt for variceal hemorrhage. A prospective study. Ann Surg. 1987;206:48–52.
65. Yang WL, Tripathi D, Therapondos G, Todd A, Hayes PC. Endoscopic use of human thrombin in bleeding gastric varices. Am J Gastroenterol. 2002;97:1381–5.
66. Yoshida T, Harada T, Shigemitsu T, Takeo Y, Miyazaki S, Okita K. Endoscopic management of gastric varices using a detachable snare and simultaneous endoscopic sclerotherapy and O-ring ligation. J Gastroenterol Hepatol. 1999;14:730–5.

Endoscopic Management of Non-variceal Upper Gastrointestinal Bleeding

15

Muhammed Sherid and Subbaramiah Sridhar

Introduction

Acute upper GI bleeding is a common, potentially life-threatening medical emergency. In the USA, it is estimated that more than 300,000 hospital admissions per year are due to upper GI bleeding, resulting in 30,000 deaths annually [25]. Upper GI bleeding is defined as any GI bleeding that occurs in any part of the GI tract proximal to the ligament of Treitz [17].

Acute upper GI bleeding manifests as one or more of the following symptoms: coffee ground emesis, hematemesis, melena, and/or hematochezia. The main determining factor for these symptoms is directly related to the rate and severity of bleeding; the slower the bleeding, the darker the appearance of the blood and vice versa. The presence of coffee ground emesis suggests more limited bleeding, whereas frank hematemesis suggests more severe or continued bleeding. Melena indicates blood that has been present in the GI tract for at least 14 h, and it is more likely to be the result of an upper GI bleeding source. However, 10% of melena can originate from the oropharynx, small bowel, and right colon [25]. Melena can be seen with as little as 50 mL of blood. Hematochezia on the other hand, which is mostly the result of lower GI bleeding, can be a manifestation of an upper GI bleeding lesion in around 15% of the instances when the blood loss is more than 1 L and transit time is less than 4 h in association with hemodynamic instability [26].

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Nasogastric (NG) lavage with blood or coffee ground material confirms upper GI bleeding, and bloody lavage increases the possibility of active bleeding; however, a clear or bile-stained NG lavage may be seen up to 18% of patient with acute upper GI bleeding [27]. In addition, NG tube is one of the most unpleasant procedures by patients in a survey in ER patients. Thus, American College of Gastroenterology 2012 guidelines stated that NG lavage is probably not necessary in most patients with upper GI bleeding [27].

Causes of Upper GI Bleeding

Older studies suggested that peptic ulcer disease accounted for 50% of upper GI bleeding; however, more recent studies suggest that, while still the most common source of upper GI bleeding, ulcer disease accounts for 20–25% of case with bleeding from gastric ulcers being more common than bleeding from duodenal ulcers [5].

The most common causes of upper GI bleeding include the following (in descending order of frequency) [5, 10, 28]:

- Gastric and/or duodenal ulcers
- Esophagogastric varices
- Severe esophagitis
- Severe gastritis/duodenitis
- Portal hypertensive gastropathy
- Angiodysplasia (arteriovenous malformation: AVMs)
- Mass lesions (polyps/cancers)
- Mallory-Weiss tear
- No lesion identified (10–15% of cases)

Other less common causes of upper GI bleeding include:

- Dieulafoy's lesion
- Gastric antral vascular ectasia (GAVE)
- Hemobilia
- Hemosuccus pancreaticus

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- Aortoenteric fistula
- Cameron lesions
- Ectopic varices

In this chapter, we focus only on the endoscopic management of peptic ulcer bleeding.

Practical Considerations

- Peptic ulcer disease is the most common source of upper GI bleeding, ulcer disease accounting for 20–25% of case with bleeding from gastric ulcers being more common than bleeding from duodenal ulcers.

Initial Evaluation of Patients with Upper GI Bleeding

The initial evaluation should always include a thorough medical history, physical examination, and laboratory tests. The goal is to evaluate the severity of the GI bleeding, recognize possible site of bleeding, and identify any comorbidities that may affect the treatment. This data should be collected as a part of the initial evaluation to help guide triaging the patients, fluid resuscitation, and medical therapy and to plan timing of endoscopy.

Hemodynamic stability of the patients is an important step prior to any endoscopic intervention. Patients with mild to moderate hypovolemia have resting tachycardia. Patients with orthostatic hypotension have at least 15–20% blood loss of their total blood volume, whereas patients with supine hypotension have more than 40% blood loss. Intravenous fluid resuscitation, blood transfusion, and oxygen therapy are extremely important initial interventions to ensure patients' stability.

Once the patient has become hemodynamically stable, upper endoscopy can be performed to provide diagnosis and gather further prognostic information, both of which will dictate subsequent management.

Several risk factors influence the outcome of an acute upper GI bleeding with regard to rebleeding and mortality. Risk assessment is useful to determine higher-risk patients for rebleeding or bad outcome, level of care, timing of endoscopy, and time of discharge [27]. Several risk assessment scoring systems have been developed including Rockall score (Table 15.1), Glasgow Blatchford score, modified Glasgow Blatchford, and AMIS65 [22, 29–31]. Both mortality and rebleeding rates increased in a stepwise fashion as the scores go up. These scoring systems can be very helpful in identifying patients who are at low risk of rebleeding and negligible risk of death and hence might be considered for early discharge or outpatient treatment. Patients with Blatchford score of 0 (BUN < 18.2 mg/dl; hemoglobin ≥13 g/dl for men and ≥12 g/dl for women; systolic blood pressure ≥110 mmHg; pulse <100 b/m; absence of melena, syncope, cardiac failure, and liver disease) have <1% chance of requiring intervention and may discharge from the emergency room without inpatient endoscopy [27, 29].

Practical Considerations

- Patients with mild to moderate hypovolemia have resting tachycardia. Patients with orthostatic hypotension have at least 15–20% blood loss of their total blood volume, whereas patients with supine hypotension have more than 40% blood loss.
- Intravenous fluid resuscitation and oxygen therapy are very important initial interventions to ensure patients' stability.
- Several risk assessment scoring systems are available (Rockall score, Glasgow Blatchford score, modified Glasgow Blatchford, and AMIS65).

Table 15.1 Mental check list for endoscopists during endoscopy (Print and put on wall of Endo Room)

	Score			
Variable	0	1	2	3
Age	<60	60–79	>80	
Shock	No shock SBP ≥ 100 HR < 100	Tachycardia HR ≥ 100 SBP ≥ 100	Hypotension SBP < 100	
Comorbidities	No major comorbidities		CHF CAD	Renal failure, liver failure, disseminated malignancy
Diagnosis	MWT No lesion No SRH	All other diagnosis	Malignant upper GI tract	
Major SRH	None or dark spot only		Blood in the upper tract, adherent clot, visible or spurting vessel	

Anatomy of a Bleeding Ulcer

Peptic ulcers usually bleed because of erosion into an underlying medium-sized arteriole in the submucosal plexus of vessels. Posterior wall duodenal bulb ulcers and lesser curve gastric ulcers usually bleed heavily because of erosion into larger caliber arterioles and, therefore, fall into high-risk group of ulcers. Endoscopic therapy usually stops the bleeding if the underlying vessel is smaller than 1 mm in size [24].

Timing of Endoscopy

The timing of endoscopy has been a subject of debate in patients with GI bleeding. Early endoscopy has been advocated, but the optimal timing is uncertain. The definition of early endoscopy has been variably described as endoscopy performed between 2 and 24 h of presentation with GI bleeding. It has been shown that patients who are undergoing early endoscopy within 8 h have more high-risk stigmata of recent bleeding (active bleeding, visible vessels, or adherent clots) and require more endoscopic interventions but have no benefits in clinical outcomes [32]. In low-risk patients who are hemodynamically stable and have no serious comorbid conditions, early endoscopy can decrease the length of hospital stay and post-discharge physician visits. Discharging patients home immediately after early endoscopy in low-risk patients is possible in 40–45% of cases which obviously lower the cost of healthcare in this subset of patients [33, 34]. However, the lack of clinical benefit argues against the need for endoscopy for low-risk patients in the emergent settings such as the middle of the night [27]. In high-risk patients such as patients with bloody NG aspirate and patients with hypotension, early endoscopy within 12 h decrease number of blood transfusion, hospital stay, and mortality [27, 35]. However, very early endoscopy, before appropriate resuscitation and stabilization of the patient, may carry a higher risk for potential complications.

Practical Considerations

- Early endoscopy within 8 h has more high-risk stigmata of recent bleeding and requires more endoscopic interventions.
- In low-risk patients who are hemodynamically stable and have no serious comorbidities, early endoscopy can decrease the length of hospital stay and post-discharge physician visits.
- In high-risk patients such as patients with bloody NG aspirate and patients with hypotension, early endoscopy within 12 h decreases number of blood transfusion, hospital stay, and mortality.
- A very early endoscopy, before appropriate resuscitation and stabilization of the patient, may carry a higher risk for potential complications.

Table 15.2 Forrest classification

Active bleeding	
Class Ia	Ulcer with arterial spurting
Class Ib	Ulcer with active oozing
Signs of recent hemorrhage	
Class IIa	Ulcer with nonbleeding visible vessel
Class IIb	Ulcer with adherent clot
Class IIc	Ulcer with flat pigmented spot
No signs of recent hemorrhage	
Class III	Ulcer with clean base

Administration of proton pump inhibitors (PPI) before endoscopy decreases the proportion of participants with high-risk stigmata of bleeding (active bleeding, non-visible vessel, and adherent clot) in patients who undergo endoscopy and decreases rebleeding and surgery in patients who do not receive endoscopy or if there is delay in endoscopy [15, 36, 37].

Endoscopic Therapy of Bleeding Peptic Ulcers

According to recent studies, peptic ulcers are the most common causes of upper GI bleeding accounting for about 20–25%. Gastric or duodenal ulcers can be classified endoscopically according to Forrest classification as shown in Table 15.2 and Fig. 15.1:

Rebleeding rates and mortality of each of the above ulcers with and without endoscopic interventions are shown in Table 15.3 [7, 12].

Class I and IIb ulcers do clearly benefit from endoscopic therapy as discussed below.

Patient Monitoring

It is important to maintain adequate oxygenation of the patient as arterial desaturation can occur during the procedure. Pulse oximetry and blood pressures should be continually recorded. Pressurized infusion bags and resuscitation equipment should be readily available. Competent assistants and nurses should be monitoring the patient and assisting the endoscopist.

Patient Position

The left lateral position is generally preferred. In this position, blood in the stomach gravitates toward the fundus and the greater curve of the body of the stomach. Occasionally, the patient is rolled to the right lateral decubitus position, and occasionally the head of the bed is elevated into a sitting position so that the cardia of the stomach can be well examined as shown in Fig. 15.2.

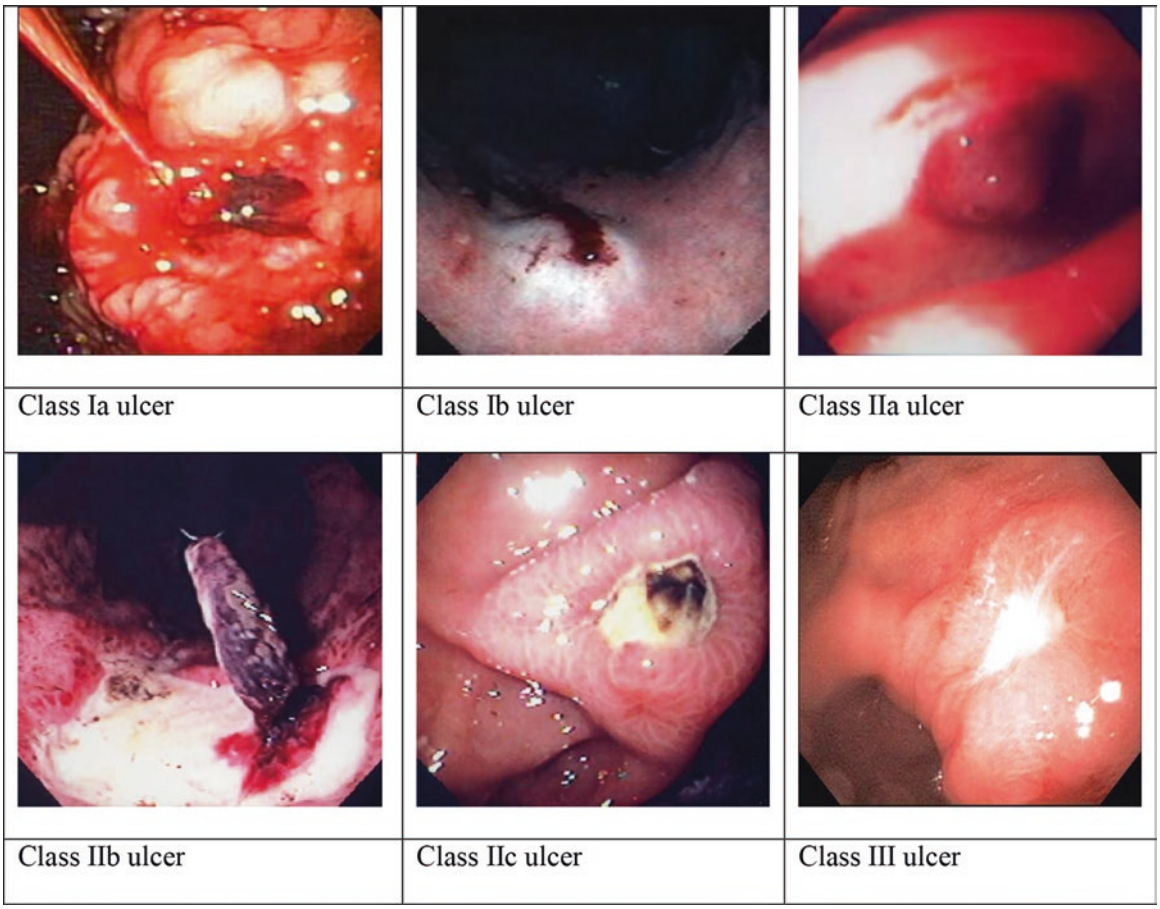


Fig. 15.1 Forrest classification: (**a**) class Ia ulcer, (**b**) class Ib ulcer, (**c**) class IIa ulcer, (**d**) class IIb ulcer, (**e**) class IIc ulcer, and (**f**) Class III ulcer

Table 15.3 Rebleeding rates and mortality of ulcers with and without endoscopic interventions

Findings	% Rebleeding without endoscopic treatment	% Mortality	Rebleeding after endoscopic therapy
Active arterial spurting	90	11	15–30
Visible vessel	50	11	15–30
Adherent clot	12–33	7	5
Oozing without stigmata	10–27		N/A
Flat pigmented spot	7	3	N/A
Clean based	<5	2	N/A

Gastric Lavage

Gastric lavage is usually unnecessary as the majority of the bleeding lesions are located in the duodenum, antrum, or lesser curvature, while most of the blood tends to pool in the fundus when the patient is lying in the left lateral decubitus position. However, if lavage is still needed, an overtube can be placed to protect the airway while repeated intubation for lavage is performed.

Practical Considerations

- Competent nurses should assist the endoscopist.
- The vital signs and oxygen saturation should be monitored continually.
- Gastric lavage is unnecessary in the majority of cases.

Endoscopic Treatment

Endoscopy can be performed using a diagnostic or a therapeutic endoscope. Each has its own advantages and limitations. The diagnostic endoscope is more flexible and easy to manipulate, but it has a smaller 2.8-mm instrument channel that limits irrigation and suctioning in addition to

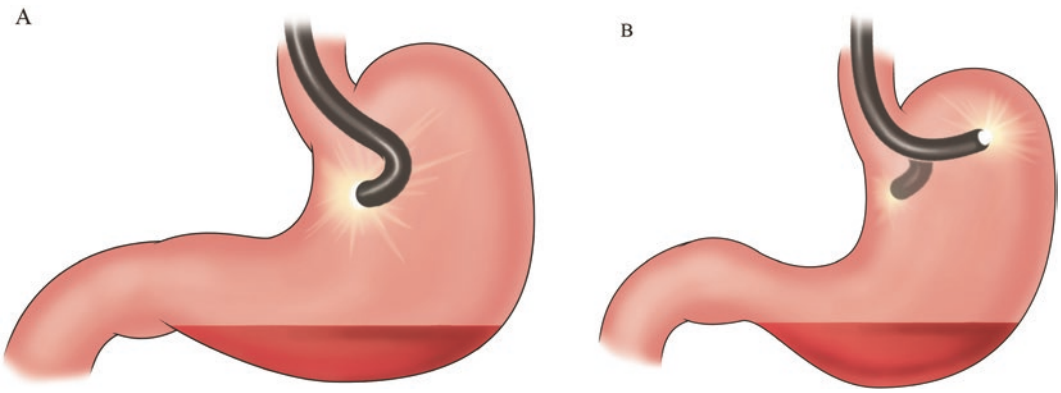


Fig. 15.2 Patient positions

Table 15.4 Instruments and accessories for the treatment of GI bleeding

Diagnostic and therapeutic endoscope in working order (therapeutic endoscope is preferred)
Gastric lavage kit
Injection needle, snare, and Roth Net
Multipolar or heat probe
Endoclips (multiple)
Epinephrine
Sclerosing agent

only accommodating a 7 Fr multipolar or heater probe. On the other hand, the therapeutic endoscope has two channels, a 2.8 mm and a 3.7 mm one. One channel can be used for irrigation and/or suctioning, while the other can be used to introduce an injection needle or even a 10 Fr probe. However, the therapeutic endoscope has a larger external diameter, is less flexible, and, therefore, is harder to manipulate.

Endoscopic therapeutic interventions include thermal and nonthermal techniques. The thermal techniques can be divided into electrocoagulation and non-electrocoagulation, while the nonthermal ones include needle injection, tissue glue, and endoclip placement.

Instruments and Accessories

The endoscopist, his assistants, the nursing team, and the anesthesiology personnel should be completely familiar with the patient's condition, indications, and the contraindications for the procedure. He or she should also be familiar with the endoscopy unit and the setup and finally be comfortable and confident in performing necessary interventions. Finally, one has to make sure that all the necessary accessories are available on hand and one should not be frantically searching for equipment (Table 15.4).

Thermal Therapy

Electrothermocoagulation

This thermal method uses direct heat therapy in combination with mechanical compression to produce a strong sealing of the bleeding vessel. Several types of probes are available for endoscopic therapy; they can be applied directly or with an acute angle, and most of them have built-in irrigation channel to help wash away blood and clots. The three currently available methods are the monopolar, liquid monopolar, and the multipolar electrocoagulation. In monopolar electrocoagulation, the current flows through the patient and exits via a ground plate. However, the depth of coagulation and tissue adherence is unpredictable, thus rendering this method less popular for use. The liquid monopolar or electrohydrothermal method allows the application of a film of water or normal saline to the tip of the probe to reduce tissue stickiness but does not solve the problem of lack of predictability of the depth of tissue injury. The multipolar probe is made of three pairs of electrodes arranged in a linear array at the tip connected to a power generator. Patient grounding is not needed since the flow of the electrical current is limited to between the electrodes on the probe where tissue can be heated up to 100 °C on contact. The depth of the injury is shallow compared to the previously mentioned two methods, with less risk for transmural damage and capability to coagulate vessels of up to 2 mm in diameter. Seven Fr and 10 Fr probes are available. The latter requires a therapeutic scope with 3.7-mm inner channel diameter.

The Technique

The probe should be pushed firmly against the blood vessel while delivering the heat to achieve good foot-printing and, hence, more lasting homeostasis. Here, the larger (10 Fr)

probe is preferred. A low current setting is recommended (15 and 25 W), and a sustained period of probe application is used (10–14, 2-s pulses).

Nonelectrothermocoagulation

This includes heat probe and microwave coagulation. A heat probe consists of a metal tip covered with Teflon that is heated by a computer-controlled coil to a temperature of 250 °C in order to deliver 15–30 joules of energy. The probe should be pushed firmly against the vessel while delivering the energy for about 8 s of contact time followed by extensive irrigation prior to retrieval of the probe in order to minimize tissue shearing and immediate rebleeding. On the other hand, microwave coagulation uses microwave energy directed to tissue via a 2.7-mm diameter coaxial cable, the terminal portion of which ends in a needlelike electrode, which projects about 2–3 mm. The bleeding lesion is penetrated by the electrode, and microwave energy is delivered to be absorbed by water-rich tissue that results in thermal coagulation. Vessels up to 3 mm in size can be coagulated.

The Technique

Here, a larger probe is preferred (10 Fr), and a firm pressure is applied over the bleeding point using three to four, 30 J pulses before changing the position. A "probe print or cavitation" at the site of the bleeding point is considered a good end point.

Injection Therapy

Agents Used

This is a nonthermal technique that uses epinephrine or sclerosants such as 1% polidocanol, 5% ethanolamine, absolute alcohol, 1.5% sodium tetradecyl sulfate, hypertonic saline, and 50% dextrose solution (Table 15.4). Epinephrine is the most commonly established and widely used agent for homeostasis of ulcers. Injection therapy can be used with standard endoscope using a disposable 23 or 25 gauge sclerotherapy needle. Epinephrine or sclerosants are injected around and into the bleeding point at the base of the ulcer to raise submucosal blebs followed by cessation of bleeding. In our unit we use 1:10,000 concentration epinephrine.

The mechanism of action of epinephrine is believed to be prolonged vasoconstriction for up to 2 h, platelet activation and aggregation, and activation of the coagulation cascade [2, 21]. With large volumes, it also exerts a local tamponade effect on the vessel [16]. It is metabolized on a first pass by the liver, and, hence, up to 20 mL can be injected safely in patient with good liver function. More care and smaller volumes should be used in patients with hepatic dysfunction because of the risk for systemic side effects, the most common of which is tachycardia [23]. Epinephrine has a low tissue-damaging potential and does not cause ulcers, necrosis, or perforation. It can be injected blindly into the pool of blood in active bleeding patients in order to slow the bleeding and localize the lesion for further direct interventions [16].

Sclerosants (Table 15.5), on the other hand, cause bowel wall spasm and early edema with subsequent inflammation and thrombosis of the vessel. Absolute alcohol causes rapid dehydration and rapid fixation of the tissue leading to obliteration of the bleeding vessel. The degree of tissue damage is directly related to the volume of the sclerosant injected with higher volumes carrying higher risk for ulceration and perforation.

Practical Considerations

- Epinephrine injection is effective to achieve initial hemostasis in patients with active bleeding.
- Epinephrine injection alone is less effective than other monotherapies in preventing rebleeding and the need for surgery.

Thrombin/Fibrin Glue

Injection of a solution of thrombin and fibrinogen via a standard injection needle can obliterate and compress the bleeding point. Thrombin promotes the conversion of fibrinogen to fibrin leading to the production of a local fibrin clot without any potential for tissue injury or necrosis. However, the potential complications include thrombosis, embolization, viral transmission, and anaphylactic reaction.

The Technique

An injection needle with a retractable tip is used. Generally, 1:10,000 concentration of epinephrine is used. We use smaller volumes of the solution in aliquots of 1–2 mL. We recommend injecting, if possible, all the four quadrants

Table 15.5 Agents for the treatment of GI bleeding

Sclerosing agents
Polidocanol, 1%
Ethanolamine, 5%
Absolute alcohol
Sodium tetradecyl sulfate, 1.5%
Hypertonic saline
Dextrose solution, 50%

at least 3–4 mm away from the bleeding point. The assistant should be instructed to retract the needle after each aliquot of injection. Generally, mucosal paleness is noted after injection of epinephrine. The nursing assistant may encounter resistance in injecting the solution. We usually inject the mucosa distal to the bleeding point first, which may raise the mucosa and tilt the bleeding point toward the endoscope. Whether the use of smaller or larger volumes of epinephrine is preferable is a matter of debate. Lin and his group have proposed larger volumes of epinephrine (mean 16.5 mL) as the rebleeding risk was lower in this group when compared with smaller volumes, 15.4% versus 30.8%, with a mean of 8 mL [19].

Mechanical Clips

Hemoclip application is a mechanical method of homeostasis. The clips can control large-sized arterioles. The clips can be cumbersome and difficult to deploy in difficult locations and especially in the retroflexed position. Clip application is not for diffuse bleeding with no identifiable vessel. Four types of endoclips are currently available on the market: the Rotating clip, the QuickClip, the TriClip, and the Resolution clip. Specifications of each of these devices are summarized in Table 15.6.

Before starting the procedure, the Rotating clip is loaded onto an applicator and kept ready for use. The applicator can be reused after sterilization. Although this device is cheaper compared to the other clips that are disposable, a major drawback is the need to reload the device with a clip in the middle of the procedure. This can be easily overcome by preloading two or three clip applicators before the start of the procedure and keeping them ready for use. QuickClip is a single-use device that comes preloaded on a disposable applicator in a sterile package. The TriClip is a three-pronged single-use device with a flushing mechanism. An advantage of the Resolution clip is that it can be opened and closed up to five times to achieve a satisfactory position prior to deployment (Fig. 15.3). Although not specifically designed to be rotated, it can be rotated counterclockwise with minimal effort, if needed.

The Technique

The operator and the assistant should be familiar with the type of clip being used and the method of clip application. It is also very important to have a rough idea of the direction of blood flow in the underlying arteriole. The clip applicator exits the endoscope at the 8 o'clock position of the endoscopic field, and therefore any lesion at this position is easier to be targeted. It is also important to rotate the shaft of the

Table 15.6 Types of clips and their specifications

Company product name	Olympus			Boston scientific	Wilson cook	
	Rotating clip	QuickClip 2	QuickClip 2 long	Resolution clip	TriClip	TriClip
Catalog number	HX-LR/QR-1 HX-6UR-1	HX-201LR/ UR-135	HX-201LR/ UR-135 L	M005226XX	TC-8–12	TC-7–12
Ready to use	No	Yes	Yes	Yes	Yes	Yes
Clip size	>2.8 mm (5LR/QR) >3.2 mm (6UR)	>2.8 mm	>2.8 mm	>2.8 mm	>3.2 mm	>2.8 mm
Working length	230 cm (6 U), 195 cm (5Q) and165 cm (5 L)	240 cm (UR) and 165 cm (LR)	240 cm (UR), 165 cm (LR)	235 cm 155 cm	205 cm	207 cm
Maximum clip length (initial)	Various Max 17 mm	15 mm	17 mm	20 mm	18.5 mm	18.5 mm
Maximum clip length (deployed)	Various Max 13 mm	11 mm	13 mm	15.5 mm	14.5 mm	14.5 mm
Maximum opening width	Various Max 11 mm	9.5 mm	11 mm	11 mm	12 mm	12 mm
Rotatability	Rotatable	Rotatable	Rotatable	Not rotatable	Not rotatable	Not rotatable
Flushing	No	No	No	No	Yes	No
Reopening capability	None	None	None	Up to five times	None	None
Clip material	Stainless steel	Stainless steel	Stainless steel	Stainless steel	Stainless steel	Stainless steel
Radiopacity	Radiopaque	Radiopaque	Radiopaque	Radiopaque	Radiopaque	Radiopaque

Modified from Kaltenbach et al. [11]

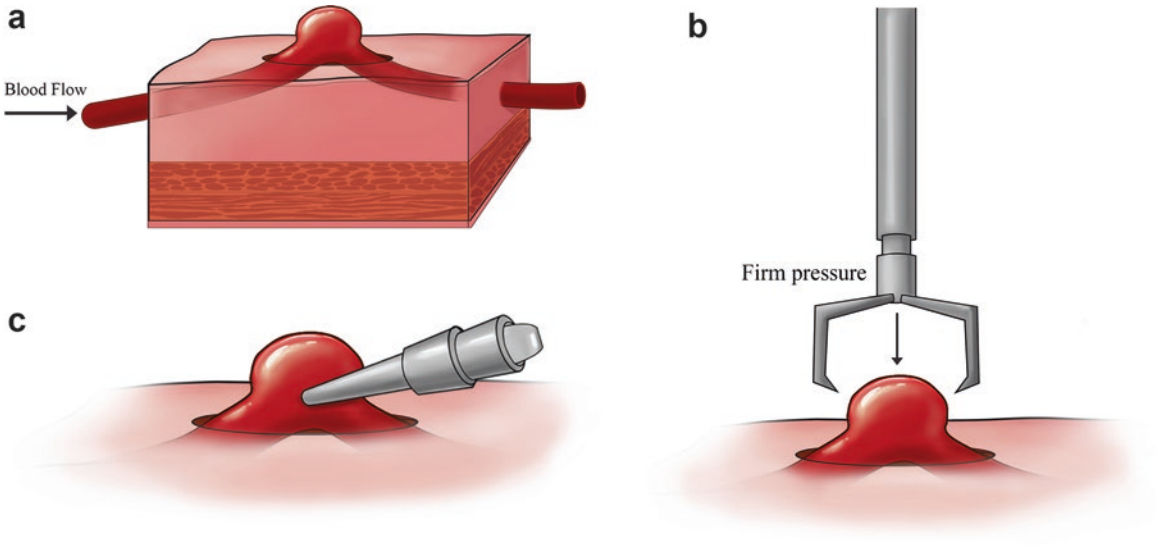
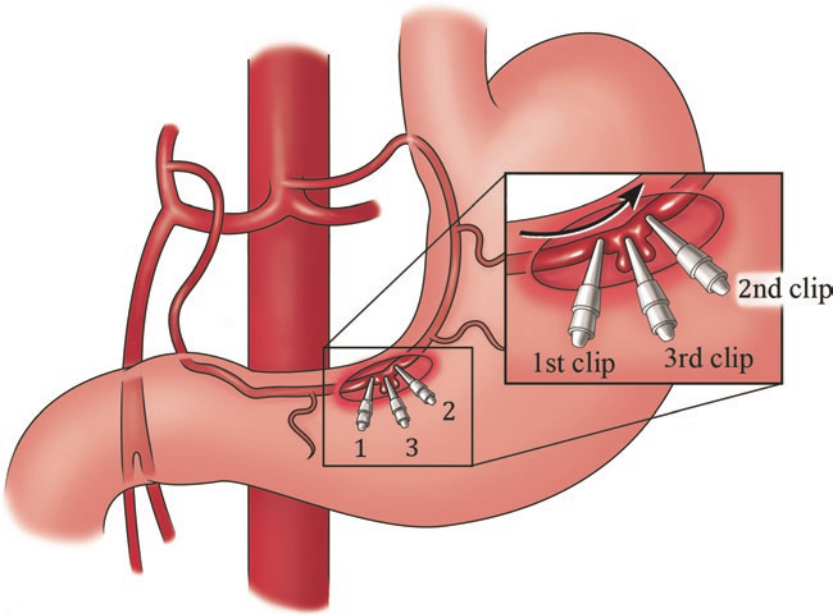


Fig. 15.3 Clip application

Fig. 15.4 Clip application with respect to blood flow



endoscope to bring the bleeding vessel to this position. First, the outer sheath should be pulled back to barely expose the tip of the clip prior to insertion into the channel. The device is then inserted into the channel of the endoscope. Once the tip is visualized on the screen, the outer sheath should be pulled further for full exposure of the clip. The clip is then opened to its "maximum" width, rotated to the desired angle (only for rotatable clips), placed over the target, closed, and deployed (note that only the resolution clip may be reopened if position is not satisfactory). The handles of different clips vary slightly in the direction of forces applied to perform each of the prementioned steps. The direction of the course of the underlying arteriole is important. We try to apply the first clip proximal to the bleeding point and the second clip distal to it on the bleeding vessel. By using this method, we achieve clipping of both sides of the underlying arteriole (Figs. 15.4 and 15.5).

Hemostatic Powder Spray (Hemospray)

A novel hemostatic powder spray has been developed by Cook Medical Inc., Winston-Salem, North Carolina (Hemospray) for management of GI bleeding. It was

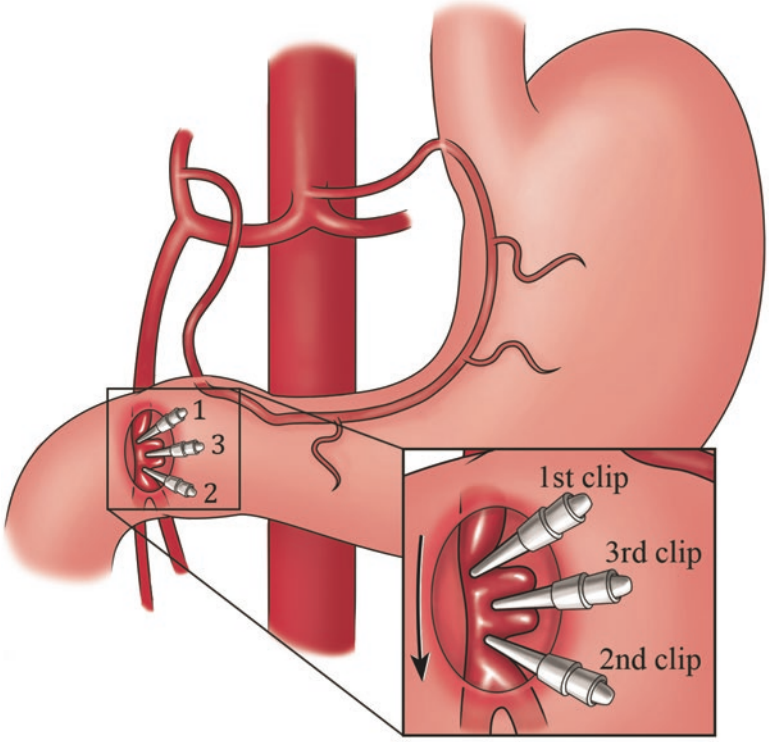


Fig. 15.5 Clip application with respect to blood flow

originally used in the military to control bleeding from the wounds. The powder achieves hemostasis by covering the bleeding site, enhancing clot formation, causing mechanical plug on the injured blood vessel, and shortening the coagulation time [38]. The rate of successful initial hemostasis with Hemospray is 94%, and the rebleeding rate within 7 days has been as high as 39% [39, 40]. Therefore, Hemospray should be considered as a temporary measure or a bridge until definitive therapy performed.

Choice of Techniques

Three therapies are currently considered to be standard with respect to endoscopic management of non-variceal upper GI bleeding (mainly bleeding ulcers). This includes epinephrine injection, thermal contact devices (multipolar or heat probe), and endoclip application; however, Hemospray has emerged as a new modality used as a temporary measure until definitive therapy is entertained.

Multiple studies have showed that epinephrine injection is effective to achieve initial hemostasis in patients with active bleeding; however, epinephrine injection alone is less effective than other monotherapies in preventing rebleeding and the need for surgery [27]. In addition, dual therapy, epinephrine with a second modality, is more effective than epinephrine monotherapy [20]. Although some data suggested epinephrine followed by thermal therapy provided better efficacy than thermal therapy alone, the data is insufficient to recommend against using thermal therapy alone [1, 27]. Injection of epinephrine is more useful in the cases of active bleeding to slow bleeding and improve the visualization of the area before applying a definitive modality. Also, preinjection of epinephrine is useful in the cases of adherent blood clots that do not dislodge with irrigation to decrease the rate of severe bleeding after clot removal. Clips are more effective than epinephrine injection in preventing rebleeding and the need for surgery. Studies comparing clips to other modalities had conflicting results. One study by Cipolletta et al. evaluated hemoclip versus heater probe in 113 patients with major stigmata of ulcer hemorrhage and showed that hemoclip was safe and effective in treatment of severe ulcer bleeding and was superior to heater probe in preventing early recurrent bleeding [4]. On the other hand, Gevers et al. evaluated sclerosant injection versus hemoclip application versus combination of the 2 in 105 patients with non-bleeding or actively bleeding visible vessels. The use of hemoclips alone appeared to fail because of difficulty with hemoclip placements and incomplete vessel compressions, and the mechanical therapy was inferior to injection therapy [6]. A randomized trial by Lin et al. studied the effectiveness of hemoclip versus heater probe in 80 patients with actively bleeding or nonbleeding visible vessels. Heater probe was shown to be superior to hemoclip in control of bleeding, with initial homeostasis achieved in 85% of the patients in the hemoclip group versus 100% in the heater probe group [18].

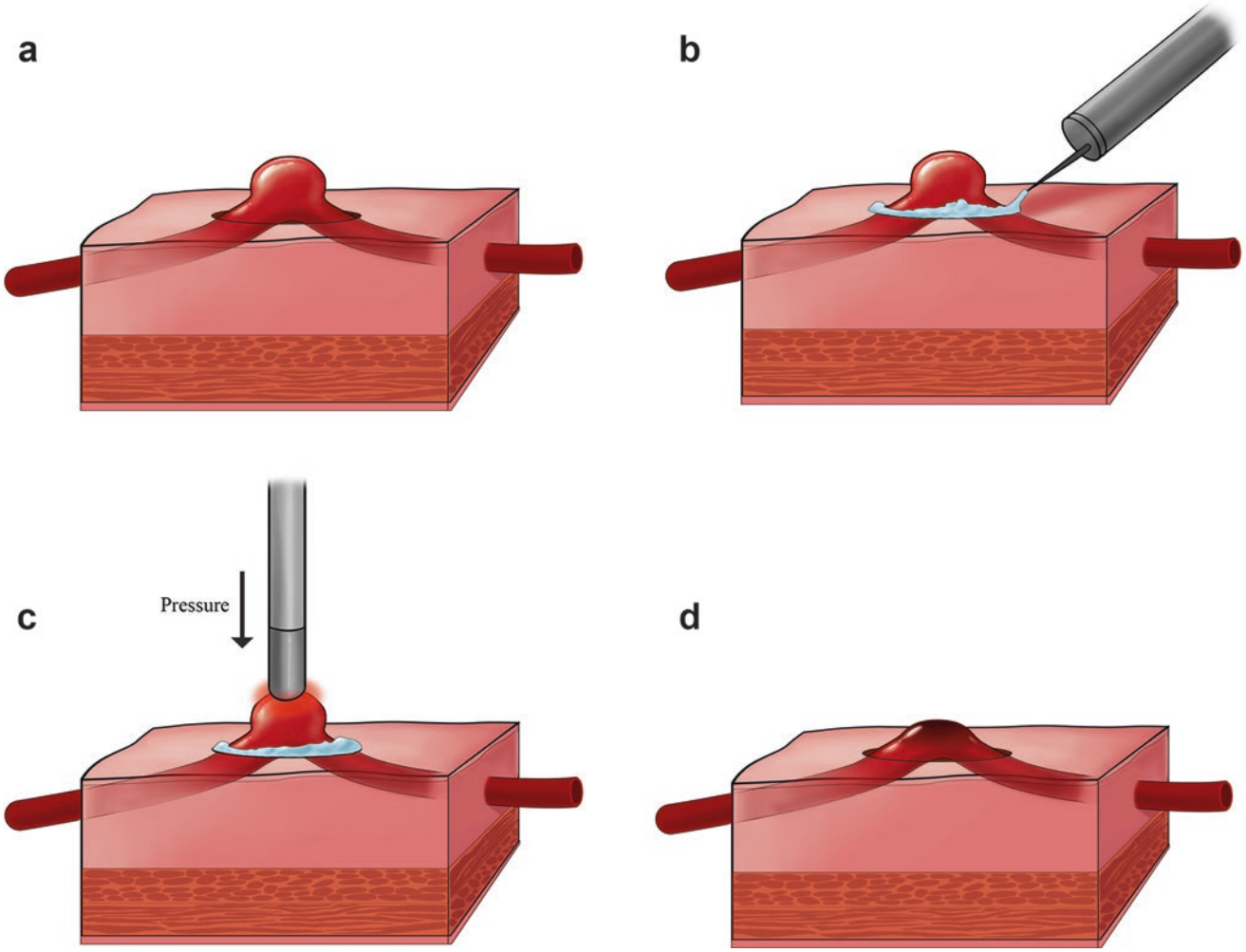


Fig. 15.6 Needle injection followed by thermal therapy

The variability of these results suggested that the effectiveness of mechanical therapy could be operator dependent. However, newer clips in the current practice have not been studied well which are easier to apply and vary in the size, depth of tissue penetration, and the duration of the attachment.

The choice of endoscopic treatment (Figs. 15.6 and 15.7) also depends on the stigmata of the underlying ulcer at the time of endoscopy (Table 15.7).

Forrest Classes Ia and Ib (Actively Bleeding Ulcers)

For these types of ulcers, the authors prefer injecting smaller volumes of 1:10,000 epinephrine, up to a total of 15–20 mL, in four quadrants within 2–4 mm of the bleeding point, followed by either mechanical clip application or thermal therapy using a large probe. The probe is applied with firm pressure, using 20–25 W power, setting 10 s with 10 s pulses. This is followed by irrigation and removal of the probe. The same method is repeated if necessary until a good probe print is visible. If clip application is chosen based on the site of the ulcer and the rough anatomical course of the underlying arteriole, then a endoclip is applied first proximally to the bleeding point, then distal to the bleeding point, and finally directly on the bleeding point [3, 8].

Forrest Class IIa (Ulcer with Nonbleeding Visible Vessel)

For this type of ulcer, we use either a combination of epinephrine plus thermal therapy or epinephrine plus clip application or thermal therapy alone. The method is the same as described above for Forrest types Ia and Ib.

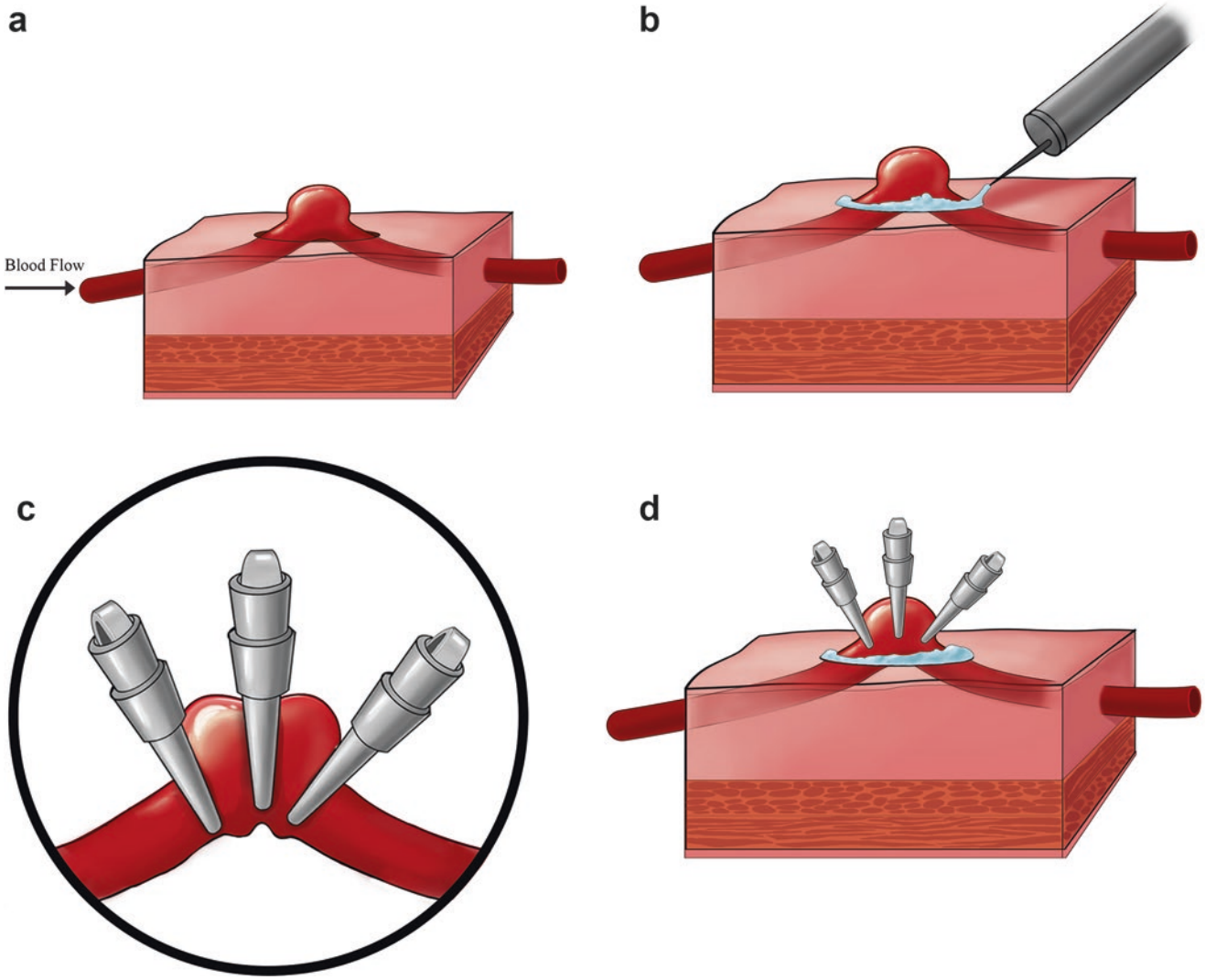


Fig. 15.7 Needle injection followed by clip placement

Table 15.7 Endoscopic therapy recommendations and end points

	Forrest class Ia (spurting)	Forrest class Ib (oozing)	Forrest II a (visible vessel)	Forrest IIb (adherent clot)
Epinephrine	Yes	Yes	Yes	Yes
Probe size	Large	Large	Large	Large
Probe pressure	Firm	Firm	Firm	Firm
Power setting	15–20 W	15–20 W	15–20 W	15–20 W
Pulse duration	8–10 s	8–10 s	8–10 s	8–10 s
Clip	Yes	Yes	Yes	Yes
End point	Bleeding stops	Oozing stops	Vessel flattens or successful clipping	Vessel flattens or successful clipping

Forrest Class IIb (Ulcer with Adherent Clot)

For this type of ulcer, our approach is to irrigate the clot with a jet of water followed by injection of aliquots of 1:10,000 epinephrine as described above. We use a snare (without current) to trim the clot very carefully, as shown in Fig. 15.8 [9]. Extra care should be taken not to guillotine the clot entirely from the base. This may shear off the underlying arteriole and precipitate torrential bleeding. If the underlying vessel is exposed well, then we use the method as described for Forrest IIa ulcers.

Forrest IIc and III types of ulcers generally do not require endoscopic therapy.

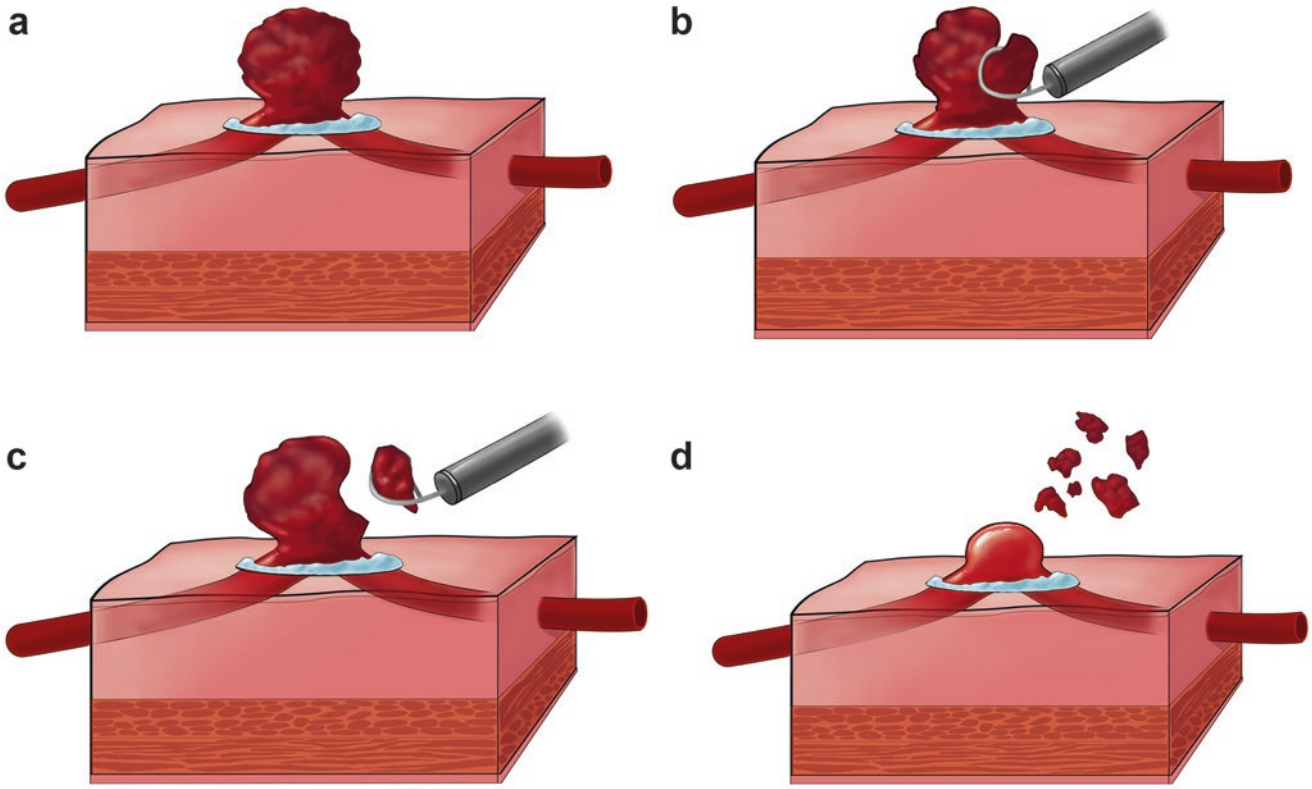


Fig. 15.8 Clot removal

Post-endoscopic Therapy

Although endoscopic therapy is effective for bleeding peptic ulcers, bleeding does recur in up to 15–20% of patients [14]. Most of the rebleeding occurs within the first 3 days, and the mortality rate in these patients is high. Vitro studies have shown that a high intragastric pH can facilitate platelet aggregation, suggesting that inhibition of gastric acid secretion to maintain a neutral pH should stabilize clots and prevent recurrent bleeding [21]. IV proton pump inhibitor (PPI) infusion after endoscopic homeostasis (80 mg IV bolus followed by 8 mg per h) for 72 h was studied in 240 patients and was shown to decrease the percent for rebleeding to around 7% [14].

Lau et al. compared endoscopic retreatment to surgery in patients who rebled. Bleeding was considered to have recurred in the event of any one of the following: vomiting of fresh blood, hypotension and melena, or a requirement of more than four units of blood in the 72-h period after endoscopy. Forty-eight patients with rebleeding were assigned to endoscopic retreatment, and 44 were assigned to surgery. Of the 48 patients, 35 had long-term control of bleeding, while the other 13 had undergone salvage surgery, 11 because retreatment failed and 2 because of perforation. Five patients in the endoscopy retreatment group died within 30 days compared to eight patients in the surgery group ($P = 0.37$). Seven patients in the endoscopy group (including six who underwent salvage surgery) had complications compared to 16 in the surgery group ($P = 0.03$). It was concluded that endoscopic retreatment reduced the need for surgery without increasing the risk of death and was associated with fewer complications [13].

Mallory–Weiss Tears

Mallory–Weiss tears usually occur on the gastric side of the gastroesophageal junction. Bleeding stops spontaneously in 80–90% of patients and recurs only in 0–5%. Endoscopic therapy is effective for actively bleeding patients but is not needed if no active bleeding is seen.

Second-Look Endoscopy

Second-look endoscopy is usually not necessary after successful endoscopic therapy unless rebleeding occurs. However, in patients with gastric ulcers, relook endoscopy in 6–8 weeks should be performed to confirm complete healing of the ulcers, while the patient is on PPI therapy and off nonsteroidal anti-inflammatory drugs. Further investigations should be performed for nonhealing ulcers.

Conclusions

Endoscopic management of acute upper GI bleeding has evolved greatly over the years. The techniques should be carefully chosen depending on the severity of the bleeding, ulcer location, availability of equipment, and, most importantly, the experience of the endoscopist.

Summary of Key Points

- Acute upper GI bleeding is a common medical emergency.
- Nasogastric (NG) lavage is not necessary in most patients with upper GI bleeding.
- Patients develop orthostatic hypotension after losing 20% of their total blood volume and develop supine hypotension after losing more than 40%.
- Upper endoscopy within 24 h is recommended in most patients with upper GI bleeding and within 12 h in "high-risk" patients.
- Very early endoscopy, before fluid resuscitation, may carry risk of complications.
- Administration of PPI before endoscopy accelerates the resolution of signs of bleeding in ulcers and reduces the need for endoscopic therapy.
- The endoscopic techniques should be carefully chosen depending on the severity of the bleeding, ulcer location, availability of equipment, and the experience of the endoscopist.

References

1. Bianco MA, Rotondano G, Marmo R, Piscopo R, Orsini L, Cipolletta L. Combined epinephrine and bipolar probe coagulation vs. bipolar probe coagulation alone for bleeding peptic ulcer: a randomized controlled trial. Gastrointest Endosc. 2004;60:910–5.
2. Chung SCS, Leung JWC, Leung FW. Effect of submucosal epinephrine injection on local gastric blood flow: a study using laser doppler flowmetry and reflectance spectrophotometry. Dig Dis Sci. 1990;35:1008–11.
3. Chung SS, Lau JY, Sung JJ, Chan AC, Lai CW, Ng EK, et al. Randomised comparison between adrenaline injection alone or adrenaline injection plus heat probe treatment for actively bleeding ulcers. Br Med J. 1997;314:1307–11.
4. Cipolletta L, Bianco MA, Marmo R, Rotondano G, Piscopo R, Vingiani AM, et al. Endoclips versus heater probe in preventing early recurrent bleeding from peptic ulcer: a prospective and randomized trial. Gastrointest Endosc. 2001;53:147–51.
5. Enestvedt BK, Gralnek IM, Mattek N, Lieberman DA, Eisen G. An evaluation of endoscopic indications and findings related to nonvariceal upper-GI hemorrhage in a large multicenter consortium. Gastrointest Endosc. 2008;67:422–9.
6. Gevers AM, De Goede E, Simoens M, Hiele M, Rutgeerts P. A randomized trial comparing injection therapy with hemoclip and with injection combined with hemoclip for bleeding ulcers. Gastrointest Endosc. 2002;55:466–9.
7. Jensen DM. Endoscopic control of nonvariceal upper gastrointestinal hemorrhage. In: Yamada T, Alpers DH, Laine L, Owyang C, Powell DW, editors. Textbook of gastroenterology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1999. p. 2857–79.
8. Jensen DM, Kovacs TO, Randall GM, et al. Prospective study of thermal coagulation (gold probe) versus combination injection and thermal treatment of high risk patients with severe ulcer or Mallory Weiss bleeding. Gastrointest Endosc. 1994;40:25.
9. Jensen DM, Kovacs TOG, Jutabha R, Savides T, Cheng S, Jensen ME, et al. Initial results of a multicenter, randomized controlled trial of medical versus combination endoscopic therapy for prevention of recurrent severe ulcer hemorrhage from non-bleeding adherent clots. Gastrointest Endosc. 1996;43:352.
10. Jutabha R, Jensen DM. Management of severe upper gastrointestinal bleeding in the patient with liver disease. Med Clin North Am. 1996;80:1035–68.
11. Kaltenbach T, Friedland S, Barro J, Soetikno R. Clipping for upper gastrointestinal bleeding. Am J Gastroenterol. 2006;101:915–8.
12. Laine L, Stein C, Sharma V. A prospective outcome study of patients with clot in an ulcer and the effect of irrigation. Gastrointest Endosc. 1996;43:107–10.199.
13. Lau JY, Sung JJ, Lam YH, Chan AC, Ng EK, Lee DW, et al. Endoscopic retreatment compared with surgery in patients with recurrent bleeding after initial endoscopic control of bleeding ulcers. N Engl J Med. 1999;340:751–6.
14. Lau JY, Sung JJ, Lee KK, Yung MY, Wong SK, Wu JC, et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. N Engl J Med. 2000;343:310–6.
15. Lau JY, Leung WK, Wu JCY, Chan FKL, Wong VWS, Chiu PWY, et al. Omeprazole before endoscopy in patients with gastrointestinal bleeding. N Engl J Med. 2007;356:1631–40.
16. Leung JW, Chung SCS. Practical management of nonvariceal upper gastrointestinal bleeding. In: Tytgat GNJ, Classen M, editors. Practice of therapeutic endoscopy. New York: Longman group; 1994. p. 1–16.
17. Lewis JD, Bilker WB, Farrar JT, Strom BL. Hospitalization and mortality rates from peptic ulcer disease and GI bleeding in the 1990s: relationship to sales of nonsteroidal anti-inflammatory drugs and acid suppression medications. Am J Gastroenterol. 2002;97:2540–9.
18. Lin HJ, Hsieh YH, Tseng GY, Perng CL, Chang FY, Lee SD. A prospective, randomized trial of large-versus small-volume endoscopic injection of epinephrine for peptic ulcer bleeding. Gastrointest Endosc. 2002;55:615–9.
19. Lin HJ, Hsieh YH, Tseng GY. A prospective, randomized trial of endoscopic hemoclip versus heater probe thermocoagulation for peptic ulcer disease. Am J Gastroenterol. 2002;97(9):2250–4.
20. Marmo R, Marmo R, Rotondano G, Piscopo R, Bianco MA, D'Angella R, et al. Dual therapy versus monotherapy in the endoscopic treatment of high-risk bleeding ulcers: a meta-analysis of controlled trials. Am J Gastroenterol. 2007;102:279–89.
21. O'Brien JR. Some effects of adrenaline and anti-adrenaline compounds on platelets in vitro and in vivo. Nature. 1963;200:763–4.
22. Rockall TA, Logan RFA, Devlin HB, Northfield TC. Risk assessment after acute gastrointestinal haemorrhage. Gut. 1996;38:316–21.
23. Sung JY, Chung SCS, Low JM, Cocks R, Ip SM, Tan P, et al. Systemic absorption of epinephrine after endoscopic submucosal injection in patients with bleeding peptic ulcers. Gastrointest Endosc. 1993;39:20–2.
24. Swain CP, Storey DW, Bown SG, Heath J, Mills TN, Salmon PR, et al. Nature of the bleeding vessel in recurrently bleeding gastric ulcers. Gastroenterology. 1986;90:595–608.
25. Cappell MS, Friedel D. Initial management of acute upper gastrointestinal bleeding: from initial evaluation up to gastrointestinal endoscopy. Med Clin North Am. 2008;92(3):491–509.
26. Jensen DM, Machicado GA. Diagnosis and treatment of severe hematochezia. The role of urgent colonoscopy after purge. Gastroenterology. 1988;95(6):1569–74.

27. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107(3):345–60. quiz 361
28. Boonpongmanee S, Fleischer DE, Pezzullo JC, Collier K, Mayoral W, Al-Kawas F, Chutkan R, Lewis JH, Tio TL, Benjamin SB. The frequency of peptic ulcer as a cause of upper-GI bleeding is exaggerated. Gastrointest Endosc. 2004;59(7):788–94.
29. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet. 2000;356(9238):1318–21.
30. Cheng DW, Lu YW, Teller T, Sekhon HK, Wu BU. A modified Glasgow Blatchford score improves risk stratification in upper gastrointestinal bleed: a prospective comparison of scoring systems. Aliment Pharmacol Ther. 2012;36(8):782–9.
31. Saltzman JR, Tabak YP, Hyett BH, Sun X, Travis AC, Johannes RS. A simple risk score accurately predicts in-hospital mortality, length of stay, and cost in acute upper GI bleeding. Gastrointest Endosc. 2011;74(6):1215–24.
32. Tsoi KK, Ma TK, Sung JJ. Endoscopy for upper gastrointestinal bleeding: how urgent is it? Nat Rev Gastroenterol Hepatol. 2009;6(8):463–9. https://doi.org/10.1038/nrgastro.2009.108. Epub 2009 Jul 14
33. Lee JG, Turnipseed S, Romano PS, Vigil H, Azari R, Melnikoff N, Hsu R, Kirk D, Sokolove P, Leung JW. Endoscopy-based triage significantly reduces hospitalization rates and costs of treating upper GI bleeding: a randomized controlled trial. Gastrointest Endosc. 1999;50(6):755–61.
34. Bjorkman DJ, Zaman A, Fennerty MB, Lieberman D, Disario JA, Guest-Warnick G. Urgent vs. elective endoscopy for acute nonvariceal upper-GI bleeding: an effectiveness study. Gastrointest Endosc. 2004;60(1):1–8.
35. Lim LG, Ho KY, Chan YH, Teoh PL, Khor CJ, Lim LL, Rajnakova A, Ong TZ, Yeoh KG. Urgent endoscopy is associated with lower mortality in high-risk but not low-risk nonvariceal upper gastrointestinal bleeding. Endoscopy. 2011;43(4):300–6.
36. Sreedharan A, Martin J, Leontiadis GI, Dorward S, Howden CW, Forman D, Moayyedi P. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2010;7:CD005415.
37. Leontiadis GI, Sharma VK, Howden CW. Proton pump inhibitor therapy for peptic ulcer bleeding: Cochrane collaboration meta-analysis of randomized controlled trials. Mayo Clin Proc. 2007;82(3):286–96.
38. Holster IL, van Beusekom HM, Kuipers EJ, Leebeek FW, de Maat MP, Tjwa ET. Effects of a hemostatic powder hemospray on coagulation and clot formation. Endoscopy. 2015;47(7):638–45.
39. Sulz MC, Frei R, Meyenberger C, Bauerfeind P, Semadeni GM, Gubler C. Routine use of Hemospray for gastrointestinal bleeding: prospective two-center experience in Switzerland. Endoscopy. 2014;46(7):619–24.
40. Yau AH, Ou G, Galorport C, Amar J, Bressler B, Donnellan F, Ko HH, Lam E, Enns RA. Safety and efficacy of Hemospray® in upper gastrointestinal bleeding. Can J Gastroenterol Hepatol. 2014;28(2):72–6.

Management of Gastric Varices

16

Jonggi Choi and Young-Suk Lim

Introduction

Gastroesophageal varices are present in approximately 50% of patients with cirrhosis and are more frequently observed in patients with poor liver function. Gastric varices (GV) bleed less frequently than esophageal varices (EV) and are the bleeding source in approximately 10–30% of patients suffering from variceal hemorrhage [62]. However, bleeding from GV tends to be more severe with higher mortality. In addition, a high proportion of patients, from 35% to 90%, rebleed after spontaneous hemostasis.

This chapter will provide an overview of the classification and pathophysiology of GV, which have direct consequences for management, management of acute gastric variceal bleeding, an introduction to current endoscopic management options for GV along with details of a practical approach to endoscopic management, endovascular management options for GV, and novel endoscopic techniques.

Prevalence and Classification of Gastric Varices

GV have been reported less prevalent than EV and present in 5–33% of patients with cirrhosis [62]. The reported bleeding from GV incidence is about 25% in 2 years, particularly with a higher incidence in fundal varices [62].

The most widely used classification for GV was initially suggested by Sarin and Kumar in 1989 [61] (Fig. 16.1). Sarin et al. divided GV into gastroesophageal varices (GOV) or isolated gastric varices (IGV) according to their relationship with EV and their location in the stomach. GOV are basically an extension of EV and are categorized as GOV1 which extend along the lesser curvature of stomach and GOV2 which extend along the fundus and tend to be longer and more tortuous. IGV occur in the absence of EV and are further categorized as IGV1 which are located in the fundus and IGV2 which are located in the body, antrum, or around the pylorus. The correct classification for GV is crucial as it is closely linked with the approach and management of GV and can be used as nomenclature in clinical studies to describe the characteristic of GV or compare the outcomes.

According to Sarin et al., GOV1 comprise approximately 75% of all GV. Even though GOV1 are the most common type of GV, GOV1 are generally regarded as an extension of EV due to the similarity in treatment strategy and response to EV. IGV2 have been reportedly rare with a prevalence of 4% among total GV, and there have been no specific recommendations for this type in guidelines due to limited data regarding prevalence, bleeding risk, and management. Therefore, the focus on this chapter will be on GOV2 and IGV1, so-called fundal varices, and both of which will be referred to as GV unless otherwise specified.

Pathophysiology of Gastric Varices and Risk Factors for Bleeding from Gastric Varices

The bleeding from GV is more severe, requiring more blood transfusions, and has a higher mortality rate than EV. The mortality from first GV bleeding remains as high as 20% within 6 weeks of occurring bleeding.

In terms of the bleeding risk from GV, in a prospective study on 132 patients with GV, the cumulative risks for bleeding at 1, 3, and 5 years were 16%, 36%, and 44%, respectively [34]. Untreated group of a small randomized trial showed the 1-year bleeding risk from GV was about 10% [43]. Several risk factors have been identified for bleeding from GV, such as the size of GV, Child-Pugh class, and endoscopic presence of red spots (defined as

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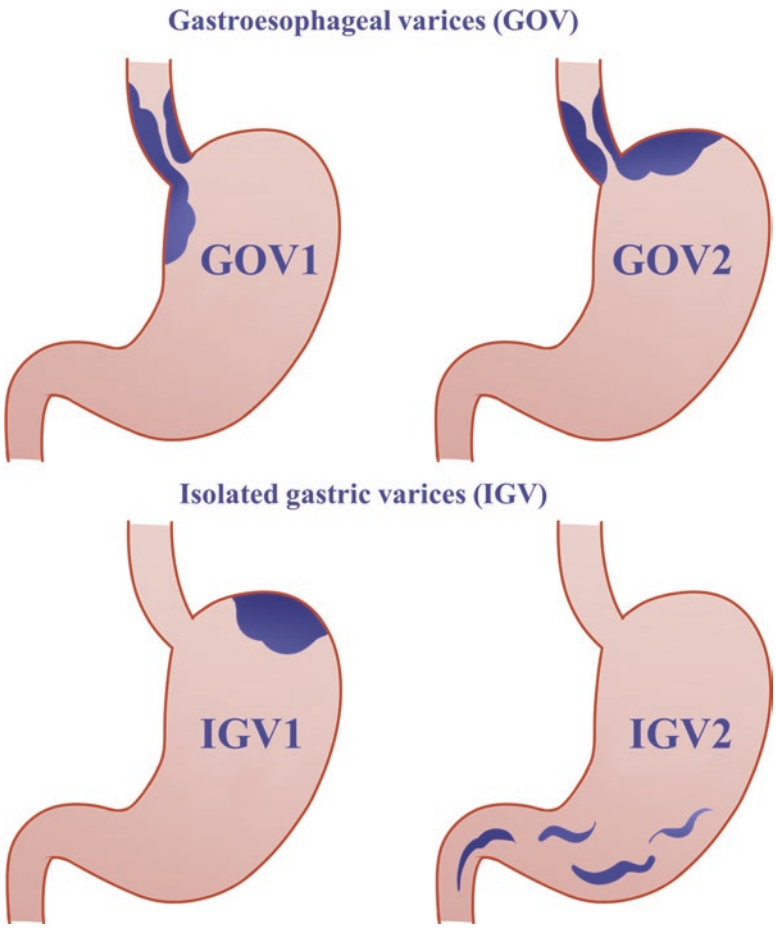

Fig. 16.1 Sarin's classification of gastric varices (Adapted from Sarin et al. [62])

localized reddish mucosal area or spots on the mucosal surface of a varix) [34].

Whether GV rupture or not depends largely on the wall stress of the varix, which is defined by the equation $\sigma = p\ (r / w)$, in which σ is the wall stress, p is the transmural pressure (the portal pressure), r is the radius, and w is the wall width [6, 52]. When the transmural pressure increases, both an enlargement of the varix (r) and a decrease in varix wall thickness (w) can occur at the same time so that small increases in portal pressure can lead to an exponential increase in the wall stress (σ), ultimately occurring rupture [6, 10, 52]. This explains in part why GV, which are usually larger than esophageal varices, can rupture despite the fact that GV have thicker walls and lower portal pressures than EV [10].

Primary Prophylaxis

A randomized controlled trial on 89 patients with GOV2 or IGV1 compared cyanoacrylate injection (n = 30), beta-blockers (n = 29), or no treatment (n = 30) as primary prophylaxis for GV with a median follow-up of 26 months, demonstrating favor of cyanoacrylate injection for preventing first GV bleeding and better survival compared to no treatment group [43]. However, compared to beta-blocker group, cyanoacrylate group showed favor of preventing rebleeding but did not differ in survival and preventing first GV [43]. Considering the paucity of randomized controlled trials regarding primary prophylaxis for GV, the above study has clinical impact on the use of cyanoacrylate injection as primary prophylaxis. Nevertheless, future larger studies are needed to evaluate the risk and benefit of using cyanoacrylate in the setting of primary prophylaxis for GV; therefore, currently no such recommendation has been made in the guidelines [16, 19].

Management of Acute Gastric Variceal Bleeding

General principle of management of acute GV bleeding is almost identical with that of acute EV bleeding, consisting of volume resuscitation, prophylactic antibiotics, vasoactive drugs, and restrictive transfusion.

The goal of resuscitation should be preserving tissue perfusion. Hemodynamic stabilization should always precede any procedures. Based on Baveno VI consensus, packed red blood cell transfusion should be done conservatively at a target hemoglobin level between 7 and 8 g/dL, although transfusion policy in individual patients should

also consider other factors such as cardiovascular disorder, age, hemodynamic status, and ongoing bleeding [16].

Antibiotic prophylaxis, due to the high possibility of bacterial infection from gastrointestinal (GI) bleeding in cirrhotic patients, should be administered from the time of admission or the occurrence of bleeding events. When determining antibiotics, local antibiotic susceptibility should be taken into account, but in general intravenous ceftriaxone 1 g/24 h should be considered as a first option, particularly in patients exposed to quinolone prophylaxis previously [16].

In suspected variceal bleeding, vasoactive drugs should be started as soon as possible, before endoscopy. Terlipressin, somatostatin, or octreotide can be used in combination with endoscopic treatment and continued for up to 5 days [16]. Regarding the efficacy of vasoactive drugs in the setting of variceal bleeding, a randomized trial compared three commonly used vasoactive drugs, suggesting no significant differences among them [65]. Hyponatremia has been reported in patients receiving terlipressin; thus, serial sodium levels should be monitored [16]. In the case of IGV1 developed by spontaneous splenorenal shunts, bleeding can occur with low portal pressure gradients compared to bleeding from EV. In this regard, more powerful vasoconstrictors are needed not only to decrease portal pressure but also to markedly reduce portal and collateral blood flow to control acute fundal variceal bleeding [19].

Sengstaken-Blakemore (SB) tube was compared with the Linton-Nachlas (LN) tube in a randomized clinical trial. In bleeding from GV, the LN tube achieved hemostasis in 50% of cases, but SB tube achieved 0% of hemostasis, whereas bleeding from EV was controlled equally by using both tubes [73]. Therefore, in the setting of hemodynamic instability prior to performing endoscopic treatment, balloon tamponade can be used as a temporary "bridge" (for a maximum of 24 h) with a caution given the high incidence of its severe adverse events. Intensive care monitoring is required, and intubation may be taken into account until definitive treatment can be instituted [16].

Therapeutic Options for Gastric Varices

- Endoscopic variceal band ligation
- Endoscopic variceal obturation with cyanoacrylate
- Endoscopic variceal obturation with thrombin injection
- Endoscopic ultrasound-guided coil embolization
- Transjugular intrahepatic portosystemic shunt
- Balloon-occluded retrograde transvenous obliteration
- Plug-assisted retrograde transvenous obliteration

Endoscopic Management

AASLD guidelines and Baveno VI consensus guidelines recommend that endoscopy should be performed within 12 h of presentation once patients are hemodynamically stabilized [16, 21]. Consensus is in favor of endoscopic variceal obturation (EVO) for initial treatment of choice for bleeding from GV. Baveno VI consensus recommends endoscopic therapy with tissue adhesive for acute bleeding from GV, and additional glue injection after 2–4 weeks can be given to prevent rebleeding from GV as well as combination of beta-blocker treatment. However, the evidence level is still low and more data are needed [16]. If EVO is not available, endoscopic variceal band ligation might be an alternative option particularly for small GOV2. However, band ligation is not a definitive treatment for large fundal varices, because it may cause delayed massive bleeding. No specific studies have evaluated the role of band ligation for managing GV [21].

Endoscopic Variceal Sclerotherapy

Before the introduction of EVO or newer techniques, sclerotherapy using ethanolamine injection had been used for GV treatment. However, due to the high complication [63] and rebleeding rates, sclerotherapy is not more recommended in the setting of bleeding from GV.

Endoscopic Variceal Obturation

Concept and Procedure

Soehendra and colleagues introduced EVO using tissue adhesives in 1987 [67]. The most widely used tissue adhesive is N-butyl-2-cyanoacrylate (Histoacryl®). Cyanoacrylate is a liquid polymer that on coming in contact with plasma instantly polymerizes and can lead to obliteration of the varices [33]. 2-Octyl cyanoacrylate (Dermabond®) approved for skin closure can be used as an alternative to N-butyl-2-cyanoacrylate.

N-butyl-2-cyanoacrylate makes rapid polymerization, being able to cause premature solidification of the glue in the needle or entrapment of the needle within the varix. Therefore, N-butyl-2-cyanoacrylate should be diluted with Lipiodol (ratios from 1:1 to 1:1.6), and the injection catheter needs to be primed with distilled water first, followed by flushing with water to deliver the entire glue contents from the catheter into the varix. Compared to N-butyl-2-cyanoacrylate, 2-octyl cyanoacrylate has a longer polymerization time so that it can be injected without dilution and more slowly [76].

Table 16.1 Results of published studies on endoscopic variceal obturation

Author, year	Design	Sample size	Type of GV[a]	Mean follow-up (mo)	Initial bleeding control (%)	Rebleeding (%)	Mortality (%)
Miyazaki et al., 1996 [14]	Retrospective	6	NR	NR	83	NR	NR
Kind et al., 2000 [36]	Retrospective	174	66/79/21/8	36	97	15%	20 (1 mo)
Huang et al., 2000 [29]	Retrospective	90	NR	36	93	23%	43 (6 years)
Iwase et al., 2001 [30]	Retrospective	37	NR	31	100	16	43
Akahoshi et al., 2002 [2]	Retrospective	52	0/25/27/0	12	96	40	40 (5 years)
Greenwald et al., 2003 [22]	Pilot	44	10/21/13/0	12	95	20	23
Rengstorff et al., 2004 [56]	Pilot	25	0/13/12/0	11	100	20	12
Cheng et al., 2007 [12]	Retrospective	146	NR	36	95	8	10
Mumtaz et al., 2007 [46]	Retrospective	50	16/15/22/0	NR	100	14	12
Marques et al., 2008 [41]	Retrospective	48	17/30/1/0	18	88	20.5	44
Paik et al., 2008 [49]	Retrospective	121	NR	1	91	13	12
Monsanto et al., 2012 [45]	Retrospective	97	36/27/30/4	19	96	14	9

[a]GOV1/GOV2/IGV1/IGV2
Abbreviations: *GV* gastric varices, *mo* months, *NR* not reported

Table 16.2 Results of published studies comparing endoscopic variceal obturation and endoscopic variceal band ligation

Author, year	Design	Sample sizeEVO	GV type[b]	Sample size EVL	GV type[b]	Mean follow-up (months)	Initial bleeding control	Rebleeding	Mortality
Lo et al., 2001 [38]	RCT	31 (15)	21/6/4	29 (11)	20/8/1	14 vs 9	87 vs 45[a]	54 vs 31[a]	29 vs 48[a]
Tan et al., 2006 [71]	RCT	49	27/9/13	48	26/16/6	20 vs 23	93 vs 93	21 vs 44[a]	65 vs 63
Tantau et al., 2014 [72]	RCT	19	11/8/0	18	11/7/0	14 vs 13	100 vs 89	32 vs 72[a]	11 vs 11
El Amin, 2010 [17]	RCT	75	75/0/0	75	75/0/0	6 vs 6	91 vs 81	6 vs 16	6.6 vs 1.3
Lo et al., 2013 [39]	Retrospective	118 (55)	118/0/0	44 (28)	44/0/0	1.4 vs 1.4	89 vs 85	14 vs 14	14 vs 23[a]
Hong et al., 2013 [28]	Retrospective	64	64/0/0	20	20/0/0	NR	97 vs 90	27 vs 17	19 vs 6

[a]Statistically significant difference
[b]GOV1/GOV2/IGV1
Abbreviations: *EVL* endoscopic variceal band ligation, *EVO* endoscopic variceal obturation, *GV* gastric varices, *NR* not reported, *RCT* randomized controlled trial

Clinical Application

Despite the limited high-quality data from randomized trials for the efficacy of EVO, uncontrolled case series and retrospective studies have reported a high rate of hemostasis, more than 90%, by using tissue adhesives such as cyanoacrylate (Table 16.1).

Endoscopic Variceal Obturation Vs Endoscopic Variceal Sclerotherapy

In a prospective nonrandomized trial comparing endoscopic sclerotherapy and EVO in patients with GV with a mean follow-up of 14 months, the rate of initial hemostasis was higher in the EVO group (93%) than in the sclerotherapy group (67%, $p = 0.014$) [48]. Additionally, the mortality was significantly lower in the EVO group (38%) compared to sclerotherapy group (67%) [48]. However, the rate of rebleeding did not differ between the two groups (30% in sclerotherapy group vs 25% in EVO group, $p = 0.921$) [48]. A randomized trial consisting of patients with IGV only showed that EVO group had a better control of bleeding with a shorter duration until complete obturation of GV than sclerotherapy group (44% vs 100% for bleeding control, $p < 0.05$) [60].

Endoscopic Variceal Obturation Vs Endoscopic Variceal Band Ligation

Table 16.2 summarizes the results of published studies comparing EVO and EVL (Table 16.2). Tan et al. reported through a randomized trial that EVL appeared not different to EVO for controlling active bleeding from GV but EVO group was associated with a lower rebleeding rate compared to EVL group (21.4% in the EVO vs 43.8% in the EVL, $p = 0.044$) [71]. However, another randomized trial comparing EVO to EVL showed better initial hemostasis (87% in EVO vs 45% in EVL, $p = 0.03$), less rebleeding (31% in EVO vs 54% in EVL, $p = 0.005$), and less complications (7% in EVO vs 28% in EVL, $p = 0.03$) in patients treated with EVO than in those treated with EVL [38]. Tantau et al. conducted randomized study consisting of 37 patients with GV treated with either EVO or EVL. This study reported EVO

group (32%) had a lower rate of rebleeding than EVL group (72%) without a significant difference in survival rates [72]. Meta-analysis that combined the above three randomized trials revealed that EVO was superior in controlling active bleeding from GV to EVL (93.9% vs 79.5%, $p = 0.032$) and EVO favored in rebleeding rate in IGV1 but not in GOV2 [53]. There was no difference in the rates of complication or mortality between two interventions [53]. However, due to the small number of patient in each study, these results should be interpreted cautiously even though it comes from meta-analysis. When expanding to 648 patients in another meta-analysis which combined randomized trials and observational studies, EVO had a better pooled odds ratio for hemostasis of GV bleeding and for rebleeding as compared to EVL without differences in complication rates and mortality [78]. It is noteworthy that substantial portion of patients in the abovementioned studies were with GOV1, which could be managed by EVL.

Complications of Endoscopic Variceal Obturation

Cyanoacrylate injection may cause several complications (Table 16.4). In a retrospective analysis of evaluating complications among 753 patients with bleeding from GV, 51 (6.8%) patients experienced complications: rebleeding because of early-onset (within 3 months) extrusion of cyanoacrylate glue cast (33 patients, 4.4%), sepsis (10 patients, 1.3%), distant embolisms (5 patients, 0.7%; pulmonary, brain, and splenic emboli), major gastric variceal bleeding (1 patient, 0.7%), a large gastric ulcer (1 patient, 0.7%), and mesenteric hematoma accompanied with hemoperitoneum and bacterial peritonitis (1 patient, 0.7%) [13]. The complication-related mortality in this study was 0.53% (three deaths from sepsis and one death from rebleeding after early-onset glue cast extrusion) [13], suggesting that EVO with cyanoacrylate in GV is relatively safe and complications occur rare. Most common complications are transient fever and chest and abdominal pain. In general, most of complications can be prevented by keeping a standardized injection technique which will be described in the next section, and the overall incidence of complication from EVO is low.

Complications of EVO

- Intractable bleeding during the procedure
- Embolization into the renal vein, IVC, and pulmonary or systemic vessels
- Septic thrombophlebitis/embolism
- Paravariceal injection with mucosal necrosis and bleeding
- Intraperitoneal injection inducing severe pain
- Needle sticking in the varix
- Adherence of the glue to the endoscope

Practical Consideration in Endoscopic Variceal Obturation for Bleeding Gastric Varices

Although EVO shows a high rate of bleeding control from GV, EVO should be performed cautiously with a standard protocol to minimize the risk of serious complications, such as systemic embolization. Seewald et al. proposed a standardized injection technique and regimen of cyanoacrylate injection for the treatment of GV as follows (Figs. 16.2 and 16.3) [64].

Practical Considerations

- For preparation before injection, cyanoacrylate is mixed with Lipiodol in a ratio of 0.5–0.8 mL.
- Not more than 1.0 mL of cyanoacrylate-Lipiodol mixture should be injected into the varix each time.
- If bleeding continued, the injection can be repeated several times, but the volume of each injection should be limited to 1.0 mL.
- The injection should be strictly intravariceal to prevent unnecessary ulceration.
- Before the injection, the dead space volume of injection catheter should be found to be around 0.8–1.0 mL in order to prevent premature solidification of the glue at the tip of the needle causing blockage.
- After puncture of GV, 1.0 mL of the mixture should be injected, followed by a second injection of 0.8 mL of distilled water.
- The needle should be quickly withdrawn after completing the injection; injection catheter then should be cleared by flushing with distilled water not to be clogged. Distilled water is better than normal saline because cyanoacrylate may coagulate in contact with saline.
- Check the remaining patent varices by probing the injected varices with the injection catheter. If it remains soft, the injection can be repeated to achieve complete obturation as evident by a feeling of hardness.
- Follow-up endoscopy can be performed 1–4 days after the initial procedure to confirm complete obturation. In case complete obturation is not achieved, another session of injection can be done.

Real-time fluoroscopy monitoring is not always necessary. An overtube should be kept readily available to easily remove and reinsert the endoscope during the procedure. Prior to EVO a routine check with dynamic CT scanning is strongly recommended to identify the presence and type of GV,

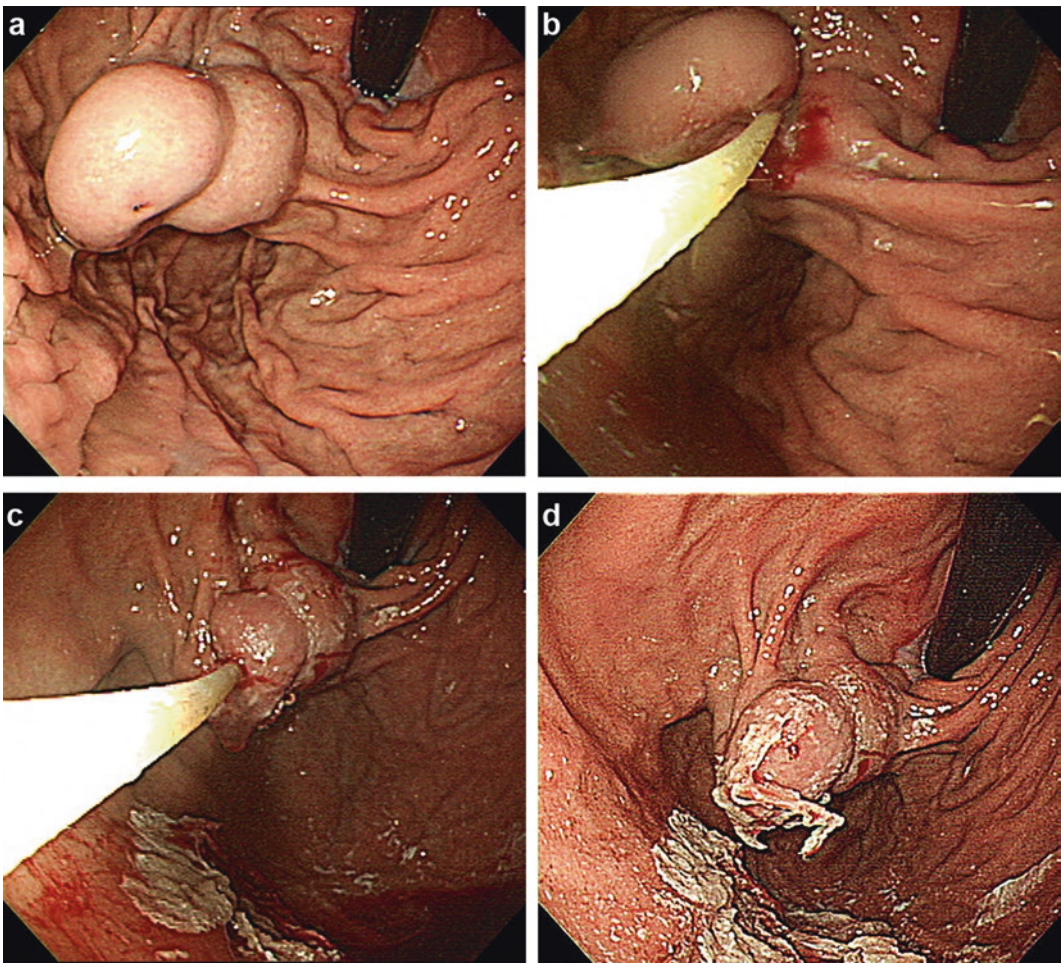

Fig. 16.2 Endoscopic injection of gastric fundal varices with N-butyl-2-cyanoacrylate. (**a**) Endoscopic image shows a large fundal varix. (**b**) A catheter was introduced and approached into the side area of varix, where the intravariceal pressure is lower compared to the top of variceal dome. (**c**) Cyanoacrylate and Lipiodol mixture was injected. (**d**) Catheter was withdrawn and the fundal varix was obturated

to assess the anatomy of GV and surrounding vasculatures such as gastrorenal shunt, and to assess the risk of systemic embolization by EVO [42]. In addition, the applicability of salvage treatments such as TIPS or BRTO can be ensured using imaging studies in case of EVO failure.

Endovascular Treatment Options for Gastric Varices

Transjugular Intrahepatic Portosystemic Shunt (TIPS)

Concept and Procedure

TIPS, first introduced by Rosch and colleagues in 1979 [58], is a percutaneous image-guided procedure in which a tract or conduit is constructed within the liver between the systemic venous system and portal system with an intent for portal decompression [51]. In general, a right internal jugular approach is preferred, but left internal jugular or femoral vein can be used as second options. Right hepatic vein is mainly chosen and a wedged venogram is obtained to identify the portal venous anatomy. Then, the targeted portal vein is punctured and stent is placed (Fig. 16.4). Initially bare metal stents were deployed, whereas polytetrafluoroethylene-covered stents have remarkably improved patency rates and now are preferred over bare metal stents [74]. TIPS has been considered the treatment of choice in patients with GV when endoscopic approach fails to control bleeding or rebleeding (Table 16.3).

TIPS Vs Endoscopic Variceal Obturation

A study evaluating cost-effectiveness of the treatment for GV bleeding between EVO (n = 23) and TIPS (n = 20) concluded EVO was more cost effective than TIPS [40]. In this study, rebleeding rate was lower in patients treated with TIPS compared to those treated with EVO (15% vs 30%, p = 0.005), but there was no difference in the overall mortality [40]. Unlike the abovementioned studies using non-coated stent for TIPS, a retrospective study of 169

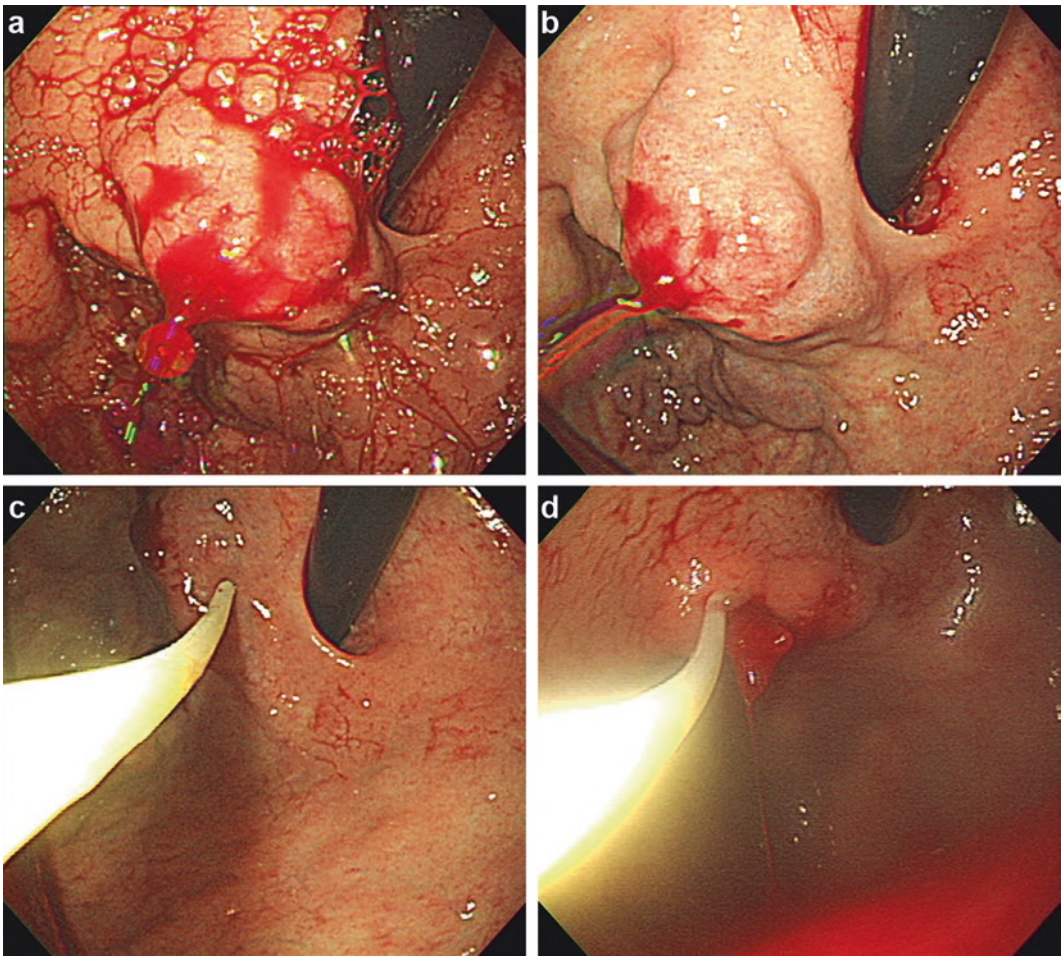

Fig. 16.3 Endoscopic obliteration of bleeding gastric fundal varices. (**a**) Active bleeding in the gastric fundus. (**b**) After clearing the endoscopic view field, a fundal varix, which is the bleeding focus, was identified. (**c**) Injection of cyanoacrylate into the fundal varix using the catheter. (**d**) After completion of injection, cyanoacrylate plug is starting to extrude

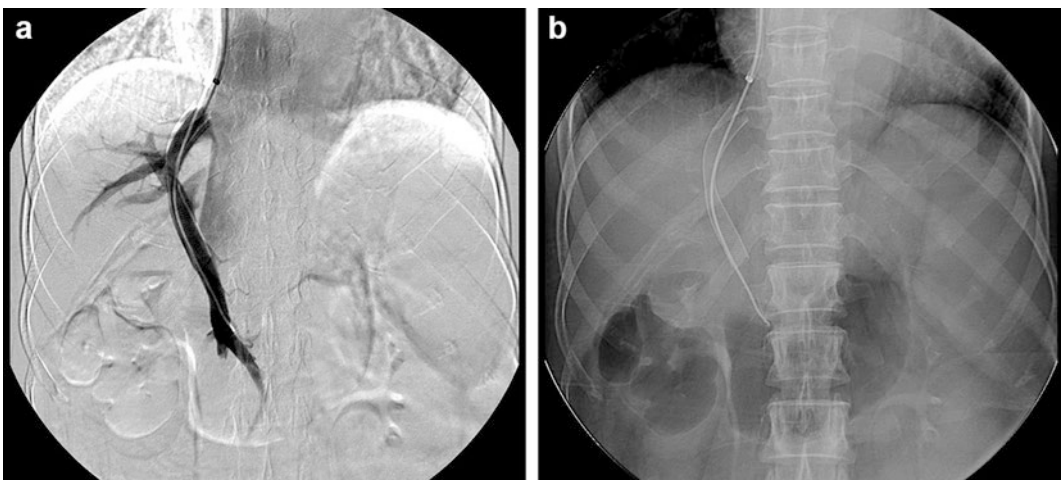

Fig. 16.4 TIPS procedure. (**a**) After puncture from inferior vena cava to portal vein, guidewire was advanced into portal system obtaining venogram. (**b**) The stent was placed in the shunt tract

Table 16.3 Results of published studies on transjugular intrahepatic portosystemic shunt

Author, year	Design	Sample size	Technical success (%)	Mean follow-up (mo)	Initial bleeding control (%)	Rebleeding (%)	Mortality (%)
Stanley et al., 1997 [69]	Retrospective	32	91	14	NR	16	40
Chau et al., 1998 [11]	Retrospective	28	NR	7	96	24	43
Barange et al., 1999 [7]	Retrospective	32	100	17	90	31	41
Rees et al., 2000 [55]	Retrospective	12	96	19	NR	16	25
Tripathi et al., 2002 [75]	Retrospective	40	NR	37	98	20	31
Song et al., 2002 [68]	Retrospective	30	100	13	100	41	21

Abbreviations: *NR* not reported

patients treated either with TIPS using covered stent ($n = 140$) or EVO ($n = 29$) showed no differences between TIPS and EVO groups in rebleeding rate within 30 days or in-hospital mortality [37].

The relatively small number of study participants, heterogeneous baseline characteristics, and the use of different types of stent in previous studies preclude a firm conclusion of the comparative effectiveness between these two modalities.

Early TIPS

A randomized trial by the Early TIPS Cooperative Study Group compared the early TIPS treatment with a polytetrafluoroethylene-covered (PTFE) stent within 72 h ($n = 32$) to continuation of pharmacologic and subsequent EVL ($n = 31$) [20]. During a median follow-up of 16 months, the 1-year actuarial survival was 81% in the early TIPS group versus 61% in the pharmacologic and EVL group ($p < 0.001$). Rebleeding or failure to control bleeding less occurred in the early TIPS group compared to the pharmacologic and EVL group ($p = 0.001$) [20]. The importance of this study lies in the fact that covered stent was used for TIPS and early TIPS was not associated with an increase of hepatic encephalopathy event, which is a major concern for TIPS. Despite favorable results of early TIPS without increase of hepatic encephalopathy, this study excluded patients with GV. In this regard, it remains to be determined whether early TIPS can provide the similar benefit in patients with GV.

Balloon-Occluded Retrograde Transvenous Obliteration

Since introduction by Kanagawa et al. [32] in the mid-1990s, balloon-occluded retrograde transvenous obliteration (BRTO) has become widely accepted from Japan to many Asian countries as an alternative option for selected cases of GV. Currently BRTO continues established in the United States and Europe. In order for BRTO to be successful, accurate assessment of the hemodynamic pattern and understanding the anatomy of vascular structures surrounding GV are essential.

Concept and Procedure

BRTO occludes the outflow veins of a spontaneous portosystemic shunt using an occlusion balloon (Fig. 16.5). Subsequently, transvenous catheter injects the sclerosing agent into the varix via transfemoral or transjugular approach. The essential part of BRTO involves dwelling the sclerosing agent inside the varix without escaping into either the portal or systemic vasculature due to the reflux flow, thereby increasing the success rate and minimizing the complication rate. When large collateral vascular structures were revealed angiographically, embolization coils are often needed to block the flow from reflux of sclerosant prior to injecting the sclerosing agent.

Technical Procedure of BRTO

Technical procedure is performed in the following orders:

- For approach to the gastrorenal or splenorenal shunt from systemic venous side, the femoral or the jugular approach is preferable to access to the left renal vein.
- Once catheter is introduced into the shunt and identifies target varix to be blocked, a balloon is placed and inflated to occlude the shunt.
- Through the balloon-occluded venography, determine the type of afferent and efferent venous anatomy that is present, and seek any escape route on venography.

(continued)

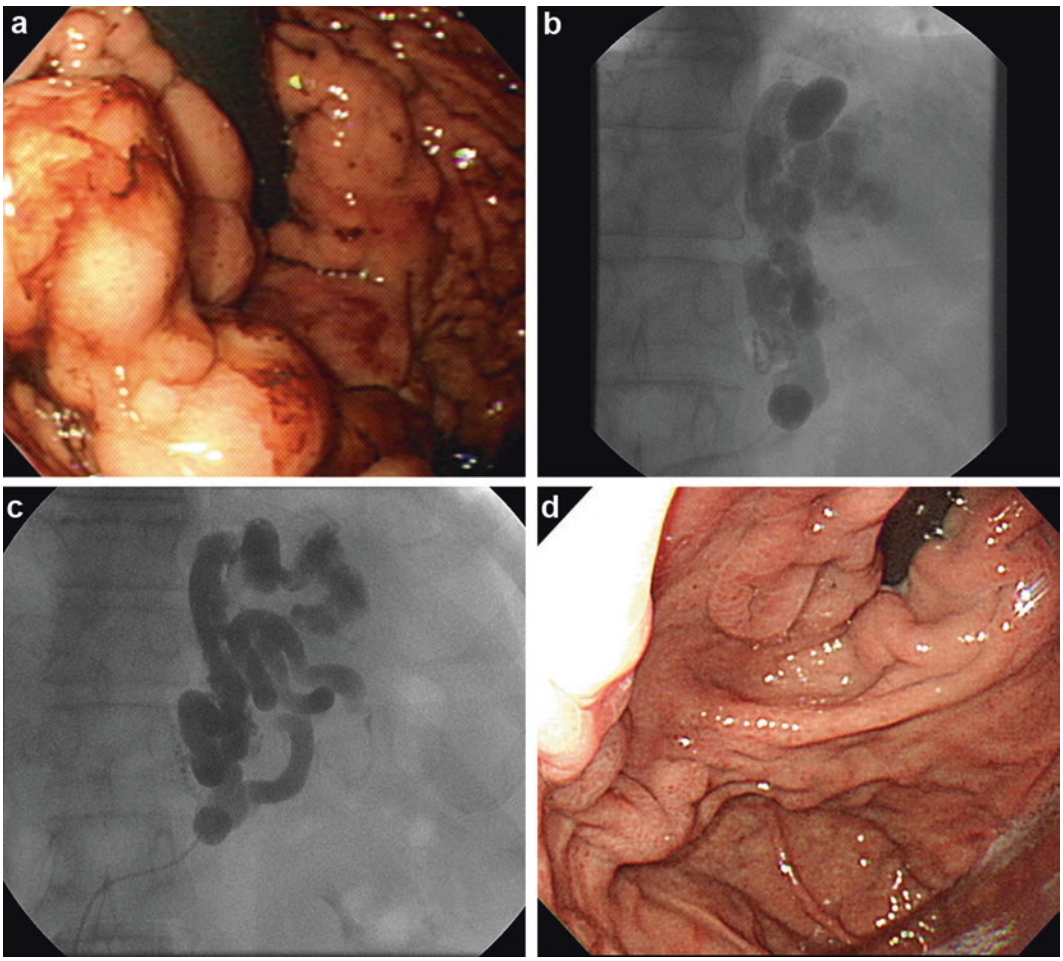

Fig. 16.5 Fundal varix in a 77-year-old man. (**a**) Large fundal varices were seen on endoscopy. (**b**) A balloon catheter was inserted into the gastrorenal shunt. Balloon-occluded venography showed fundal varices. (**c**) Gastric varices and gastrorenal shunt were filled with sclerosant. (**d**) Endoscopy 6 months after BRTO shows obliteration of the varices

- If there is an escape route on venography, several methods can be applied including a coil embolization to afferent veins, selective injection of the agent via a microcatheter, and staged instilment of the sclerosing agent.
- Injection of the sclerosing agents via transvenous catheter. The type of the sclerosing agent may differ depending on the institution or region due to its availability. However, ethanolamine oleate is the predominant and traditional sclerosing agent used, particularly in Asia.
- The occlusive balloon is usually left inflated for 6–12 h and then deflated under fluoroscopic observation. These time periods allow the sclerosing agent to make thrombus inside the varix.
- Check the absence of blood flow in the target varix on angiogram.

Clinical Application

The technical success rate of BRTO ranges from 79% to 100% (Table 16.4). In a long-term follow-up study of BRTO for GV bleeding, variceal eradication was achieved in 96.6%, and the 8-year cumulative rebleeding rate was 14% [3]. There was no ectopic variceal bleeding after BRTO instituted in the above long-term follow-up study.

TIPS vs BRTO

In a single-center retrospective study on 50 patients with bleeding from IGV, the technical success rate was 100% in the TIPS group ($n = 27$) and 91% in the BRTO group ($n = 23$; $p = 0.21$) [59]. The incidence of rebleeding from GV was 11% and 0% in the TIPS and BRTO group ($p = 0.25$) [59]. Although the statistical significance was not achieved, TIPS group had a high rate of hepatic encephalopathy after procedure compared to BRTO (15% in TIPS vs 0% in the BRTO, $p = 0.12$) [59].

Table 16.4 Published studies of balloon-occluded retrograde transvenous obliteration for bleeding from gastric varices

Author, year	Design	Sample size	Technical success (%)	Mean follow-up (mo)	Initial bleeding control (%)	Rebleeding (%)
Ninoi et al., 2005 [47]	Retrospective	35	87	23	87	3.1
Arai et al., 2005 [5]	Retrospective	11	100	37	100	0
Hiraga et al., 2007 [26]	Retrospective	34	95	33	91	0
Akahoshi et al., 2008 [3]	Retrospective	20	93	66	94	5.5

Advantages and Concerns

Compared to TIPS, BRTO can increase portal blood flow potentially leading to improve liver function [1]. A small retrospective analysis of nine patients that performed BRTO demonstrated a significant increase in portal blood flow with decreasing in GV size [1]. In this study, seven (77.8%) patients increased in the level of albumin after BRTO, whereas two of nine showed worsening of EV [1]. Another study with 14 patients who underwent BRTO reported a significant increase in portal blood flow and the intrinsic clearance of indocyanine green which assesses liver function [44]. In addition, GV were obliterated in all patients, in which hepatic encephalopathy was improved [44]. In the same vein, a retrospective cohort study consisting of patients with spontaneous portosystemic shunt and hepatic encephalopathy demonstrated that BRTO lowered the recurrence rate of 2-year hepatic encephalopathy, improved liver function, and had a better survival compared to control group [4].

On the contrary, increase portal pressure can lead to aggravate EV. In a retrospective analysis consisting of 67 patients who underwent BRTO for GV, total bilirubin (≥1.6 mg/dL) and hepatic venous pressure gradient (≥13 mmHg) were significant risk factors for EV aggravation after BRTO was applied [31]. Therefore, patients with EV which are expected to worsen after BRTO may need a surveillance for EV aggravation and corresponding treatment for EV. However, the 8-year long-term follow-up study with 68 patients did not report any ectopic varices [3]. In this regard, long-term follow-up study with large population is still needed to evaluate whether BRTO will seriously worsen the EV in a real clinical practice.

Another concern in BRTO lies on the complication from sclerosing agents. Ethanolamine oleate (EO) and pure ethanol were used for sclerosing agents for BRTO. Due to its effectiveness and ability allowing mixed with contrast medium to track down on angiography, EO has been more widely used in Asia. However, EO has several complications such as pulmonary edema, disseminated intravascular coagulation, anaphylactic reaction, and renal insufficiency [35]. Recently another approach using sodium tetradecyl sulfate (STS) instead of sclerosing agents has been introduced based on the fact that STS has faster sclerosing effect than EO with lower dose theoretically. Drawback of BRTO is a time-consuming procedure requiring certain time for allowing the balloon to be in place for sclerosing effect. Therefore, patients should have bed rest for such time. Balloon rupture, which can cause systemic embolization, recurrent variceal bleeding, and even in-hospital mortality can also occur as complication during the BRTO procedure [35].

Plug-Assisted Retrograde Transvenous Obliteration (PARTO)

Concept and Advantages

The idea of vascular plug-assisted retrograde transvenous obliteration (PARTO) arises from the complications and disadvantages from BRTO such as systemic embolization due to sclerosing agents or balloon rupture during the BRTO procedure. Some centers in Asia have introduced PARTO using vascular plug and gelatin sponges instead of using sclerosing agents [24]. Compared to BRTO, PARTO seems less invasive and to be technically easier for interventional radiologists to perform with shorter procedure time. Moreover, PARTO has several advantages: [24]

1. PARTO does not require both balloon catheter and sclerosing agents, which are associated with complications including pulmonary edema, systemic embolization, and renal insufficiency.
2. PARTO does not require repeated procedures. For BRTO, although previous studies varied the balloon indwelling time from 30 minutes to overnight, leaving balloon in place may entail the risk of bleeding, infection, and patient inconvenience.
3. PARTO does not require selective embolization of efferent veins, as it does not require sclerosing agents.

Clinical Application

Most studies of PARTO have been published in Korea. The first retrospective study of 20 patients who performed PARTO showed a technical success rate of 100% without procedure-related complications [24]. Complete thrombosis of GV and gastrorenal shunts were achieved in all patients [24]. In a larger multicenter retrospective analysis, PARTO was technically successful in all 73 patients (57 had GV, 28 had GV in danger of rupture, 23 had previous bleeding from GV, and 6 had active bleeding from GV) without procedure-related complications. During follow-up period (mean

544 days), no cases of variceal bleeding were observed, and complete thrombosis of GV and gastrorenal shunts were achieved in 72 patients (98.6%) [23]. In a case report of PARTO in the United States, PARTO was successfully applied to patients with history of bleeding from varices and hepatic encephalopathy [50]. Recently, a study comparing among BRTO using sclerosing agents ($n = 49$), BRTO using Gelfoam ($n = 25$), and PARTO ($n = 21$) concluded BRTO using Gelfoam or PARTO is better than BRTO using sclerosing agents for treatment of GV in terms of complication or procedure time. However, in this study PARTO showed more recurrence of GV compared to BRTO in long-term follow-up (Fig. 16.6) [35].

Novel Endoscopic Techniques for the Management of Gastric Varices

EUS-Guided Therapy

From a technical point of view, using EUS-guided therapy for GV may benefit compared to conventional endoscopy in terms of more accurate localizing the submucosal venous structure or confirming variceal obturation using Doppler. Consequently, the use of Doppler before and after the injection of coils and/or cyanoacrylate permits monitoring of the treatment success [18].

EUS-Guided Coil Embolization

A retrospective study evaluating the efficacy between EUS-guided coil embolization ($n = 11$) and EVO ($n = 19$) reported the similar rate of GV obliteration in both interventions [57]. Recently another retrospective analysis of 152 patients treated with EUS-guided combined coil and cyanoacrylate injection reported >99% of technical success, 93% of complete obliteration as evidenced by Doppler study, and 3% of posttreatment bleeding during long-term follow-up (median follow-up, 324 days) [8]. EUS-guided therapy is considered to be promising techniques as an alternative option for difficult-to-treat cases with conventional endoscopy. However, EUS-guided therapy has some limitations: [18] (1) EUS-guided guided injection therapy along with coil embolization requires fluoroscopic guidance which will make difficult in the setting of limited space such as intensive care unit. (2) The echoendoscope has a smaller aspiration channel with decreased suction power as compared to conventional endoscope. (3) Compared to conventional endoscopic procedure, EUS might be a more time-consuming procedure as well as more cost is needed.

Transesophageal Injection

Binmoeller and colleagues proposed transesophageal injection for GV obliteration by using EUS. They treated 30 patients using this approach with a hemostasis rate of 100% and a rebleeding rate of 96% [9]. Transesophageal approach merits easy approach without interruption by gastric contents, such as blood and food, which tend to accumulate in the fundus [76].

Thrombin Injection

Thrombin induces clot formation by transforming from fibrinogen to fibrin clot. Bovine thrombin is no longer available due to the risk of transmission of prion. Human thrombin currently is used as an effective treatment option for bleeding from GV with a satisfactory hemostasis rate around 70–100% in the case series [54, 66, 77]. However, lack of data in large studies and affordability hinder use of human thrombin to routine clinical practice as an alternative option for GV bleeding.

Beriplast-P is a fibrin glue with factor VIII and human thrombin that has been used extensively in surgical procedures for hemostasis in oozing bleeding sites. A case series reported successful hemostasis (93%) with Beriplast-P in 15 patients with GV [15]. In another case series, immediate hemostasis was achieved in seven of ten patients with a single Beriplast-P injection without rebleeding in patients with GV bleeding [25].

Endoscopic Hemostatic Spray

Hemospray powder is highly adsorptive with a multimodal mechanism of action. Contacting with moisture such as blood or tissue in the GI tract makes powder become cohesive and adhesive; subsequently powder forms a stable mechanical barrier and then enables to cover the bleeding site and achieves hemostasis [70]. An advantage of hemostatic spray is its ease of use, allowing for less precise targeting and ability to treat poorly accessible areas [18]. Hemospray is recently introduced for the management of non-variceal upper GI bleeding, and its safety and efficacy have been shown in the peptic ulcer bleeding. However, few case reports exist in the use of hemostatic spray in patients with refractory GV bleeding following EVO [27]. Future studies are required to accumulate the evidence of clinical applications for use of hemostatic spray.

Conclusion

Gastric varices are present in 5–30% of patients with portal hypertension. Bleeding from gastric varices is a life-threatening condition requiring immediate resuscitation, vasoactive drugs, prophylactic antibiotics, and immediate hemostasis using either endoscopic or endovascular treatment. After bleeding controlled, GV should be managed

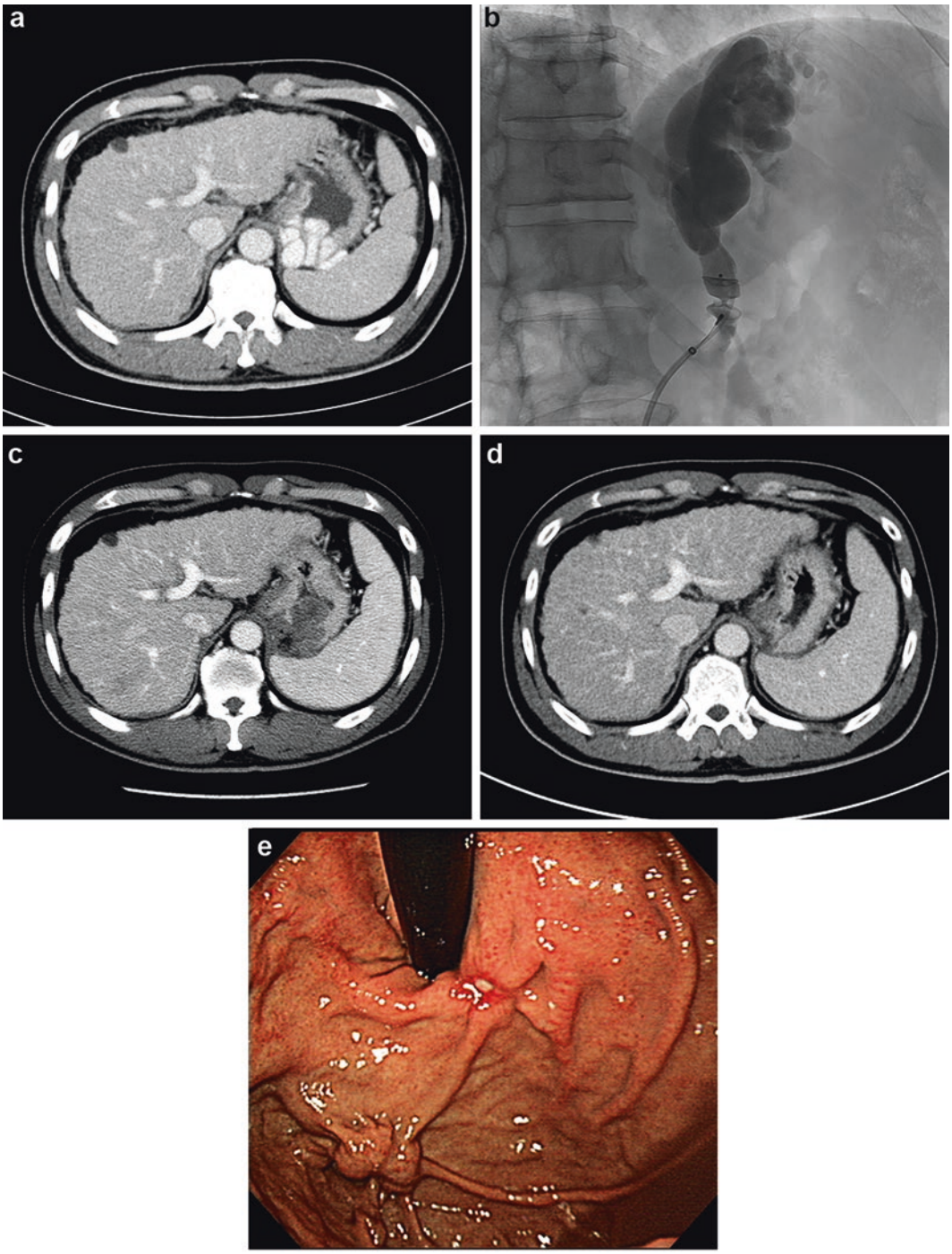

Fig. 16.6 Fundal varix in a 48-year-old man. (**a**) Contrast-enhanced CT image obtained before PARTO shows fundal varices. (**b**) After vascular plug placement, venogram revealed a large gastrorenal shunt and fundal varices. (**c**) CT image obtained 2 days after PARTO shows thrombosis of the gastrorenal shunt and fundal varices. (**d**) CT image obtained 6 months after PARTO shows complete obliteration of the fundal varices. (**e**) Endoscopy 6 months after PARTO shows obliteration of the fundal varices with submucosal lesion filled with thrombosis from PARTO

continuously considering the risk of rebleeding. EVO can be used as a first option for management of GV, and TIPS or BRTO can be chosen as alternative options if EVO is not applicable. TIPS or BRTO for first option for management of GV should be further studied. Unlike management of esophageal varices, limited prospective randomized studies are available and previous published studies consisted of relatively small number of patients. Therefore, prospective

randomized trials are warranted to guide optimal treatment strategy for GV, particularly for each categorization such as primary prophylaxis, acute management option, and secondary prophylaxis.

References

1. Akahane T, Iwasaki T, et al. Changes in liver function parameters after occlusion of gastrorenal shunts with balloon-occluded retrograde transvenous obliteration. Am J Gastroenterol. 1997;92(6):1026–30.
2. Akahoshi T, Hashizume M, et al. Long-term results of endoscopic Histoacryl injection sclerotherapy for gastric variceal bleeding: a 10-year experience. Surgery. 2002;131(1 Suppl):S176–81.
3. Akahoshi T, Hashizume M, et al. Long-term results of balloon-occluded retrograde transvenous obliteration for gastric variceal bleeding and risky gastric varices: a 10-year experience. J Gastroenterol Hepatol. 2008;23(11):1702–9.
4. An J, Kim KW, et al. Improvement in survival associated with embolisation of spontaneous portosystemic shunt in patients with recurrent hepatic encephalopathy. Aliment Pharmacol Ther. 2014;39(12):1418–26.
5. Arai H, Abe T, et al. Emergency balloon-occluded retrograde transvenous obliteration for gastric varices. J Gastroenterol. 2005;40(10):964–71.
6. Arakawa M, Masuzaki T, et al. Pathomorphology of esophageal and gastric varices. Semin Liver Dis. 2002;22(1):73–82.
7. Barange K, Peron JM, et al. Transjugular intrahepatic portosystemic shunt in the treatment of refractory bleeding from ruptured gastric varices. Hepatology. 1999;30(5):1139–43.
8. Bhat YM, Weilert F, et al. EUS-guided treatment of gastric fundal varices with combined injection of coils and cyanoacrylate glue: a large U.S. experience over 6 years (with video). Gastrointest Endosc. 2016;83(6):1164–72.
9. Binmoeller KF, Weilert F, et al. EUS-guided transesophageal treatment of gastric fundal varices with combined coiling and cyanoacrylate glue injection (with videos). Gastrointest Endosc. 2011;74(5):1019–25.
10. Chao Y, Lin HC, et al. Hepatic hemodynamic features in patients with esophageal or gastric varices. J Hepatol. 1993;19(1):85–9.
11. Chau TN, Patch D, et al. "Salvage" transjugular intrahepatic portosystemic shunts: gastric fundal compared with esophageal variceal bleeding. Gastroenterology. 1998;114(5):981–7.
12. Cheng LF, Wang ZQ, et al. Treatment of gastric varices by endoscopic sclerotherapy using butyl cyanoacrylate: 10 years' experience of 635 cases. Chin Med J. 2007;120(23):2081–5.
13. Cheng LF, Wang ZQ, et al. Low incidence of complications from endoscopic gastric variceal obturation with butyl cyanoacrylate. Clin Gastroenterol Hepatol. 2010;8(9):760–6.
14. D'Imperio N, Piemontese A, et al. Evaluation of undiluted N-butyl-2-cyanoacrylate in the endoscopic treatment of upper gastrointestinal tract varices. Endoscopy. 1996;28(2):239–43.
15. Datta D, Vlavianos P, et al. Use of fibrin glue (beriplast) in the management of bleeding gastric varices. Endoscopy. 2003;35(8):675–8.
16. de Franchis R, Baveno VIF. Expanding consensus in portal hypertension: report of the Baveno VI Consensus Workshop: stratifying risk and individualizing care for portal hypertension. J Hepatol. 2015;63(3):743–52.
17. El Amin H, Abdel Baky L, et al. A randomized trial of endoscopic variceal ligation versus cyanoacrylate injection for treatment of bleeding junctional varices. Trop Gastroenterol. 2010;31(4):279–84.
18. Fujii-Lau LL, Law R, et al. Novel techniques for gastric variceal obliteration. Dig Endosc. 2015;27:189–96.
19. Garcia-Pagan J-C, Barrufet M, et al. Management of gastric varices. Clin Gastroenterol Hepatol. 2014;12:919–28.e1. quiz e51–2
20. Garcia-Pagan JC, Caca K, et al. Early use of TIPS in patients with cirrhosis and variceal bleeding. N Engl J Med. 2010;362(25):2370–9.
21. Garcia-Tsao G, Sanyal AJ, et al. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology. 2007;46(3):922–38.
22. Greenwald BD, Caldwell SH, et al. N-2-butyl-cyanoacrylate for bleeding gastric varices: a United States pilot study and cost analysis. Am J Gastroenterol. 2003;98(9):1982–8.
23. Gwon DI, Kim YH, et al. Vascular plug-assisted retrograde transvenous obliteration for the treatment of gastric varices and hepatic encephalopathy: a prospective multicenter study. J Vasc Interv Radiol. 2015;26(11):1589–95.
24. Gwon DI, Ko G-Y, et al. Gastric varices and hepatic encephalopathy: treatment with vascular plug and gelatin sponge-assisted retrograde transvenous obliteration–a primary report. Radiology Radiological Society of North America Inc. 2013;268:281–7.
25. Heneghan MA, Byrne A, et al. An open pilot study of the effects of a human fibrin glue for endoscopic treatment of patients with acute bleeding from gastric varices. Gastrointest Endosc. 2002;56(3):422–6.
26. Hiraga N, Aikata H, et al. The long-term outcome of patients with bleeding gastric varices after balloon-occluded retrograde transvenous obliteration. J Gastroenterol. 2007;42(8):663–72.
27. Holster IL, Poley JW, et al. Controlling gastric variceal bleeding with endoscopically applied hemostatic powder (Hemospray). J Hepatol. 2012;57(6):1397–8.
28. Hong HJ, Jun CH, et al. Comparison of endoscopic variceal ligation and endoscopic variceal obliteration in patients with GOV1 bleeding. Chonnam Med J. 2013;49(1):14–9.
29. Huang YH, Yeh HZ, et al. Endoscopic treatment of bleeding gastric varices by N-butyl-2-cyanoacrylate (Histoacryl) injection: long-term efficacy and safety. Gastrointest Endosc. 2000;52(2):160–7.
30. Iwase H, Maeda O, et al. Endoscopic ablation with cyanoacrylate glue for isolated gastric variceal bleeding. Gastrointest Endosc. 2001;53(6):585–92.
31. Jogo A, Nishida N, et al. Factors associated with aggravation of esophageal varices after B-RTO for gastric varices. Cardiovasc Intervent Radiol. 2014;37(5):1243–50.
32. Kanagawa H, Mima S, et al. Treatment of gastric fundal varices by balloon-occluded retrograde transvenous obliteration. J Gastroenterol Hepatol. 1996;11(1):51–8.
33. Kapoor A, Dharel N, et al. Endoscopic diagnosis and therapy in gastroesophageal variceal bleeding. Gastrointest Endosc Clin N Am. 2015;25:491–507.
34. Kim T, Shijo H, et al. Risk factors for hemorrhage from gastric fundal varices. Hepatology. 1997;25(2):307–12.
35. Kim YH, Kim YH, et al. Comparison of balloon-occluded retrograde transvenous obliteration (BRTO) using ethanolamine oleate (EO), BRTO using sodium tetradecyl sulfate (STS) foam and vascular plug-assisted retrograde transvenous obliteration (PARTO). Cardiovasc Intervent Radiol. 2016;39(6):840–6.
36. Kind R, Guglielmi A, et al. Bucrylate treatment of bleeding gastric varices: 12 years' experience. Endoscopy. 2000;32(7):512–9.
37. Kochhar GS, Navaneethan U, et al. Comparative study of endoscopy vs. transjugular intrahepatic portosystemic shunt in the management of gastric variceal bleeding. Gastroenterol Rep (Oxf). 2015;3(1):75–82.
38. Lo GH, Lai KH, et al. A prospective, randomized trial of butyl cyanoacrylate injection versus band ligation in the management of bleeding gastric varices. Hepatology. 2001;33(5):1060–4.
39. Lo GH, Lin CW, et al. A retrospective comparative study of histoacryl injection and banding ligation in the treatment of acute type 1 gastric variceal hemorrhage. Scand J Gastroenterol. 2013;48(10):1198–204.

40. Mahadeva S, Bellamy MC, et al. Cost-effectiveness of N-butyl-2-cyanoacrylate (histoacryl) glue injections versus transjugular intrahepatic portosystemic shunt in the management of acute gastric variceal bleeding. Am J Gastroenterol. 2003;98(12):2688–93.
41. Marques P, Maluf-Filho F, et al. Long-term outcomes of acute gastric variceal bleeding in 48 patients following treatment with cyanoacrylate. Dig Dis Sci. 2008;53(2):544–50.
42. Matsumoto A, Kitamoto M, et al. Three-dimensional portography using multislice helical CT is clinically useful for management of gastric fundic varices. AJR Am J Roentgenol. 2001;176(4): 899–905.
43. Mishra SR, Sharma BC, et al. Primary prophylaxis of gastric variceal bleeding comparing cyanoacrylate injection and beta-blockers: a randomized controlled trial. J Hepatol. 2011;54(6):1161–7.
44. Miyamoto Y, Oho K, et al. Balloon-occluded retrograde transvenous obliteration improves liver function in patients with cirrhosis and portal hypertension. J Gastroenterol Hepatol. 2003;18(8): 934–42.
45. Monsanto P, Almeida N, et al. Endoscopic treatment of bleeding gastric varices with histoacryl (N-butyl-2-cyanoacrylate): a South European single center experience. Indian J Gastroenterol. 2013;32(4):227–31.
46. Mumtaz K, Majid S, et al. Prevalence of gastric varices and results of sclerotherapy with N-butyl 2 cyanoacrylate for controlling acute gastric variceal bleeding. World J Gastroenterol. 2007;13(8):1247–51.
47. Ninoi T, Nishida N, et al. Balloon-occluded retrograde transvenous obliteration of gastric varices with gastrorenal shunt: long-term follow-up in 78 patients. AJR Am J Roentgenol. 2005;184(4):1340–6.
48. Oho K, Iwao T, et al. Ethanolamine oleate versus butyl cyanoacrylate for bleeding gastric varices: a nonrandomized study. Endoscopy. 1995;27(5):349–54.
49. Paik CN, Kim SW, et al. The therapeutic effect of cyanoacrylate on gastric variceal bleeding and factors related to clinical outcome. J Clin Gastroenterol. 2008;42(8):916–22.
50. Park JK, Cho SK, et al. Vascular plug-assisted retrograde transvenous obliteration of portosystemic shunts for refractory hepatic encephalopathy: a case report. Case Rep Radiol. 2014;2014:391420.
51. Patidar KR, Sydnor M, et al. Transjugular intrahepatic portosystemic shunt. Clin Liver Dis. 2014;18(4):853–76.
52. Polio J, Groszmann RJ. Hemodynamic factors involved in the development and rupture of esophageal varices: a pathophysiologic approach to treatment. Semin Liver Dis. 1986;6(4):318–31.
53. Qiao W, Ren Y, et al. Cyanoacrylate injection versus band ligation in the endoscopic management of acute gastric variceal bleeding: meta-analysis of randomized, controlled studies based on the PRISMA statement. Medicine (Baltimore). 2015;94(41):e1725.
54. Ramesh J, Limdi JK, et al. The use of thrombin injections in the management of bleeding gastric varices: a single-center experience. Gastrointest Endosc. 2008;68(5):877–82.
55. Rees CJ, Nylander DL, et al. Do gastric and oesophageal varices bleed at different portal pressures and is TIPS an effective treatment? Liver. 2000;20(3):253–6.
56. Rengstorff DS, Binmoeller KF. A pilot study of 2-octyl cyanoacrylate injection for treatment of gastric fundal varices in humans. Gastrointest Endosc. 2004;59(4):553–8.
57. Romero-Castro R, Ellrichmann M, et al. EUS-guided coil versus cyanoacrylate therapy for the treatment of gastric varices: a multicenter study (with videos). Gastrointest Endosc. 2013;78(5):711–21.
58. Rosch J, Hanafee W, et al. Transjugular intrahepatic portacaval shunt. An experimental work. Am J Surg. 1971;121(5):588–92.
59. Sabri SS, Abi-Jaoudeh N, et al. Short-term rebleeding rates for isolated gastric varices managed by transjugular intrahepatic portosystemic shunt versus balloon-occluded retrograde transvenous obliteration. J Vasc Interv Radiol. 2014;25(3):355–61.
60. Sarin SK, Jain AK, et al. A randomized controlled trial of cyanoacrylate versus alcohol injection in patients with isolated fundic varices. Am J Gastroenterol. 2002;97(4):1010–5.
61. Sarin SK, Kumar A. Gastric varices: profile, classification, and management. Am J Gastroenterol. 1989;84(10):1244–9.
62. Sarin SK, Lahoti D, et al. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology. 1992;16(6):1343–9.
63. Schuman BM, Beckman JW, et al. Complications of endoscopic injection sclerotherapy: a review. Am J Gastroenterol. 1987;82(9):823–30.
64. Seewald S, Ang TL, et al. A standardized injection technique and regimen ensures success and safety of N-butyl-2-cyanoacrylate injection for the treatment of gastric fundal varices (with videos). Gastrointest Endosc. 2008;68(3):447–54.
65. Seo YS, Park SY, et al. Lack of difference among terlipressin, somatostatin, and octreotide in the control of acute gastroesophageal variceal hemorrhage. Hepatology. 2014;60(3):954–63.
66. Smith MR, Tidswell R, et al. Outcomes of endoscopic human thrombin injection in the management of gastric varices. Eur J Gastroenterol Hepatol. 2014;26(8):846–52.
67. Soehendra N, Grimm H, et al. N-butyl-2-cyanoacrylate: a supplement to endoscopic sclerotherapy. Endoscopy. 1987;19(6):221–4.
68. Song HG, Lee HC, et al. Therapeutic efficacy of transjugular intrahepatic portosystemic shunt on bleeding gastric varices. Taehan Kan Hakhoe Chi. 2002;8(4):448–57.
69. Stanley AJ, Jalan R, et al. A comparison between gastric and oesophageal variceal haemorrhage treated with transjugular intrahepatic portosystemic stent shunt (TIPSS). Aliment Pharmacol Ther. 1997;11(1):171–6.
70. Sung JJ, Luo D, et al. Early clinical experience of the safety and effectiveness of Hemospray in achieving hemostasis in patients with acute peptic ulcer bleeding. Endoscopy. 2011;43(4):291–5.
71. Tan PC, Hou MC, et al. A randomized trial of endoscopic treatment of acute gastric variceal hemorrhage: N-butyl-2-cyanoacrylate injection versus band ligation. Hepatology. 2006;43(4):690–7.
72. Tantau M, Crisan D, et al. Band ligation vs. N-Butyl-2-cyanoacrylate injection in acute gastric variceal bleeding: a prospective follow-up study. Ann Hepatol. 2013;13(1):75–83.
73. Teres J, Cecilia A, et al. Esophageal tamponade for bleeding varices. Controlled trial between the Sengstaken-Blakemore tube and the Linton-Nachlas tube. Gastroenterology. 1978;75(4):566–9.
74. Tripathi D, Redhead D. Transjugular intrahepatic portosystemic stent-shunt: technical factors and new developments. Eur J Gastroenterol Hepatol. 2006;18(11):1127–33.
75. Tripathi D, Therapondos G, et al. The role of the transjugular intrahepatic portosystemic stent shunt (TIPSS) in the management of bleeding gastric varices: clinical and haemodynamic correlations. Gut. 2002;51(2):270–4.
76. Weilert F, Binmoeller KF. Endoscopic management of gastric variceal bleeding. Gastroenterol Clin N Am. 2014;43:807–18.
77. Yang WL, Tripathi D, et al. Endoscopic use of human thrombin in bleeding gastric varices. Am J Gastroenterol. 2002;97(6):1381–5.
78. Ye X, Huai J, et al. Cyanoacrylate injection compared with band ligation for acute gastric variceal hemorrhage: a meta-analysis of randomized controlled trials and observational studies. Gastroenterol Res Pract. 2014;2014:806586.

Percutaneous Endoscopic Gastrostomy and Jejunostomy for Feeding

17

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Percutaneous endoscopic feeding tube placement as suggested by its name is an endoscopy-guided artificially created ostomy connecting the gastric cavity and the skin surface. Enteral nutrition has been shown to be superior to parenteral nutrition in improving immunity, but enteral access can be a challenge in patients who cannot swallow safely [1, 2]. The need for a percutaneous enteral access arises in patients who are expected to be dependent on tube feeds for a long time, usually for more than 1 month. The most common source of tube feeding is via a nasogastric (NG) or orogastric tube extending into the stomach or nasojejunal (Dobhoff) tube which extends into the proximal small bowel. The tube is used for delivering tube feeds, water, and medications to the gut. The most common requirements for such a nutritional access are cancers involving upper airways, oral cavity, pharynx, or esophagus; dementia and cerebrovascular accidents with loss of ability to swallow. The procedures performed by gastroenterologists for enteral access include percutaneous endoscopic gastrostomy (PEG), percutaneous endoscopic gastrojejunostomy (PEGJ), and direct percutaneous endoscopic jejunostomy (DPEJ). The most commonly employed technique is the PEG.

Percutaneous Endoscopic Gastrostomy

Introduction

Percutaneous endoscopic gastrostomies were first reported in 1980 by Gauderer and colleagues. They reported a small case series of 12 children and 19 adults in whom they performed PEG tube placement with minimal anesthesia and declared that the procedure carried a low risk of morbidity and mortality [3]. At first the procedure was performed mainly in children, but over the years, it has been utilized in adults and geriatric populations as well. Surgically performed gastrostomy was initially the procedure of choice for enteral access through the stomach. Subsequently studies have shown PEG to be superior to surgical gastrostomy, especially in reducing overall complication rates and shortening the duration of the procedure, hence reducing risk of anesthesia-related complications [4–6].

Among stroke patients, PEG tube feeding has shown to improve nutritional status when compared to NG tube feeding [7, 8]. PEG tube feeding has been shown to be superior to NG tube feeding in terms of survival, providing adequate nutritional support and risk of developing aspiration pneumonia [9–11]. Major bacterial pathogens, mainly gram-negative species like proteus and pseudomonas, were more frequently found in gastric secretions of patients with a NG tube when compared to ones with a PEG tube [12]. It is also important to note there have been studies that have shown lack of superiority of PEG when compared to NG tube for enteral access [13]. They show no survival benefit with use of PEG [8, 14].

Head and neck cancer patients who undergo chemoradiation sometimes undergo prophylactic PEG tube placement in order to maintain adequate nutritional status. This practice in fact has no superior benefit when compared to NG tube feeding with regard to treatment outcome or nutritional status [15–17]. But such use of prophylactically placed PEG tubes is a matter of discussion and it may be placed due to patient preferences and ease of management of nutrition or when prolonged treatment is anticipated. Patients tend to prefer PEG tube for long-term feeding due to lesser discomfort when compared to a NG tube [18].

Indications

The gastrointestinal tract is a one single luminal tube-like structure extending from the oral cavity to the anus. Any blockage in the GI tract can be bypassed with a percutaneous ostomy connecting to the lumen distal to the blockage. For

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example, in individuals who have oral cancer or esophageal cancers, a PEG tube can bypass the area of obstruction in the oral cavity or esophagus, respectively, and deliver the nutritional substrates directly into the stomach. Just like tumors which can arise in any segment of the GI tract, benign strictures too can form in any section of the GI tract leading to obstruction to flow of luminal contents. If such an obstruction develops in the proximal part of the GI tract up to the cardia of the stomach, then a PEG tube can be placed to bypass it. Although the PEG is iatrogenically created, once the tube that traverses the ostomy site is removed, the opening closes by itself within hours to days. This gives the patients an opportunity to have a PEG tube placed even in a condition which is temporary and when the luminal obstruction is likely to be resolved in the near future. The list of possible indications for placement of a PEG tube have been mentioned in Table 17.1.

Another major indication for PEG tube placement is dysphagia of either the oral phase or the pharyngeal phase. Inability to masticate also can warrant a PEG tube placement. But in this case, it puts one at risk for aspiration of oral contents (food or secretions) into the bronchial tree leading to complications like aspiration pneumonia or obstruction of the airways which can be fatal. The outcomes in patients with severely debilitating disease like amyotrophic lateral sclerosis (ALS) are suggesting improved survival in those who get adequate caloric nutrition [19]. Hence, early placement of PEG is recommended in individuals who are only going to progressively deteriorate, as seen in conditions like ALS, Parkinson's, Alzheimer's, and other forms of progressive dementias or in case of untreatable cancers. Whatever may be the case, the use of PEG tubes has not shown to add any overall survival benefit [20]. The prophylactic placement of PEG tube in patients with advanced head and neck cancers has been shown to improve quality of life [21].

Table 17.1 Indications for percutaneous endoscopic gastrostomy tube placement [27]

Cancers
Oral cancer
Tonsillar cancer
Pharyngeal cancer
Laryngeal cancer
Esophageal cancer
Cancer of the stomach (gastroesophageal junction, cardia)
Neurologic conditions
Cerebrovascular accidents
Amyotrophic lateral sclerosis
Advanced dementia
Multiple sclerosis
Parkinsonism
Cerebral palsy
Cerebral tumor
Psychomotor retardation
Altered mental status (head injury, prolonged coma)
Other causes
Mediastinal tumors compressing or invading the esophagus
Erosive esophagitis (caustic ingestion, radiation exposure)
Burns
Fistula formation (Crohn's disease)
Intensive care patients (long-term intubation)
Esophageal stricture
Cystic fibrosis
Short bowel syndrome
Weight loss
Gastric venting (severe gastroparesis, gastric outlet obstruction, proximal small bowel strictures)
Congenital anomaly (tracheoesophageal fistula)

The assessment of who has or does not have dysphagia can be performed by a swallow evaluation, usually conducted by a speech pathologist. In critically ill patients, detailed neurologic examinations to evaluate swallow function may not be feasible, especially among those who are extubated and carry a high risk of having undiagnosed underlying risk of aspiration. In such patients, a simple bedside evaluation by a speech pathologist called the "fiber-optic endoscopic evaluation of swallow" (FEES) can be performed [22]. While performing FEES, the speech pathologist orally administers various textures of meals and observes the glottis move under direct visualization using a fiber-optic scope placed behind the tongue. They can also assess what types of foods are better tolerated, for example, certain patients with head and neck cancers may be able to tolerate puree diet or mechanical soft diet and can continue to be fed via oral route. Another test to evaluate swallow function is modified barium swallow which is a radiologic test that assesses the oral, pharyngeal, and esophageal phases of swallowing using foods to which radiopaque barium is added, and the mechanism of swallowing is studied closely under fluoroscopy. Usually barium-labeled "cookie" meal is used for performing the test.

In individuals who have inability to empty their stomach either due to gastric outlet obstruction or severe gastroparesis, they may require a venting gastrostomy [23]. This essentially serves as a PEG tube but is used mainly to remove gastric secretions and not for feeding purposes. The use of venting gastrostomy has been shown to provide greater relief when compared to maximal medical therapy [23, 24]. Patients with severe gastroparesis with a venting gastrostomy have better weight gain than ones without it [23]. These patients also tend to have a percutaneous jejunostomy tube that is used for feeding purposes, and in some cases, they are placed on total parenteral nutrition.

Some newer applications of PEG have been in the field of bariatrics with the use of gastric aspiration systems used for weight loss where a PEG tube with a detachable port at the cutaneous end is placed [25, 26]. This port can be attached to

a gastric suction bag which empties food after a meal, hence lowering the amount of food passing into the small bowel.

Contraindications

Percutaneous gastrostomy tube insertion is a surgical procedure associated with various risk factors. Therefore, it is a prerequisite to establish the absolute need for the procedure and also be aware of potential contraindications to performing the procedure. Majority of the contraindications are associated with other coexisting disease states like sepsis, hemodynamic instability, bleeding diathesis, or anatomical factors. We have listed the major contraindications for this procedure in Table 17.2 [27]. The principle behind anatomical factors is that if the endoscope cannot be passed up to the stomach or if there is insufficient transillumination of the light from the endoscope onto the external surface of the abdominal wall, then the PEG tube cannot be safely placed. This can arise when individuals have a tumor blocking the passage of the endoscope through the oral cavity, oropharynx, esophagus, and the gastroesophageal junction. Such an obstruction can be due to cancer at any of these locations or benign conditions like non-malignant stricture. In a case of an esophageal stricture, dilation of the stricture can be performed prior to placing a PEG tube. But in case of cancers, a NG tube for feeding may be placed temporarily, and once the cancer is treated partially or completely, then one can be reassessed for PEG tube placement. Even in patients with malignant esophageal cancers on palliative treatment, placement of an esophageal stent may facilitate PEG tube placement [28]. In other advanced cancer cases, we can consider radiographically placed gastrostomy tubes where the interventional radiologist places a feeding gastrostomy tube under radiologic visualization by directly puncturing the abdominal wall and entering the gastric cavity. Another reason for considering the radiologically placed feeding tube is to avoid the risk of causing endoscopic direct spread of the cancer cells from the upper airways to the stomach or ostomy site, which has been reported to occur in few cases [29].

Table 17.2 List of contraindications for percutaneous endoscopic gastrostomy tube placement

Hemodynamic instability
Coagulopathy (elevated partial thromboplastin time of >50 or INR of >1.5)
Thrombocytopenia (platelet count <50,000)
Sepsis or infection of the abdominal wall at PEG tube insertion site
Peritonitis
Hepatomegaly, splenomegaly, interposed bowel
Obstruction of upper airways (oral cavity, pharynx) due to cancer or stenosis
Esophageal obstruction due to stricture or malignancy
Diffuse peritoneal carcinomatosis[a]
Gastric outflow obstruction[a]
Proximal small bowel strictures[a]
Total gastrectomy
Relative contraindications: severe abdominal obesity, ascites, pregnancy, gastric varices, peritoneal dialysis

[a]*In these cases, PEG tube may be placed for venting gastric secretions only*

Among the risk factors listed in Table 17.2, some are reversible like bleeding-related risk factors, which can be corrected with platelet transfusion or fresh-frozen plasma infusion. A newly available vitamin K-related 4-factor prothrombin complex (Kcentra™) has been utilized for quick reversal of INR, especially in patients who are on warfarin for anticoagulation [30]. The presence of systemic infection requires intravenous antibiotic therapy, and resolution of infection should be confirmed with repeat blood cultures prior to proceeding with the procedure. Abdominal organs can sometimes get interposed between the stomach and the abdominal wall making it challenging to place a PEG tube. In these situations, surgically placed PEG tubes are considered with laparoscopic technique.

Some of the relative contraindications are listed in Table 17.2; they are termed relative since their severity determines whether the PEG tube may or may not be placed. For example, obesity has not limited PEG tube placement and has been safely performed even in individuals with super obesity (BMI > 50) [31–33]. Performing the procedure in overtly obese individuals is also dependent on the experience of the endoscopist [32]. In rare circumstances it may be very challenging to place a PEG tube, and an alternate method to establish enteral access must be considered. The presence of ascites can be treated with diuretics, but refractory ascites may require transjugular intrahepatic portosystemic shunt (TIPS) placement. The placement of TIPS itself is associated with risk factors and hence in advanced cirrhotics may not be feasible. Ascitic tap followed by PEG tube placement has been performed but can put one at risk for complications once the ascites reaccumulates [34, 35]. The placement of PEG tube in cirrhotics has been associated with increased mortality and hence is discouraged [36]. According to the American Society of Gastrointestinal Endoscopy (ASGE), the presence of ascites has been labeled a relative contraindication for PEG tube placement. Pregnancy-related hyperemesis gravidarum can be debilitating to such an extent that PEG tube for feeding is considered as an option for enteral feeding and has been shown to be effective in multiple reported cases [37, 38]. Placing a PEG tube during pregnancy requires a multidisciplinary approach, with obstetricians available to deliver the child in case of an emergency and the presence of personnel who can monitor the fetus during the PEG tube placement [39]. It is generally unsafe to perform the procedure after 29 weeks of gestation [27].

Practical Considerations

- Consider early application of PEG in individuals who are going to progressively deteriorate, as seen in conditions like ALS, Parkinson's, Alzheimer's, and other forms of progressive dementias or untreatable cancers.
- Establish the absolute need for the procedure, and also consider potential contraindications prior to performing PEG.
- It is unsafe to perform the procedure after 29 weeks of gestation.

Techniques of PEG Tube Placement

The procedure can be performed in the endoscopy suite and operating room or at bedside (especially in case of critical patients). It can be performed as an outpatient procedure with minimal distress and reduced cost [40]. An informed consent of the patient, legally appointed person or next of kin must be obtained prior to the procedure. Also, obtaining a consent for blood transfusion in case of severe uncontrolled bleeding is advisable. In addition to an endoscopy technician, the endoscopist will need assistance of an additional person who can be another technician, a physician, or a trained nurse. A adult gastroscope with a diameter of 9.9 mm is used. A standard PEG tube kit contains the following sterile equipment (Fig. 17.1): PEG tube with bumper (button-type device), endoscope snare, scissors, dilators, needle with a catheter, guidewire, lidocaine solution, needles for injection, syringe, scalpel, stopcock with inlet openings, sterile gauze, curved artery forceps, antibacterial ointment, sterile drape, and iodine solution with applicators. The first half of the procedure is performed under sterile precautions. To prevent local and systemic infections, it is recommended to administer a single dose of an intravenous broad-spectrum antibiotic at least 30 min prior to the procedure. The usually preferred antibiotics of choice are cefazolin 1 g (ASGE recommendation), ceftriaxone 1 g, cefotaxime 2 g, or piperacillin 4 g/ tazobactam 0.5 g [41–44].

The Pull-Through Technique First the adult gastroscope is advanced from the mouth to the second portion of the duodenum, to determine any obvious obstruction. Then the scope is withdrawn until it reaches the gastric body, which is insufflated with air. A second physician, nurse, or a trained assistant is present who serves as a "procedure assistant" and observes for transillumination of the endoscope light onto the surface of the abdomen. The brightness of the endoscope light can be increased and the room darkened by turning off the lights and pulling the curtains, for better visualization of the transilluminated light. The Olympus™ endoscopy processor has a special transillumination setting which when turned on can increase the endoscope light intensity for a brief period. The assistant then presses on the abdomen, usually in the left upper quadrant which indents gastric mucosa as visualized by the endoscopist. Then the appropriate skin surface is sterilized with Betadine or chlorhexidine.

The PEG tube kit is opened and the assistant wears sterile gloves and then picks up the sterile section of the kit. The PEG tube kit usually contains a 20 or 24 Fr size PEG tube with its external bumper and clamp (Fig. 17.1). First the sterile drape is applied around the sterile area keeping the sterilized area exposed. A local anesthetic (usually lidocaine 1%) solution is then infiltrated into the skin and subcutaneous tissues using a 22 gauge needle. Then the needle is vertically pushed, and more lidocaine is injected, especially to anesthetize the parietal peritoneum which carries the pain-producing somatic sensory nerve fibers. While pushing the needle, it may be seen to enter or cause an indentation on the gastric mucosa as noted by the endoscopist. Then after waiting for a minute allowing for the effect of the local anesthetic, a gentle 1-cm-wide and about 1–1.5 cm deep incision is made using a sterile scalpel in the area that was anesthetized. It is recommended to slightly dilate the incised skin and subcutaneous tissues using the blunt end artery forceps. This makes it easier to pull the tube in the later part of the procedure. Then a catheter with a trochar needle is inserted at the surgical incision with minimal pressure. Throughout the course of these steps, endoscopic visualization of the gastric lumen has to be maintained; usually continuous air insufflation is required to keep the lumen sufficiently distended. The endoscopist has to stay focused on the area of the mucosa that indented initially. As the trochar needle enters the gastric mucosa, it is seen as a dent of the mucosal lining. The needle

Fig. 17.1 PEG tube placement kit

is further advanced until the tip of the trochar is seen by the endoscopist. Once the needle with catheter tip enters the gastric lumen, then the needle is removed, and a guidewire is passed through the catheter. The wire is then seen to come out of the catheter into the gastric lumen. The luminal end of the wire is then grabbed with the endoscope using a snare. The wire is firmly held with a snare; then the scope with the wire is withdrawn and brought to the outside of the patient's mouth. The catheter that was used to feed the guidewire is then removed leaving the guidewire at ostomy site in place. Then a feeding tube with a snare-like end is tied to the guidewire at the oral end. The feeding tube is sufficiently lubricated with lubricant jelly to prevent mucosal trauma, and then the guidewire is pulled from the ostomy site. As the guidewire is being pulled, some resistance is encountered initially when the bumper of the PEG tube passes the upper esophageal sphincter. With constant pressure, the guidewire is pulled along with the tied end of the feeding tube until it passes smoothly across the upper esophageal sphincter. When the proximal end of the tube comes in contact with the gastric wall, resistance is again appreciated. With a constant vertical pull the tube is slowly pulled out until the markings of the gastrostomy tube appear. At this point, the bumper at the luminal end of the tube is moving closer to the gastrostomy opening. The guidewire is then cut, and an external bolster is inserted over the tapered end of the feeding tube until it is held firmly against the abdominal wall; this is around 4–5 cm mark on the gastrostomy tube. About 1 fingerbreadth (1–2 cm) of space is left between the skin and the external bolster. The endoscope is then reintroduced into the stomach to confirm location of the PEG tube bumper. The details of the procedure have been visually explained in Figs. 17.2 and 17.3.

Once the tube placement is confirmed with endoscopic visualization, then the tube is rotated to make sure it is not very firmly placed against the abdominal wall, since it can lead to tissue necrosis from ischemia, ostomy site infection, ulceration, pain, or buried bumper syndrome (BBS) [45]. Then the tube is cut to leave about 15 cm of its length, and the end of the tube is attached to a feeding adapter. Antibiotic ointment is applied under the external bolster, and then single sterile gauze is placed under the external bolster, interspaced between the external bolster and the skin. The tube is not used for 4 h, folllowed by initiation of tube feeds [46].

The material of the PEG tube used can be silicone or latex based. A randomized controlled trial demonstrated that the silicone PEG tubes were more durable and required less frequent replacement when compared to the latex ones [47]. In the recent years, the use PEG tubes made up of polyurethane has been found to be more durable and less susceptible to degradation by gastric and biliary juices when compared to the more conventional silicone-based PEG tubes [48, 49]. Traditionally, upper GI endoscopy procedures employ air for insufflations, but in case of PEG tube placement, there is a potential risk of pneumoperitoneum, and air is not well absorbed by the tissues. During laparoscopy surgeons use carbon dioxide for insufflation which has shown to be reabsorbed easily. The use of CO_2 for PEG tube placement has been associated with lesser incidences of pneumoperitoneum when compared to air [50]. There has been no observed difference between air and CO_2 with respect to laboratory or clinical parameters. Hence, we recommend insufflation with CO_2 while performing EGD for PEG tube placement.

The placement of a PEG tube via pull method drags the oral secretions and the bacterial colonies from the oropharynx to the stomach. This has been theoretically considered as one of the etiologies responsible for PEG tube-related periosteal infection. A modification to the standard PEG tube system includes using a covered PEG tube which is introduced into the stomach with the standard method. Once in the stomach, the covering over the tube is removed, and only the PEG tube is pulled out from the stomach and secured with the bumper. This form of covered PEG tube has shown to cause fewer infection rates, even if prophylactic antibiotics are not given prior to the procedure [51].

The Push Technique The push technique of PEG tube placement is based on the Russell technique of PEG tube insertion [52]. Once transillumination is achieved and the tube insertion site is anesthetized, a needle is subsequently introduced into the stomach cavity under endoscopic visualization with continuous air insufflation to keep the stomach dilated and well approximated to the abdominal wall. Alternatively, four T-fasteners can be percutaneously introduced in the corners of a 2 cm square area within which the gastrostomy insertion site is located in the middle [53]. The T-fasteners are introduced under endoscopic visualization, and this helps pull the gastric wall close to the abdominal wall. Using Seldinger technique, a guidewire is passed into the stomach, and the needle is removed. Then a small 1 cm incision is made with a scalpel up to the depth of the skin and subcutaneous tissues. Multiple dilators are passed over the guidewire, and then a 14 Fr or 18 Fr gastrostomy tube with an internal Foley balloon is inserted into the stomach over the guidewire. The balloon of the Foley is inflated using 5–10 ml of saline depending on the size of the catheter. Then the guidewire is removed, and the gastrostomy tube is held in place either with an external bumper or external skin sutures that are tied to the PEG tube. The entire procedure is performed under endoscopic visualization, and once the tube is secured, the scope is removed. The external feeding adapter is attached in those tubes that have an external bumper to secure them in place. The push technique has been found to be associated with lower risk of complications than the pull-through technique among individuals with head and neck cancers [54].

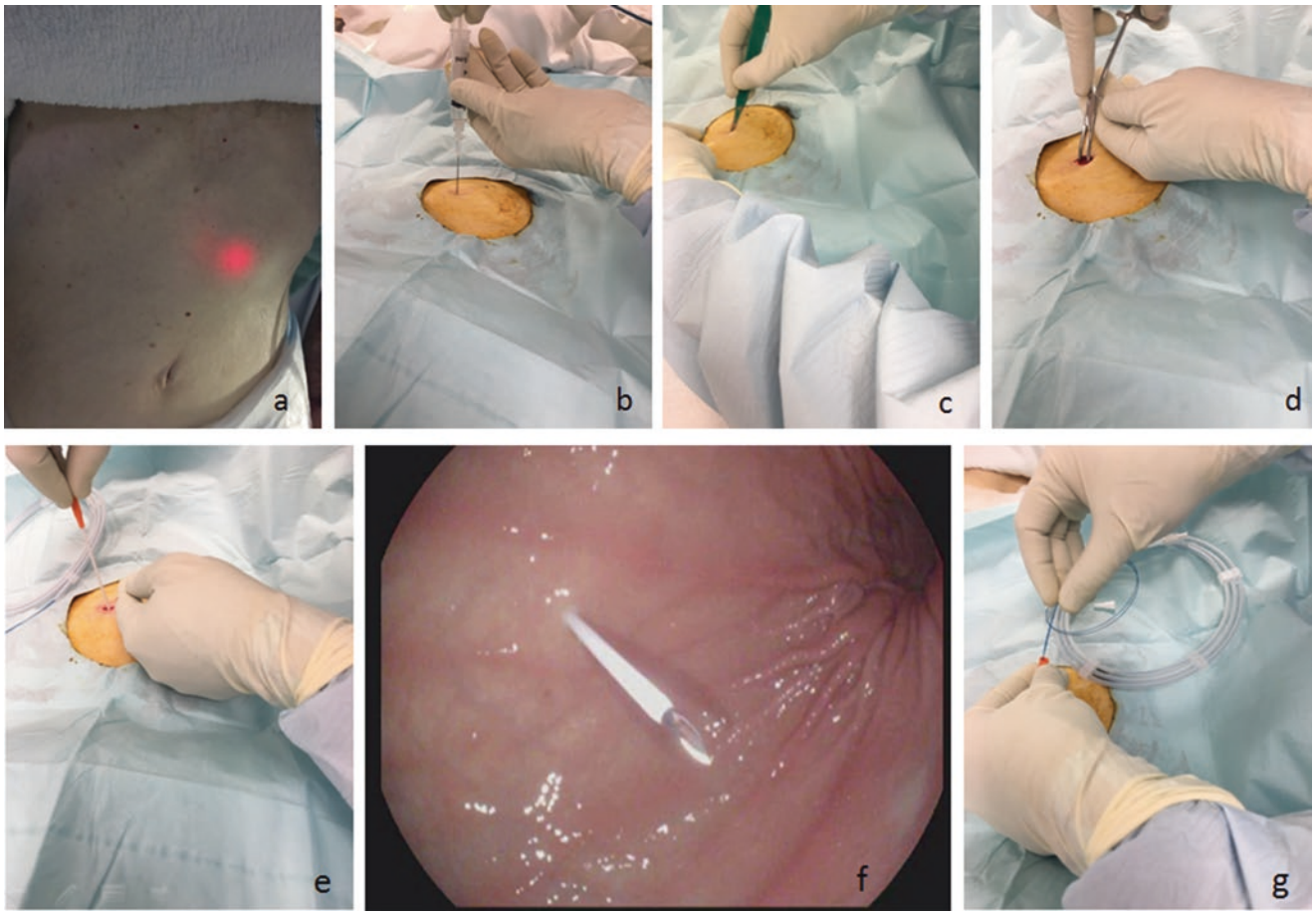

Fig. 17.2 PEG tube placement procedure. (**a**) Transillumination onto abdominal wall. (**b**) Injection of local anesthetic. (**c**) Incision of the skin and subcutaneous tissues. (**d**) Dilation of the incised area. (**e**) Insertion of PEG tube placement catheter with trochar needle. (**f**) Identification of inserted catheter with endoscope. (**g**) Feeding guidewire through the catheter *(Images provided courtsey of S.N. Merwat & H. Salameh)*

Practical Considerations

- To prevent local and systemic infections, a single dose of an intravenous broad-spectrum antibiotic should be administered at least 30 min prior to the procedure. The usually preferred antibiotics of choice are cefazolin 1 g (recommended in ASGE guidelines), ceftriaxone 1 g, cefotaxime 2 g, or piperacillin 4 g/tazobactam 0.5 g.

Complications

Percutaneous gastrostomy tube placement procedure is associated with major and minor complications (Table 17.3). The complication rate from PEG tube placement ranges between 4% and 10.3% [55]. It also carries risk of mortality. In a US nationwide (national inpatient sample or NIS) study, it was found that the risk of mortality for hospitalized patients who underwent PEG tube placement was 10.8% for the year 2006; similar results were also obtained for the year 2007 [56]. The study also showed that the risk of death increased when patients had other comorbidities like cardiopulmonary disorders, metastatic cancers, renal failure, coagulopathy, and liver disease. Hence, it is strongly recommended that selection of inpatient population for PEG tube placement must be made based on clinical and ethical grounds keeping in mind this short-term risk of inpatient mortality. In a study conducted on Medicare population (≥65 years) for the year 1991 involving 81,105 patients; the overall 30-day post-hospitalization mortality rate after PEG tube placement was 23.9%, and it rose to 63% at the end of 1 year [57]. But we must also keep in mind that these patients are very sick in the first place and death may or may not have been directly associated with PEG tube placement. There is no randomized clinical trial that directly compares individuals with PEG and no PEG tube placement since it may be considered ethically incorrect to perform such a study. In a Swedish retrospective study of 484 patients who underwent PEG tube placement between 2005 and 2009, the

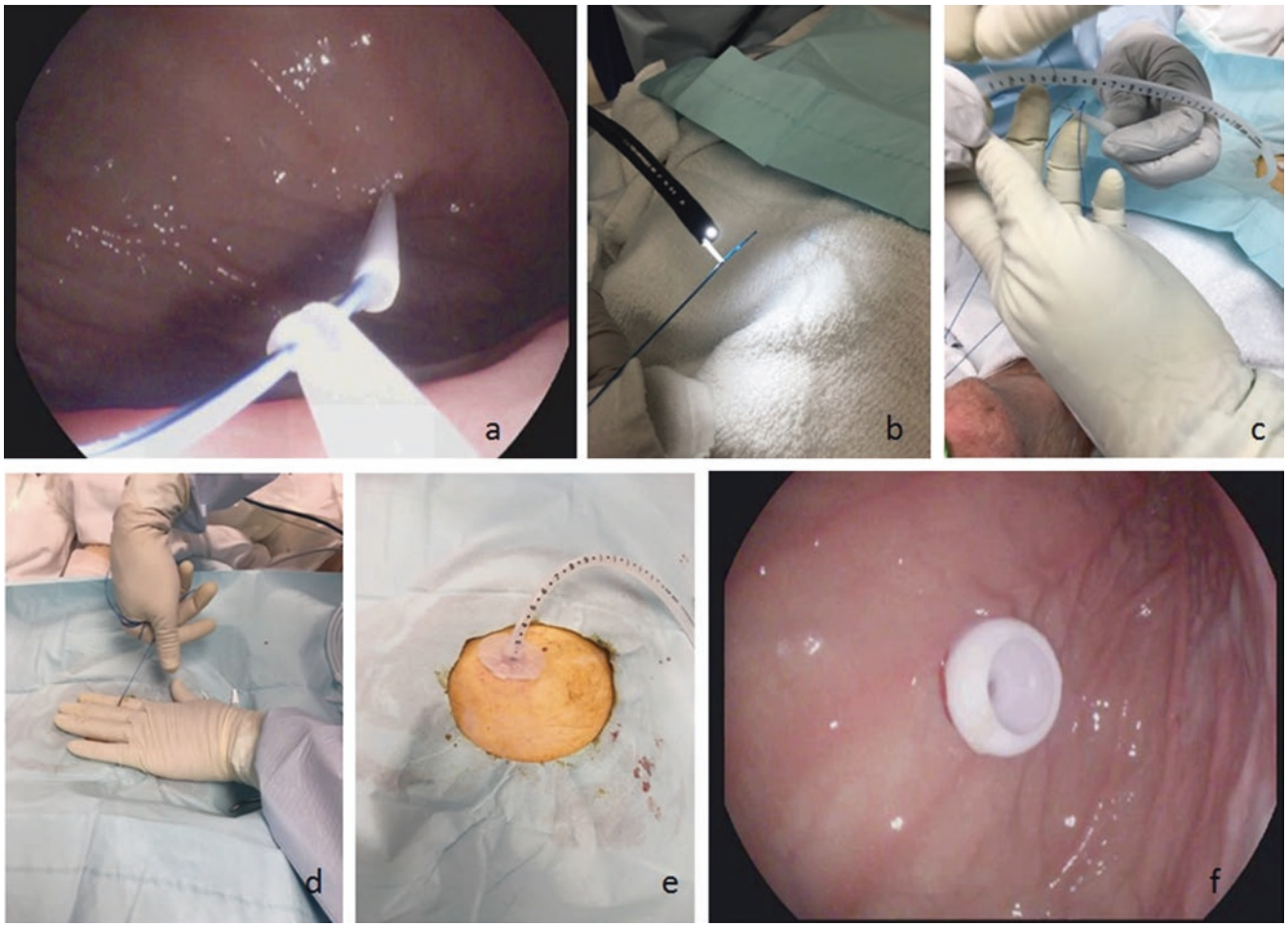

Fig. 17.3 PEG tube placement procedure (contd.). (**a**) Endoscopic snare used to grab the guidewire. (**b**) Withdrawing the endoscope with the guidewire. (**c**) Tying PEG tube with the guidewire. (**d**) Pulling the guidewire with PEG tube. (**e**) PEG tube with an external bumper attached to it. (**f**) Endoscopic visualization of the secured internal bumper

Table 17.3 Complications of percutaneous endoscopic gastrostomy tube placement

Major complications
Aspiration
Bleeding
Seeding of malignant cells
Visceral organ injury
Buried bumper syndrome
Minor complications
Peristomal infection
Pneumoperitoneum
Tube dislodgement
Periosteal leak
Gastric outlet obstruction

mortality rate was 18% with overall complication rate of 27% (diarrhea, leakage, and peristomal infection) at the end of 2 months of follow-up [58].

Aspiration Risk of aspiration exists in several endoscopic procedures and especially when patients are sedated. Neurologically impaired patients at risk for aspiration frequently undergo PEG tube placement, as seen in a study of stroke patients among which 18% individuals developed aspiration pneumonia [59, 60]. But these patients have no reduction in risk of aspiration even after the procedure [61]. Aspiration of oropharyngeal or gastric contents into the airways leads to aspiration pneumonia and can sometimes be fatal. The two factors associated with aspiration of gastric contents are infusing high volume of feeds and resting in prone position [27]. PEG tube feeding of bedridden patients using elemental diet when compared to standard liquid diet has been associated with lower risk of aspiration and better gastric emptying times [61]. Pump-assisted tube feeding has shown to reduce risk of developing aspiration pneumonia and also reduce incidence of diarrhea, vomiting, and regurgitation and improve glucose control [62]. The use of devices

like PEG with jejunal extension or a DPEJ has shown to theoretically reduce risk of aspiration and is discussed later in this chapter.

Bleeding This procedure like any surgical or endoscopic procedure carries risk of hemorrhage during or after the procedure. The source of bleeding can be the splenic vein, gastric varices, superior epigastric artery, or capillary bleeding in coagulopathic states [63]. Although persistent bleeding is a concerning complication, it is rarely seen [64, 65]. The ventral abdominal wall is a soft tissue structure with no bony or cartilaginous structures; hence, local application of pressure is not an effective strategy to control bleeding. Preprocedural evaluation must include checking a platelet count and prothrombin time (PT/INR). Patients with a known history of bleeding disorder should be further evaluated by a hematologist prior to being considered for PEG tube placement. The 2016 ASGE guidelines do not recommend stopping aspirin or NSAIDS prior to or after the procedure [66, 67]. Similarly for thienopyridines like ticagrelor or clopidogrel, the latest guidelines suggest that there is no need to stop either of them during periprocedural period. Studies have shown that use of either aspirin or clopidogrel was not associated with increased risk of bleeding [64, 67, 68]. But there is no available data regarding the safety of using dual antiplatelet therapy. Anticoagulants like warfarin or newer anticoagulants (apixaban or rivaroxaban) must be stopped at least 5 days prior to procedure in individuals who are at low risk for thrombosis. In individuals at high risk of thrombosis, bridging to low molecular weight heparin 5–7 days prior to procedure and hold the low molecular weight heparin on the day of procedure is recommended. There have been reported cases of gastric pseudoaneurysm formation after PEG tube placement that can present with recurrent hemorrhage [69].

Seeding of Malignant Cells The pull-through insertion technique for PEG tube placement in cases of head and neck cancer has been a subject of debate with previously reported cases of metastatic spread of tumor from the primary to the gastrostomy site due to seeding of malignant cells as the PEG tube is pulled across the area where the tumor is present. In a study of 40 patients, 22.5% cases had malignant cells seen at the PEG insertion site or the tubing immediately after PEG tube placement, and at end of follow-up of 3–6 months, 9.4% cases still had malignant cells at the site [29]. In cases with advanced head and neck cancers we recommend radiologically directed gastrostomy tube placement.

Visceral Organ Injury The procedure is carried out using transillumination technique to localize the site of needle insertion and then confirmed with indentation. The needle is inserted under endoscopic guidance. When these steps are followed correctly, the chances of damage to other visceral organs are minimal. Yet there have been reported cases of injury to organs like the colon, liver, spleen, and small bowel [70–73]. Inaccurate localization and insertion of needle can lead to colo-cutaneous fistula formation; this is likely to occur usually in children and elderly in whom the mesentery is lax and the colon can easily interpose between the abdominal wall and stomach. In a review of cases of colonic perforation during PEG tube placement published in 2007, a total of 28 cases were reported. Majority of cases presented with diarrhea and feculent discharge around the tube, whereas some were asymptomatic. Ten patients were treated surgically, and 14 cases underwent non-surgical removal of gastrostomy tube with conservative management. Liver injury usually occurs to the left lobe of the liver when the lobe gets interposed between the abdominal wall and the stomach. Surgical repair was required in one reported case, and conservative approach was followed in two other cases [71, 72]. There has been an unusual reported case of gastrohepatic fistula formation with hepatic abscesses which formed due to a dislodged PEG tube [74]. This form of liver damage was not caused by direct injury from the PEG placement procedure itself. There have been no reported cases of splenic parenchymal injury, but there was a reported case of retroperitoneal hemorrhage caused due to splenic vein injury close to the hilum [75]. Small bowel injury can be a potentially fatal complication from PEG tube placement and can lead to peritonitis due to spillage of luminal contents. A case of duodenal perforation as a result of compressive necrosis by the tip of the PEG tube has been reported in literature, and perhaps it can be considered a long-term complication of the procedure [76].

Buried Bumper Syndrome It is the displacement of the internal bumper of the PEG tube, and the bumper can end up anywhere along the PEG tube tract, from the gastric mucosa to the skin. There have been reported cases of the bumper being buried within the abdominal wall and gastric wall, hence the name buried bumper syndrome (BBS). The tube gets blocked and feeds cannot be pushed into the tube. The first case of BBS was described in 1989, and the incidence of this major complication is about 1% [77]. The etiology of this condition is suspected to be due to very firm apposition between the internal and external bumper leading to compression of the tissue in between the bumpers. It is common practice to keep the bumpers tightly opposed to prevent leakage, but they should subsequently be loosened after a few days of PEG tube placement in order to prevent BBS. Also, leakage commonly occurs within few days and stops once a tract is formed. Even when it is tightly apposed, as a rule of thumb, a safe distance of 1 cm between the skin and external bolster must always be maintained [78]. Patients can develop an infection at the ostomy site causing pain and erythema.

On endoscopy the internal ostomy site may appear like a pressure ulcer (flat or elevated edges) with inflammation and granulation tissue formation, sometimes giving the appearance of a tumor. The bumper may be partially visible or not visible at all. Localization of the site is conducted with methylene blue or a guidewire, injected or inserted, respectively, from the external tube. The condition is almost always treated with removal of tube, and conservative approach is rarely recommended. A savory dilator can be used to dilate the tube and the surrounding tissue, this will make the bumper stiff and helps push the bumper into the gastric lumen, and this is called the "Quill" technique [79]. Some try to loosen the bumper with the help of a clamp from the outside and an endoscopically placed snare on the inside, called the "push-pull technique" [80]. Bumpers that are buried close to the skin and subcutaneous tissues can be released with a surgical incision; those close to the gastric wall can be released using laparoscopic approach [77]. Although a rare complication, BBS can sometimes be fatal due to peritonitis and severe GI bleeding [81].

Periosteal Infection The incidence of periosteal site infection in the pull-through and direct introducer technique is the same [82, 83]. In order to prevent local and systemic infections that can occur as a result of this invasive procedure, it is recommended to administer broad-spectrum antibiotic intravenously 30 min prior to the procedure [41–43]. Studies have shown that antibiotic prophylaxis prior to placing PEG tubes significantly reduced the risk of developing periosteal site infection [84, 85]. The use of glycerin hydrogel for dressing at the peristomal site decreases risk of infection at the gastrostomy site when compared to traditional wound dressing [86].

Pneumoperitoneum The occurrence of pneumoperitoneum after PEG tube placement is not uncommon. In fact, it is frequently brought to the attention of a gastroenterologist after any radiologic investigation of abdomen that shows free air under the diaphragm. This should be regarded as benign and self-limiting unless the patient shows signs of peritonitis or infection. But we must also be aware of patients on antibiotics or with altered mental status who may not complain of abdominal pain even in the presence of peritonitis. The incidence of pneumoperitoneum after PEG tube placement is fairly common, with studies showing a risk of 38% in a study from the 1980's [87] . In a recent Korean retrospective analysis of 193 patients who underwent a PEG tube placement, 4.6% were found to have pneumoperitoneum on radiologic testing within 24 h after procedure [88]. And among sick patients in intensive care units, the incidence of pneumoperitoneum was found to be 16% [89]. In a well-designed prospective study of 65 patients, 13 of them developed pneumoperitoneum seen on chest X-rays 3 h after procedure, with 10 having complete resolution within 72 h and the other 3, although had persistent air, were of no clinical significance. Therefore, we can safely conclude that pneumoperitoneum frequently occurs after PEG tube placement, and watchful waiting or clinical evaluation with serial abdominal exams with or without radiological imaging is helpful in determining if any further intervention is needed. The risk of pneumoperitoneum is higher with the use of air during endoscopy when compared to CO_2 alone [50].

Tube Dislodgement This can occur intentionally which is mainly seen in confused and combative patients. It may also occur due to improperly placed tubes or when adequate education about using the tube is not provided to the personnel handling the tube. It is one of the most commonly encountered complications seen in about 7.8% of cases during their lifetime [90]. The gastrocutaneous fistulous tract matures within 10–14 days in healthy individuals, and it can take up to 1 month among those who are malnourished. Tube dislodgement that occurs within 1 month after placement usually requires new a new tube to be placed through the old track if patent and if not a new tract is created. However, in case of tube dislodgement occurring in individuals over a month after PEG tube placement, a new tube can be placed directly through the exiting tract, as it can be safely assumed that the tract has fully matured. Prior to placing the new PEG tube, the tract can be kept patent by placing a Foley catheter and inflating it.

Peristomal Leakage Leakage of gastric contents after placement of a PEG tube usually occurs within few days after the tube is placed. Sometimes it may persist for a long duration and can be uncomfortable for the patient due to constant soakage of clothing or dressing. Factors that can precipitate tube leakage are ulceration or infection at the ostomy site, BBS, tube dislodgement, gastric hypersecretion, excessive residuals, and factors that are responsible for poor wound healing like uncontrolled diabetes, malnutrition, deficiency of certain micronutrients like zinc, and chronic disease states [55]. Replacing the existing tube with a tube of larger diameter can only worsen the leak by increasing the size of the ostomy. The leak is managed with removal of the tube, allowing the site to heal and then replacing with a new tube [91].

Gastric Outlet Obstruction This is a rare complication of PEG tube placement where the internal bumper of the tube migrates distally to block the pyloric channel or the proximal small bowel. This can occur due to displacement of the bumper from the tube itself or when the internal bumper is not firmly opposed to the gastric mucosa. The inflatable PEG tubes (ballon-type device) that are used to replace the originally placed tube (button-type device) tend to cause gastric

outlet obstruction more commonly due to the globe-like shape of the internal balloon when compared to the flat bumper of the initially placed tube. The patient presents with nausea, vomiting, and feeling of fullness [92]. The abnormal location of the bumper can be determined radiographically [93]. The condition is treated with pulling out a section of the tube until the internal bumper is firmly apposed to the gastric mucosa but without too much tension.

Risk of Endoscopy and Anesthesia Care Last but not the least, we must always consider the risk of performing endoscopy and the risks of administering anesthetics/sedatives during the procedure. The adverse effects of endoscopy itself will be discussed in a different section of this book.

Post-PEG Tube Placement Care

After placement of a PEG tube, the patient may experience significant pain at the ostomy site which can arise due to the trauma of surgical incision or due to abdominal distension as a result of air insufflation during the procedure. Narcotic analgesic medications or acetaminophen can be administered in varying doses for pain control. Intravenous form of medication is preferred since the PEG tube is not used for at least 4 h after the procedure. Once the PEG tube is cleared for use, the analgesics can subsequently be administered through the tube.

The ostomy site requires appropriate wound care. Generally the external bumper covers the ostomy site; hence, an antiseptic ointment (iodine based or bacitracin) is applied under the external bumper. The PEG tube insertion site is covered with dry gauze for a couple of days. The healthcare staff should monitor for wound healing, if there are signs of leakage, or non-healing wound; appropriate measures must be taken to manage these complications. The PEG tube must be slightly loosened on the day after the procedure so that the external bumper is not firmly opposing the skin surface, and there must be at least 1 fingerbreadth of space between the external bumper and the skin.

Only liquid form of material can be delivered through a PEG tube, and the type of nutrition provided to the individual needs to be carefully monitored by trained personnel. Regular follow-up by a nutrition specialist or a nutrition team has been shown to reduce cost of care following PEG tube placement [94]. There is an external attachment to the end of PEG tube through which the tube feeds are administered. Avoid administering medications that can clog the PEG tube; in such cases there is anecdotal evidence that use of carbonated drinks for flushing the tube has been sometimes found to be helpful to unclog it.

The PEG tube needs to be replaced yearly and can be performed endoscopically or percutaneously. The percutaneously placed tubes have an inflatable balloon that is inflated with water once the tube is inserted. The button-type device can be used for longer periods of time, usually 1 year, whereas the balloon-type device usually is replaced in 3–6 months due to a tendency for it to be damaged easily and deflate [95]. A softer version of the button-type device can be inserted percutaneously, avoiding the need for endoscopy, and can function for longer times and can be easily pulled out with minimal traction. These softer tubes were evaluated in a study of 1126 and 139 replacements in 317 and 46 patients with PEG and DPEJ, respectively; the overall complication rate was 1.3% (16 cases) [96]. The most commonly encountered complication was fistula disruption due to misplacement of the device outside the GI tract seen in eight (0.7%) of PEG tubes and two (1.4%) of DPEJ tubes that were replaced; none of them developed peritonitis.

Practical Considerations

- The occurrence of pneumoperitoneum after PEG tube placement is expected and should be regarded as benign and self-limiting unless the patient shows signs of peritonitis or infection.

Percutaneous Endoscopic Gastro-jejunostomy

In patients with gastric outlet obstruction or gastroparesis, who cannot handle intragastric feeding, a PEGJ tube placement is recommended. It may also be considered for jejunal feeding in cases of chronic pancreatitis [46]. This technique involves adding an attachment, referred to as the J tube extension to the intragastric end of the PEG tube. We recommend initially placing a PEG tube prior to attaching the J tube extension; this prevents intragastric coiling of the J tube. Once the J tube is attached to the PEG tube, its distal end is dragged into the jejunum usually with help of endoscopic forceps. It is recommended to advance the distal end of the tube, beyond the ligament of Treitz [97]. Only a 24 Fr-sized PEG tube can be used to attach a J tube extension. The smaller-sized PEG tube of 20 Fr or lower cannot be used due to tubing fit incompatibility.

PEGJ tube can also be useful in individuals with a PEG tube who have recurrent aspirations since the feeds in case of the PEGJ are delivered directly into the jejunum and the gastric contents are minimized thereby reducing the risk of aspiration [98]. In severe cases of gastroparesis or gastric

outlet obstruction which cannot be relieved (advanced malignancy), PEGJ tube may help in enteral feeding directly into the jejunum, but the gastric secretions are not drained, and the patient will be at higher risk for aspiration of gastric secretions. Placing an additional PEG tube which serves as a venting channel for the gastric secretions is sometimes recommended [99, 100]. In a retrospective study of 158 cases that had a PEG tube placed, 28 developed aspiration of which 8 patients had improvement of symptoms by changing the consistency and timing of the feeds [101]. The other 20 patients underwent PEGJ tube placement. On subsequent follow-up, no evidence of aspiration was noted ($p = 0.047$). In a study utilizing US national hospitalization database, the placement of a PEGJ tube did not increase risk of mortality and length of stay when compared to placement of only a PEG tube [102]. In a study of 89 trauma patients with an intact GI tract, PEG tube was placed in 43 and PEGJ tube in 46, and they were followed for 14 days [103]. The nutritional goals for each patient were calculated using Harris-Benedict equation and based on their stress-related requirements. On day 3 after the enteral access was established, 15 PEG patients (35%) and 9 PEGJ patients (20%) failed to achieve nutritional goals. By the end of the study, among the PEGJ group 93% ($n = 43$) of patients and among PEG group 79% ($n = 34$) of patients achieved their calculated nutritional goals. Overall, PEGJ tube placement in acute presentations is perhaps superior if not the same as PEG tube placement in terms of achieving nutritional goals and reducing mortality. A rare use of PEGJ tube is in pregnant women who have severe hyperemesis gravidarum, but this procedure requires skillful placement of the tube due to risk of damaging the distended uterus [104].

The most common complication of this procedure is tube displacement back into the stomach. This is seen in about 30–40% of the cases within a period of 2 months. Repositioning of the J tube must be attempted with the endoscope. It is advisable not to rotate the external PEG tube to check if it is loosely placed, because this may lead to pulling out of the J tube out of the small bowel and into the stomach. A study comparing 64 PEGJ with 65 PEG tube placement cases showed that the average time taken for replacement of PEGJ tube was 160 ± 26.3 days compared to 331 ± 53.6 days ($p = 0.01$) [105]. In case the patient has recurrent failures and displacements of a PEGJ tube, a DPEJ tube can be placed. A newer type of a J tube with a balloon tip has been found to be associated with less frequent displacement into the stomach [106]. There has been a reported case of duodenal perforation due to retrograde migration of a J tube [107]. The other complications of a PEGJ tube placement are similar to the ones for PEG tube placement (Table 17.3).

Direct Percutaneous Endoscopic Jejunostomy

Enteral access that establishes access directly to the jejunum through a stoma is called the DPEJ. It is an endoscopically created artificial enterocutaneous fistula connecting the jejunal lumen and the skin of the abdominal wall. A feeding tube is placed across this fistula and held in place with an outer bumper and an inner bumper (or an inflated balloon). The tube is attached to a system of tubes that run the feeds and water to the jejunum through the ostomy site. It has a function similar to that of a more traditional PEG tube, but in this case the feeds are delivered directly into the jejunum. The first case of DPEJ tube placement was reported in 1987 in a patient with gastric cancer who underwent gastrectomy. In a study of 307 patients who underwent DPEJ tube placement the success rate was 68% [108].

Indications

The most common indications for placement of DPEJ are listed in Table 17.4. The DPEJ tube does not have a jejunal tube extension like in the case of PEGJ; hence, there is no risk of coiling of a tube or displacement into the stomach. It is preferred in cases that need enteral feeding in whom PEGJ has failed. In some cases that need enteral access, it may not be possible to place a PEG tube due to stomach pathology or altered gastric anatomy [109]. In a study of 90 patients who were referred for PEG tube placement, about 10% required a DPEJ instead due to gastroparesis, gastric herniation, or organ interpositioning [110].

Although the technique of DPEJ is similar to PEG tube placement, there are certain conditions that can make it technically more challenging. The contraindications to DPEJ are similar to PEG tube placement with intestinal obstruction being an absolute contraindication to either surgical or endoscopic enteral access. Severe obesity, altered anatomy, and thickening of bowel loops due to edema are some relative contraindications. The amount of body wall fat plays a role in success of the DPEJ tube placement. In a study conducted at a tertiary referral center, the overall success rate of DPEJ

Table 17.4 Indications for placement of percutaneous endoscopic jejunostomy

Severe gastroparesis
Gastric outlet obstruction
Organ interpositioning or altered anatomy
High risk of aspiration
Status post-gastrectomy or esophagogastrectomy
Displaced or blocked PEGJ tube
Damaged gastric mucosa (burns, caustic injury, malignancy)

tube placement was found to be 81% in 80 attempts among 75 patients [111]. The rates of success among different groups of patients based on their weight were 96% in underweight, 81% in normal weight, 73% in overweight, and 60% in obese patients. Among patients with gastroparesis, the risk of aspiration is significantly reduced with DPEJ tube-based feeding. In a study of 83 patients who underwent DPEJ tube placement, 30 of them had gastroparesis, and after tube placement, there was no reported case of aspiration during a long-term follow-up of 10 years [112].

Technique

The technique of placing a DPEJ is similar to that of a PEG, but in this case the ostomy is created to gain access directly to the jejunum with the use of transillumination technique. To prevent infections a dose of intravenous antibiotic is given about 30 min prior to starting the procedure. The standard PEG tube kit is used in a similar fashion as for PEG tube placement. DPEJ tube placement requires clear endoscopic visualization. Firstly push enteroscopy is performed using a pediatric colonoscope or enteroscope. The scope is advanced up to the jejunum and insufflated with air. The procedure assistant looks for transillumination of the endoscope's light onto the surface of the abdomen. Once an appropriate area is localized, which is usually in the left upper quadrant, the skin surface is sterilized with Betadine or chlorhexidine. Local anesthetic (lidocaine 1% solution) is then infiltrated into the skin and subcutaneous tissues. Then the needle is vertically pushed, and more lidocaine is injected to anesthetize the parietal peritoneum which carries somatic sensory nerve fibers. Sometimes the needle may enter the jejunal lumen, which can be seen on endoscopy. Then after waiting for a minute allowing for the effect of the local anesthetic, a 1-cm-wide and about 1–1.5-cm-deep incision is made using a sterile scalpel. Then a catheter with a trochar is inserted at the surgical incision with minimal pressure. Throughout the course of these actions, endoscopic visualization of the jejunal lumen has to be maintained; usually continuous air or preferable CO_2 insufflation is required to keep the lumen sufficiently distended. As the trochar needle enters the jejunal mucosa, it is seen with endoscopic visualization, then the trochar is removed, and a guidewire is passed through the catheter. Once the wire appears out of the catheter into the jejuna lumen, the luminal end of the wire is grabbed with a snare of the endoscope. The wire is firmly held by closing the loop of the snare, and then the scope with the wire is removed and brought to the outside of the patient's mouth. Then a feeding tube with a snare-like end is tied to the guidewire at the mouth end. The feeding tube is sufficiently lubricated with jelly to prevent mucosal trauma, and then the guidewire is pulled from the surgical incision site. As the guidewire is being pulled, there is some resistance when the bumper of the DPEJ tube passes the upper esophageal sphincter. When the proximal end of the tube comes in contact with the jejunal wall, resistance is again appreciated. A constant vertical pull is to be maintained to slowly pull the tube out until the markings of the tube appear. The guidewire is then cut, and an external bumper is then inserted over the tapered end of the tube until it is held firmly against the abdominal wall with about one finger gap between the external bumper and the skin surface or about 4 cm marking on the tube. It is generally advisable not to use the tube for 24 h following the procedure.

In case of PEG tube placement, air is insufflated into the stomach, and the stomach responds by distending with ease. In case of DPEJ tube placement, air is insufflated into jejunum which is a segment of long loops of small bowel, and air easily can escape in either direction making it challenging to distend the jejunum. Adequate distension is required to bring the wall of jejunum close to abdominal wall and decrease the risk of perforating the bowel wall through and through. With excess use of air, abdominal bloating can develop; to prevent this, CO_2 can be used which can get absorbed into the wall of the bowel as bicarbonate and hydrogen ion.

The use of adult gastroscope to place DPEJ has been shown to fail in at least one third of the cases, whereas single balloon enteroscopy has been found to be a successful alternative to perform this procedure [113, 114]. Among patients with altered anatomy (Billroth operation, gastrectomy, gastric and bowel anastomosis), it can sometimes be difficult to pass the enteroscope into the jejunum, and the use of double balloon enteroscopy has been shown to be helpful in reaching the jejunum [115, 116]. In children the pediatric gastroscope or enteroscope is used for DPEJ placement. Due to the narrow diameter of these scopes, they can be very flimsy and coil within the gastric lumen, making it technically challenging to advance them beyond the ligament of Treitz [117]. An alternate approach to such a situation is to advance the scope via the PEG tube and into the jejunum, then insufflate air in the jejunum, and transilluminate and insert T-fasteners to approximate bowel and abdominal walls. Then the push technique is used to place a DPEJ tube. There have been seven reported cases of such a technique of DPEJ placement in children [117–119].

Complications

The types of complications associated with DPEJ placement are similar to those seen in case of PEG tube placement. Infection of the ostomy site is reported to be the most common complication [120]. In a large reported series by Maple et al., of 307 patients who underwent DPEJ tube

placement performed at a single center, the overall complication rate was 22.5% with some having a combination of minor, moderate, or severe complications [108]. About 15.3% of the cases had minor complications which consisted mainly of ostomy site pain and infection, whereas 5.8% of the patients had moderate adverse events like leakage from ostomy site, persistent enterocutaneous fistula after removal of the tube, severe pain at ostomy site, significant ostomy site infection, large jejunal hematoma formation, jejuno-colonic fistula formation, aspiration pneumonia, jejunal ulcer, and buried bumper syndrome. About 4% of the patients developed bowel perforation, severe bleeding, jejunal volvulus or aspiration with an overall mortality rate of 0.3%. In another study reported by Lim et al., 83 patients underwent DPEJ tube placement; the study showed that 13% of cases developed perioperative (30 day) complications which comprised of infection, minor bleeding, leakage around the stoma, aspiration, and one case of gastric perforation with no reported deaths. In order to prevent perforation, it has been recommended to avoid performing deep enteroscopy soon after a DPEJ tube is placed or recently removed since the tract is still fresh and not completely healed. One of the rare complications of DPEJ tube placement is the risk of developing small bowel intussusception, with two cases reported till date [121, 122]. One case was managed conservatively, whereas the other required surgical correction.

Post-procedure Care

The post-procedure management and care of the DPEJ tube is similar to the management of PEG tube, as discussed earlier in this chapter. The nutritional feeds are to be carefully managed by trained personnel or family members. Frequent oversight by a dietician or a trained nurse is advisable. Use of DPEJ tube feeding when compared to PEG tube feeding is associated with micronutrient deficiency like copper deficiency [123]. This has been attributed to the type of feeds that are used. The tube can get blocked or displaced and sometimes even fall outside the ostomy site requiring tube exchange/replacement. The average time taken for tube exchange has been reported to be 8.2 ± 2.1 months in a 10-year follow-up study with 7% cases requiring tube exchange in less than 6 months due to blockage [112].

The DPEJ just like the PEG can be closed by removing the tube and allowing the tract to heal by itself. It may close as early as 24–48 h after the tube is removed. Trauma, burns, or caustic injury-related damage to upper GI tract may require temporary DPEJ that can be removed once the mucosa has healed [124]. In cases of chemosensitive advanced lymphomas of the stomach, the patient may be treated conservatively with chemotherapy while receiving enteral nutrition via DPEJ [125].

Conclusion

The methods of enteral access such as percutaneous endoscopic gastrostomy tube, percutaneous endoscopic gastrojejunostomy tube, and direct percutaneous endoscopic jejunostomy tube are gaining popularity. One should be familiar with not just the techniques for placement of these tubes but also the indications and contraindications prior to considering such an invasive procedure.

References

1. Alverdy J, Chi HS, Sheldon GF. The effect of parenteral nutrition on gastrointestinal immunity. The importance of enteral stimulation. Ann Surg. 1985;202(6):681–4.
2. Deitch EA, Ma WJ, Ma L, Berg RD, Specian RD. Protein malnutrition predisposes to inflammatory-induced gut-origin septic states. Ann Surg. 1990;211(5):560–7. discussion 7–8
3. Gauderer MW, Ponsky JL, Izant RJ Jr. Gastrostomy without laparotomy: a percutaneous endoscopic technique. J Pediatr Surg. 1980;15(6):872–5.
4. Himal HS, Schumacher S. Endoscopic vs surgical gastrostomy for enteral nutrition. Surg Endosc. 1987;1(1):33–5.
5. Ljungdahl M, Sundbom M. Complication rate lower after percutaneous endoscopic gastrostomy than after surgical gastrostomy: a prospective, randomized trial. Surg Endosc. 2006;20(8):1248–51.
6. Jones M, Santanello SA, Falcone RE. Percutaneous endoscopic vs surgical gastrostomy. JPEN J Parenter Enteral Nutr. 1990;14(5):533–4.
7. Hamidon BB, Abdullah SA, Zawawi MF, Sukumar N, Aminuddin A, Raymond AA. A prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with acute dysphagic stroke. Med J Malaysia. 2006;61(1):59–66.
8. Gomes CA Jr, Lustosa SA, Matos D, Andriolo RB, Waisberg DR, Waisberg J. Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for adults with swallowing disturbances. Cochrane Database Syst Rev. 2012;3:CD008096.
9. Norton B, Homer-Ward M, Donnelly MT, Long RG, Holmes GK. A randomised prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding after acute dysphagic stroke. BMJ. 1996;312(7022):13–6.
10. Dwolatzky T, Berezovski S, Friedmann R, Paz J, Clarfield AM, Stessman J, Hamburger R, Jaul E, Friedlander Y, Rosin A, Sonnenblick M. A prospective comparison of the use of nasogastric and percutaneous endoscopic gastrostomy tubes for long-term enteral feeding in older people. Clin Nutr. 2001;20(6):535–40.
11. Park RH, Allison MC, Lang J, Spence E, Morris AJ, Danesh BJ, Russell RI, Mills PR. Randomised comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with persisting neurological dysphagia. BMJ. 1992;304(6839):1406–9.
12. Segal R, Dan M, Pogoreliuk I, Leibovitz A. Pathogenic colonization of the stomach in enterally fed elderly patients: comparing percutaneous endoscopic gastrostomy with nasogastric tube. J Am Geriatr Soc. 2006;54(12):1905–8.
13. Jaafar MH, Mahadeva S, Morgan K, Tan MP. Percutaneous endoscopic gastrostomy versus nasogastric feeding in older individuals with non-stroke dysphagia: a systematic review. J Nutr Health Aging. 2015;19(2):190–7.
14. Wang J, Liu M, Liu C, Ye Y, Huang G. Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for patients with head and neck cancer: a systematic review. J Radiat Res. 2014;55(3):559–67.

15. Corry J, Poon W, McPhee N, Milner AD, Cruickshank D, Porceddu SV, Rischin D, Peters LJ. Randomized study of percutaneous endoscopic gastrostomy versus nasogastric tubes for enteral feeding in head and neck cancer patients treated with (chemo) radiation. J Med Imaging Radiat Oncol. 2008;52(5):503–10.
16. Corry J, Poon W, McPhee N, Milner AD, Cruickshank D, Porceddu SV, Rischin D, Peters LJ. Prospective study of percutaneous endoscopic gastrostomy tubes versus nasogastric tubes for enteral feeding in patients with head and neck cancer undergoing (chemo)radiation. Head Neck. 2009;31(7):867–76.
17. Nugent B, Parker MJ, McIntyre IA. Nasogastric tube feeding and percutaneous endoscopic gastrostomy tube feeding in patients with head and neck cancer. J Hum Nutr Diet. 2010;23(3):277–84.
18. Baeten C, Hoefnagels J. Feeding via nasogastric tube or percutaneous endoscopic gastrostomy. A comparison. Scand J Gastroenterol Suppl. 1992;194:95–8.
19. Dorst J, Dupuis L, Petri S, Kollewe K, Abdulla S, Wolf J, Weber M, Czell D, Burkhardt C, Hanisch F, Vielhaber S, Meyer T, Frisch G, Kettemann D, Grehl T, Schrank B, Ludolph AC. Percutaneous endoscopic gastrostomy in amyotrophic lateral sclerosis: a prospective observational study. J Neurol. 2015;262(4):849–58.
20. Mitchell SL, Tetroe JM. Survival after percutaneous endoscopic gastrostomy placement in older persons. J Gerontol A Biol Sci Med Sci. 2000;55(12):M735–9.
21. Silander E, Nyman J, Bove M, Johansson L, Larsson S, Hammerlid E. Impact of prophylactic percutaneous endoscopic gastrostomy on malnutrition and quality of life in patients with head and neck cancer: a randomized study. Head Neck. 2012;34(1):1–9.
22. Hafner G, Neuhuber A, Hirtenfelder S, Schmedler B, Eckel HE. Fiberoptic endoscopic evaluation of swallowing in intensive care unit patients. Eur Arch Otorhinolaryngol. 2008;265(4):441–6.
23. Kim CH, Nelson DK. Venting percutaneous gastrostomy in the treatment of refractory idiopathic gastroparesis. Gastrointest Endosc. 1998;47(1):67–70.
24. Laval G, Arvieux C, Stefani L, Villard ML, Mestrallet JP, Cardin N. Protocol for the treatment of malignant inoperable bowel obstruction: a prospective study of 80 cases at Grenoble University Hospital Center. J Pain Symptom Manag. 2006;31(6):502–12.
25. Forssell H, Noren E. A novel endoscopic weight loss therapy using gastric aspiration: results after 6 months. Endoscopy. 2015;47(1):68–71.
26. Sullivan S, Stein R, Jonnalagadda S, Mullady D, Edmundowicz S. Aspiration therapy leads to weight loss in obese subjects: a pilot study. Gastroenterology. 2013;145(6):1245–52.e1-5.
27. Rahnemai-Azar AA, Rahnemaiazar AA, Naghshizadian R, Kurtz A, Farkas DT. Percutaneous endoscopic gastrostomy: indications, technique, complications and management. World J Gastroenterol. 2014;20(24):7739–51.
28. Adler DG, Baron TH, Geels W, Morgan DE, Monkemuller KE. Placement of PEG tubes through previously placed self-expanding esophageal metal stents. Gastrointest Endosc. 2001;54(2):237–41.
29. Ellrichmann M, Sergeev P, Bethge J, Arlt A, Topalidis T, Ambrosch P, Wiltfang J, Fritscher-Ravens A. Prospective evaluation of malignant cell seeding after percutaneous endoscopic gastrostomy in patients with oropharyngeal/esophageal cancers. Endoscopy. 2013;45(7):526–31.
30. Milling TJ Jr, Refaai MA, Sarode R, Lewis B, Mangione A, Durn BL, Harman A, Lee ML, Goldstein JN. Safety of a 4-factor prothrombin complex concentrate versus plasma for vitamin K antagonist reversal: an integrated analysis of two phase IIIb clinical trials. Acad Emerg Med. 2016;23(4):466–75.
31. Bender JS. Percutaneous endoscopic gastrostomy placement in the morbidly obese. Gastrointest Endosc. 1992;38(1):97–8.
32. Bochicchio GV, Guzzo JL, Scalea TM. Percutaneous endoscopic gastrostomy in the supermorbidly obese patient. JSLS. 2006;10(4):409–13.
33. Karhadkar AS, Naini P, Dutta SK. PEG-tube placement in a patient with extreme obesity: overcoming the technical challenges. Gastrointest Endosc. 2007;65(4):731–3.
34. Kynci JA, Chodash HB, Tsang TK. PEG in a patient with ascites and varices. Gastrointest Endosc. 1995;42(1):100–1.
35. Horiuchi A, Nakayama Y, Tanaka N. Transgastric diversion of transnasal long tube placement using a percutaneous endoscopic gastrostomy site in a patient with bowel obstruction and massive ascites due to ovarian carcinoma. Case Rep Gastroenterol. 2008;2(3):326–9.
36. Baltz JG, Argo CK, Al-Osaimi AM, Northup PG. Mortality after percutaneous endoscopic gastrostomy in patients with cirrhosis: a case series. Gastrointest Endosc. 2010;72(5):1072–5.
37. Godil A, Chen YK. Percutaneous endoscopic gastrostomy for nutrition support in pregnancy associated with hyperemesis gravidarum and anorexia nervosa. JPEN J Parenter Enteral Nutr. 1998;22(4):238–41.
38. Serrano P, Velloso A, Garcia-Luna PP, Pereira JL, Fernadez Z, Ductor MJ, Castro D, Tejero J, Fraile J, Romero H. Enteral nutrition by percutaneous endoscopic gastrojejunostomy in severe hyperemesis gravidarum: a report of two cases. Clin Nutr. 1998;17(3):135–9.
39. Senadhi V, Chaudhary J, Dutta S. Percutaneous endoscopic gastrostomy placement during pregnancy in the critical care setting. Endoscopy. 2010;42(Suppl 2):E358–9.
40. de Souza e MGF, Lukashok HP, Meine GC, Small IA, de Carvalho RL, Guimaraes DP, Mansur GR. Outpatient percutaneous endoscopic gastrostomy in selected head and neck cancer patients. Surg Endosc. 2009;23(7):1487–93.
41. Dormann AJ, Wigginghaus B, Risius H, Kleimann F, Kloppenborg A, Rosemann J, Padel Y, Pohl R, Baum HH, Lubbesmeier A, Schwab J, Kuhlkamp V, Gutjahr W, Lindenburger W, Schutz H, Huchzermeyer H. Antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG)–results from a prospective randomized multicenter trial. Z Gastroenterol. 2000;38(3):229–34.
42. Dormann AJ, Wigginghaus B, Risius H, Kleimann F, Kloppenborg A, Grunewald T, Huchzermeyer H. A single dose of ceftriaxone administered 30 minutes before percutaneous endoscopic gastrostomy significantly reduces local and systemic infective complications. Am J Gastroenterol. 1999;94(11):3220–4.
43. Gossner L, Keymling J, Hahn EG, Ell C. Antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG): a prospective randomized clinical trial. Endoscopy. 1999;31(2):119–24.
44. Khashab MA, Chithadi KV, Acosta RD, Bruining DH, Chandrasekhara V, Eloubeidi MA, Fanelli RD, Faulx AL, Fonkalsrud L, Lightdale JR, Muthusamy VR, Pasha SF, Saltzman JR, Shaukat A, Wang A, Cash BD. Antibiotic prophylaxis for GI endoscopy. Gastrointest Endosc. 2015;81(1):81–9.
45. DeLegge MH. Percutaneous endoscopic gastrostomy. Am J Gastroenterol. 2007;102(12):2620–3.
46. Fukami N, Anderson MA, Khan K, Harrison ME, Appalaneni V, Ben-Menachem T, Decker GA, Fanelli RD, Fisher L, Ikenberry SO, Jain R, Jue TL, Krinsky ML, Maple JT, Sharaf RN, Dominitz JA. The role of endoscopy in gastroduodenal obstruction and gastroparesis. Gastrointest Endosc. 2011;74(1):13–21.
47. Campoli P, Cardoso D, Turchi M, Mota O. Clinical trial: a randomized study comparing the durability of silicone and latex percutaneous endoscopic gastrostomy tubes. Dig Endosc. 2011;23(2):135–9.
48. DeLegge RL, DeLegge MH. Percutaneous endoscopic gastrostomy evaluation of device materials: are we "failsafe"? Nutr Clin Pract. 2005;20(6):613–7.
49. Blacka J, Donoghue J, Sutherland M, Martincich I, Mitten-Lewis S, Morris P, Meredith G. Dwell time and functional failure in percutaneous endoscopic gastrostomy tubes: a prospective randomized-controlled comparison between silicon polymer

and polyurethane percutaneous endoscopic gastrostomy tubes. Aliment Pharmacol Ther. 2004;20(8):875–82.
50. Nishiwaki S, Araki H, Hayashi M, Takada J, Iwashita M, Tagami A, Hatakeyama H, Hayashi T, Maeda T, Saito K. Inhibitory effects of carbon dioxide insufflation on pneumoperitoneum and bowel distension after percutaneous endoscopic gastrostomy. World J Gastroenterol. 2012;18(27):3565–70.
51. Suzuki Y, Urashima M, Ishibashi Y, Abo M, Mashiko H, Eda Y, Kusakabe T, Kawasaki N, Yanaga K. Covering the percutaneous endoscopic gastrostomy (PEG) tube prevents peristomal infection. World J Surg. 2006;30(8):1450–8.
52. Russell TR, Brotman M, Norris F. Percutaneous gastrostomy. A new simplified and cost-effective technique. Am J Surg. 1984;148(1):132–7.
53. Boswell WC, Boyd CR, Lord SA. Percutaneous endoscopic gastrostomy with T-bar fixation in children. Surg Laparosc Endosc. 1996;6(4):262–5.
54. Tucker AT, Gourin CG, Ghegan MD, Porubsky ES, Martindale RG, Terris DJ. 'Push' versus 'pull' percutaneous endoscopic gastrostomy tube placement in patients with advanced head and neck cancer. Laryngoscope. 2003;113(11):1898–902.
55. McClave SA, Chang WK. Complications of enteral access. Gastrointest Endosc. 2003;58(5):739–51.
56. Arora G, Rockey D, Gupta S. High in-hospital mortality after percutaneous endoscopic gastrostomy: results of a nationwide population-based study. Clin Gastroenterol Hepatol. 2013;11(11):1437–44. e3
57. Grant MD, Rudberg MA, Brody JA. Gastrostomy placement and mortality among hospitalized Medicare beneficiaries. JAMA. 1998;279(24):1973–6.
58. Blomberg J, Lagergren J, Martin L, Mattsson F, Lagergren P. Complications after percutaneous endoscopic gastrostomy in a prospective study. Scand J Gastroenterol. 2012;47(6):737–42.
59. Ramczykowski T, Gruning S, Gurr A, Muhr G, Horch C, Meindl R, Swol J. Aspiration pneumonia after spinal cord injury. Placement of PEG tubes as effective prevention. Unfallchirurg. 2012;115(5):427–32.
60. James A, Kapur K, Hawthorne AB. Long-term outcome of percutaneous endoscopic gastrostomy feeding in patients with dysphagic stroke. Age Ageing. 1998;27(6):671–6.
61. Horiuchi A, Nakayama Y, Sakai R, Suzuki M, Kajiyama M, Tanaka N. Elemental diets may reduce the risk of aspiration pneumonia in bedridden gastrostomy-fed patients. Am J Gastroenterol. 2013;108(5):804–10.
62. Shang E, Geiger N, Sturm JW, Post S. Pump-assisted enteral nutrition can prevent aspiration in bedridden percutaneous endoscopic gastrostomy patients. JPEN J Parenter Enteral Nutr. 2004;28(3):180–3.
63. Ubogu EE, Zaidat OO. Rectus sheath hematoma complicating percutaneous endoscopic gastrostomy. Surg Laparosc Endosc Percutan Tech. 2002;12(6):430–2.
64. Singh D, Laya AS, Vaidya OU, Ahmed SA, Bonham AJ, Clarkston WK. Risk of bleeding after percutaneous endoscopic gastrostomy (PEG). Dig Dis Sci. 2012;57(4):973–80.
65. Ermis F, Ozel M, Oncu K, Yazgan Y, Demirturk L, Gurbuz AK, Akyol T, Nazik H. Indications, complications and long-term follow-up of patients undergoing percutaneous endoscopic gastrostomy: a retrospective study. Wien Klin Wochenschr. 2012;124(5–6):148–53.
66. Acosta RD, Abraham NS, Chandrasekhara V, Chathadi KV, Early DS, Eloubeidi MA, Evans JA, Faulx AL, Fisher DA, Fonkalsrud L, Hwang JH, Khashab MA, Lightdale JR, Muthusamy VR, Pasha SF, Saltzman JR, Shaukat A, Shergill AK, Wang A, Cash BD, DeWitt JM. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc. 2016;83(1):3–16.
67. Richter JA, Patrie JT, Richter RP, Henry ZH, Pop GH, Regan KA, Peura DA, Sawyer RG, Northup PG, Wang AY. Bleeding after percutaneous endoscopic gastrostomy is linked to serotonin reuptake inhibitors, not aspirin or clopidogrel. Gastrointest Endosc. 2011;74(1):22–34.e1.
68. Lee C, Im JP, Kim JW, Kim SE, Ryu DY, Cha JM, Kim EY, Kim ER, Chang DK. Risk factors for complications and mortality of percutaneous endoscopic gastrostomy: a multicenter, retrospective study. Surg Endosc. 2013;27(10):3806–15.
69. Fatade F, Axelrod D, Lien K, Kaplan D, Nagula S. Percutaneous endoscopic gastrostomy tube placement complicated by a gastric pseudoaneurysm and recurrent hemorrhage. Endoscopy. 2012;44(Suppl 2 UCTN):E38–9.
70. Ahmad J, Thomson S, McFall B, Scoffield J, Taylor M. Colonic injury following percutaneous endoscopic-guided gastrostomy insertion. BMJ Case Rep. 2010;2010 pii: bcr0520102976.
71. Wiggins TF, Kaplan R, DeLegge MH. Acute hemorrhage following transhepatic PEG tube placement. Dig Dis Sci. 2007;52(1):167–9.
72. Siegel TR, Douglass M. Perforation of an ileostomy by a retained percutaneous endoscopic gastrostomy (PEG) tube bumper. Surg Endosc. 2004;18(2):348.
73. Friedmann R, Feldman H, Sonnenblick M. Misplacement of percutaneously inserted gastrostomy tube into the colon: report of 6 cases and review of the literature. JPEN J Parenter Enteral Nutr. 2007;31(6):469–76.
74. Rafiq A, Abbas N, Tariq H, Nayudu SK. Gastro-hepatic fistula with liver abscess: a rare complication of a common procedure. Am J Case Rep. 2015;16:652–7.
75. Lau G, Lai SH. Fatal retroperitoneal haemorrhage: an unusual complication of percutaneous endoscopic gastrostomy. Forensic Sci Int. 2001;116(1):69–75.
76. Moriwaki Y, Arata S, Tahara Y, Toyoda H, Kosuge T, Suzuki N. Duodenal perforation due to compression necrosis by the tip of percutaneous endoscopic gastrostomy tube. Nutrition. 2011;27(9):979–81.
77. Cyrany J, Rejchrt S, Kopacova M, Bures J. Buried bumper syndrome: a complication of percutaneous endoscopic gastrostomy. World J Gastroenterol. 2016;22(2):618–27.
78. Itkin M, MH DL, Fang JC, SA MC, Kundu S, d'Othee BJ, Martinez-Salazar GM, Sacks D, Swan TL, Towbin RB, Walker TG, Wojak JC, Zuckerman DA, Cardella JF. Multidisciplinary practical guidelines for gastrointestinal access for enteral nutrition and decompression from the society of interventional radiology and American Gastroenterological Association (AGA) Institute, with endorsement by Canadian Interventional Radiological Association (CIRA) and Cardiovascular and Interventional Radiological Society of Europe (CIRSE). Gastroenterology. 2011;141(2):742–65.
79. Radhakrishnan N, Sharma RK, Ellul P, George R. The "Quill" technique–another method for managing buried bumper syndrome. Gastrointest Endosc. 2006;64(4):668.
80. Furlano RI, Sidler M, Haack H. The push-pull T technique: an easy and safe procedure in children with the buried bumper syndrome. Nutr Clin Pract. 2008;23(6):655–7.
81. Anagnostopoulos GK, Kostopoulos P, Arvanitidis DM. Buried bumper syndrome with a fatal outcome, presenting early as gastrointestinal bleeding after percutaneous endoscopic gastrostomy placement. J Postgrad Med. 2003;49(4):325–7.
82. Shigoka H, Maetani I, Tominaga K, Gon K, Saitou M, Takenaka Y. Comparison of modified introducer method with pull method for percutaneous endoscopic gastrostomy: prospective randomized study. Dig Endosc. 2012;24(6):426–31.
83. Martins FP, Sousa MC, Ferrari AP. New "introducer" PEG-gastropexy with T fasteners: a pilot study. Arq Gastroenterol. 2011;48(4):231–5.

84. Lipp A, Lusardi G. Systemic antimicrobial prophylaxis for percutaneous endoscopic gastrostomy. Cochrane Database Syst Rev. 2013;11:CD005571.
85. Lipp A, Lusardi G. Systemic antimicrobial prophylaxis for percutaneous endoscopic gastrostomy. Cochrane Database Syst Rev. 2006;4:CD005571.
86. Blumenstein I, Borger D, Loitsch S, Bott C, Tessmer A, Hartmann F, Stein J. A glycerin hydrogel-based wound dressing prevents peristomal infections after percutaneous endoscopic gastrostomy (PEG): a prospective, randomized study. Nutr Clin Pract. 2012;27(3):422–5.
87. Gottfried EB, Plumser AB, Clair MR. Pneumoperitoneum following percutaneous endoscopic gastrostomy. A prospective study. Gastrointest Endosc. 1986;32(6):397–9.
88. Park WY, Lee TH, Lee JS, Hong SJ, Jeon SR, Kim HG, Cho JY, Kim JO, Cho JH, Lee SW, Cho YK. Reappraisal of pneumoperitoneum after percutaneous endoscopic gastrostomy. Intest Res. 2015;13(4):313–7.
89. Nazarian A, Cross W, Kowdley GC. Pneumoperitoneum after percutaneous endoscopic gastrostomy among adults in the intensive care unit: incidence, predictive factors, and clinical significance. Am Surg. 2012;78(5):591–4.
90. Rosenberger LH, Newhook T, Schirmer B, Sawyer RG. Late accidental dislodgement of a percutaneous endoscopic gastrostomy tube: an underestimated burden on patients and the health care system. Surg Endosc. 2011;25(10):3307–11.
91. Tsang TK, Eaton D, Falconio MA. Percutaneous ostomy dilation: a technique for dilating the closed percutaneous endoscopic gastrostomy sites and reinserting gastrostomies. Gastrointest Endosc. 1989;35(4):336–7.
92. Schrag SP, Sharma R, Jaik NP, Seamon MJ, Lukaszczyk JJ, Martin ND, Hoey BA, Stawicki SP. Complications related to percutaneous endoscopic gastrostomy (PEG) tubes. A comprehensive clinical review. J Gastrointestin Liver Dis. 2007;16(4):407–18.
93. Singh A, Gelrud A. Adverse events associated with percutaneous enteral access. Gastrointest Endosc Clin N Am. 2015;25(1):71–82.
94. Scott F, Beech R, Smedley F, Timmis L, Stokes E, Jones P, Roffe C, Bowling TE. Prospective, randomized, controlled, single-blind trial of the costs and consequences of systematic nutrition team follow-up over 12 mo after percutaneous endoscopic gastrostomy. Nutrition. 2005;21(11–12):1071–7.
95. Heiser M, Malaty H. Balloon-type versus non-balloon-type replacement percutaneous endoscopic gastrostomy: which is better? Gastroenterol Nurs. 2001;24(2):58–63.
96. Nishiwaki S, Araki H, Fang JC, Hayashi M, Takada J, Iwashita M, Tagami A, Hatakeyama H, Hayashi T, Maeda T, Saito K. Retrospective analyses of complications associated with transcutaneous replacement of percutaneous gastrostomy and jejunostomy feeding devices. Gastrointest Endosc. 2011;74(4):784–91.
97. Westaby D, Young A, O'Toole P, Smith G, Sanders DS. The provision of a percutaneously placed enteral tube feeding service. Gut. 2010;59(12):1592–605.
98. Mathus-Vliegen EM, Koning H, Taminiau JA, Moorman-Voestermans CG. Percutaneous endoscopic gastrostomy and gastrojejunostomy in psychomotor retarded subjects: a follow-up covering 106 patient years. J Pediatr Gastroenterol Nutr. 2001;33(4):488–94.
99. Fonseca J, Santos CA. Percutaneous endoscopic gastrostomy with jejunal extension plus percutaneous endoscopic gastrostomy (PEG-j plus PEG) in patients with gastric/duodenal cancer outlet obstruction. Arq Gastroenterol. 2015;52(1):72–5.
100. Li Y, Wang Z, Ni X, Jiang Z, Ding K, Li N, Li J. Double percutaneous endoscopic gastrojejunostomy tubes for decompression and refeeding together with enteral nutrients: three case reports and a review of the literature. Surg Laparosc Endosc Percutan Tech. 2009;19(5):e167–70.
101. Lawinski M, Gradowski L, Bzikowska A, Goszczynska A, Jachnis A, Forysinski K. Gastrojejunostomy inserted through PEG (PEG-J) in prevention of aspiration pneumonia. Clinical nutrition complication in dysphagic patients. Pol Przegl Chir. 2014;86(5):223–9.
102. Poteet SJ, Holzman MD, Melvin WV, Sharp KW, Poulose BK. Inpatient mortality and length of stay comparison of percutaneous endoscopic gastrostomy and percutaneous endoscopic gastrojejunostomy. J Laparoendosc Adv Surg Tech A. 2010;20(7):587–90.
103. Adams GF, Guest DP, Ciraulo DL, Lewis PL, Hill RC, Barker DE. Maximizing tolerance of enteral nutrition in severely injured trauma patients: a comparison of enteral feedings by means of percutaneous endoscopic gastrostomy versus percutaneous endoscopic gastrojejunostomy. J Trauma. 2000;48(3):459–64. discussion 64–5
104. Irving PM, Howell RJ, Shidrawi RG. Percutaneous endoscopic gastrostomy with a jejunal port for severe hyperemesis gravidarum. Eur J Gastroenterol Hepatol. 2004;16(9):937–9.
105. Ao P, Sebastianski M, Selvarajah V, Gramlich L. Comparison of complication rates, types, and average tube patency between jejunostomy tubes and percutaneous gastrostomy tubes in a regional home enteral nutrition support program. Nutr Clin Pract. 2015;30(3):393–7.
106. Kim KJ, Victor D, Stein E, Valeshabad AK, Saxena P, Singh VK, Lennon AM, Clarke JO, Khashab MA. A novel ballooned-tip percutaneous endoscopic gastrojejunostomy tube: a pilot study. Gastrointest Endosc. 2013;78(1):154–7.
107. Kalkan IH, Disibeyaz S, Onder FO, Oztas E, Odemis B, Ozogul Y, Parlak E. A rare complication of percutaneous endoscopic gastrojejunostomy (PEG-J): duodenal bulb perforation due to retrograde migration. Acta Gastroenterol Belg. 2012;75(2):276–7.
108. Maple JT, Petersen BT, Baron TH, Gostout CJ, Wong Kee Song LM, Buttar NS. Direct percutaneous endoscopic jejunostomy: outcomes in 307 consecutive attempts. Am J Gastroenterol. 2005;100(12):2681–8.
109. Kav T. Direct percutaneous endoscopic jejunostomy in patients with altered anatomy. Arch Iran Med. 2012;15(3):176.
110. Del Piano M, Ballare M, Carmagnola S, Orsello M, Garello E, Pagliarulo M, Sartori M, Montino F. DPEJ placement in cases of PEG insertion failure. Dig Liver Dis. 2008;40(2):140–3.
111. Mackenzie SH, Haslem D, Hilden K, Thomas KL, Fang JC. Success rate of direct percutaneous endoscopic jejunostomy in patients who are obese. Gastrointest Endosc. 2008;67(2):265–9.
112. Lim AH, Schoeman MN, Nguyen NQ. Long-term outcomes of direct percutaneous endoscopic jejunostomy: a 10-year cohort. Endosc Int Open. 2015;3(6):E610–4.
113. Aktas H, Mensink PB, Kuipers EJ, van Buuren H. Single-balloon enteroscopy-assisted direct percutaneous endoscopic jejunostomy. Endoscopy. 2012;44(2):210–2.
114. Song LM, Baron TH, Saleem A, Bruining DH, Alexander JA, Rajan E. Double-balloon enteroscopy as a rescue technique for failed direct percutaneous endoscopic jejunostomy when using conventional push enteroscopy (with video). Gastrointest Endosc. 2012;76(3):675–9.
115. Monkemuller K, Vormbrock K, Kassalik M, Sancar A. Direct percutaneous endoscopic jejunostomy tube placement using double-balloon enteroscopy. Gastrointest Endosc. 2012;75(2):463–5.
116. Despott EJ, Gabe S, Tripoli E, Konieczko K, Fraser C. Enteral access by double-balloon enteroscopy: an alternative method of direct percutaneous endoscopic jejunostomy placement. Dig Dis Sci. 2011;56(2):494–8.
117. Alberca-de-Las-Parras F, Navalon-Rubio M, Egea-Valenzuela J, Alvarez-Higueras FJ, Anton-Rodenas G, Alajarin-Cervera M, Serrano-Gimenez A, Gil-Ortega D, Munoz-Tornero M, Ono-Ono A, Carballo-Alvarez LF. Direct percutaneous endoscopic jejunostomy

in pediatric age with a pexies triangulation system: report of a case and literature review. Rev Esp Enferm Dig. 2015;107(4):240–2.
118. Auvin S, Michaud L, Guimber D, Sfeir R, Gottrand F, Turck D. Percutaneous endoscopic jejunostomy for decompression in an infant with short-bowel syndrome. Endoscopy. 2002;34(3):240.
119. Virnig DJ, Frech EJ, Delegge MH, Fang JC. Direct percutaneous endoscopic jejunostomy: a case series in pediatric patients. Gastrointest Endosc. 2008;67(6):984–7.
120. Zhu Y, Shi L, Tang H, Tao G. Current considerations of direct percutaneous endoscopic jejunostomy. Can J Gastroenterol. 2012;26(2):92–6.
121. Ishii M, Teramoto S, Yakabe M, Yamamato H, Yamaguchi Y, Hanaoka Y, Ouchi Y. Small intestinal intussusceptions caused by percutaneous endoscopic jejunostomy tube placement. J Am Geriatr Soc. 2007;55(12):2093–4.
122. Satoh T, Sawada K, Satoh M, Yohko K, Yamada M, Zaitsu M, Osada T, Sawaya R, Nata T, Ueno N, Moriichi K, Ikuta K, Mizukami Y, Watari J, Fujiya M, Kohgo Y. Small intestinal intussusceptions due to the placement of a percutaneous endoscopic jejunostomy tube. BMJ Case Rep. 2011;2011 pii: bcr0720103169.
123. Nishiwaki S, Iwashita M, Goto N, Hayashi M, Takada J, Asano T, Tagami A, Hatakeyama H, Hayashi T, Maeda T, Saito K. Predominant copper deficiency during prolonged enteral nutrition through a jejunostomy tube compared to that through a gastrostomy tube. Clin Nutr. 2011;30(5):585–9.
124. Rondanelli M, Peroni G, Miccono A, Guerriero F, Guido D, Perna S. Nutritional management in an elderly man with esophageal and gastric necrosis after caustic soda ingestion: a case report. Ther Clin Risk Manag. 2016;12:129–33.
125. Khadraoui H, Feigin KN, Fox JJ, Ong L, Shike M, Yahalom J, Noy A. Successful management of gastric perforation in stage IV diffuse large B-cell lymphoma with chemoradiation therapy, percutaneous endoscopy gastrostomy for gastric drainage, and percutaneous endoscopy jejunostomy for nutrition. Clin Lymphoma Myeloma Leuk. 2013;13(3):327–30.

Capsule Endoscopy

18

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Introduction

A noninvasive endoscopic tool which is comprised of a swallowed capsule that is a self-contained camera and antenna, video capsule endoscopy (VCE), sometimes referred to as wireless capsule endoscopy, is a significant advancement in gastrointestinal (GI) imaging. Developed by the complementary pioneering innovations originating as early as the 1980s by Iddan, Avni, Fossum, Glukhovsky, Meron, Scapa, Swain, and others, VCE has become an established method of evaluating the GI tract without intubation and need for sedation [1]. Developed formally under Given Imaging and initially approved by the Food and Drug Administration (FDA) in 2001, VCE was a novel way of evaluating the small bowel in patients presenting with obscure gastrointestinal bleeding (OGIB), now referred to as small bowel bleeding, after conventional upper and lower GI endoscopy has not made the diagnosis [2]. Over a decade later, it continues to be very useful for this indication. Since the inception of VCE with small bowel capsule endoscopy (SBCE), there has been an expansion of its applications beyond GI bleeding evaluation, including inflammatory bowel disease (IBD), celiac disease, and others, with extension of VCE modalities to include esophageal capsule endoscopy (ECE) and colon capsule endoscopy (CCE), further expanding its indications. The limitation of all the VCE modalities is the general lack of control over capsule movement and inability to insufflate with the possibility that lesions may still hide behind folds, and debris and bubbles may obscure mucosal visualization. VCE remains a diagnostic technique, and clinically suspicious findings still require formal endoscopic and/or surgical techniques to obtain tissue for biopsy and perform intervention. Recent clinical practice guidelines support the use of VCE as a complementary test in patients with GI bleeding, Crohn's disease, and celiac disease or who have had negative or inconclusive endoscopic or imaging studies [3].

The technology of VCE has evolved over time, and the basic video capsule (VC) characteristics are essential to understanding the differences between how the different VCs perform in different fields of application [4].

Practical Considerations: Limitations of VCE

- Lack of control over capsule movement.
- Inability to insufflate may allow lesions to remain hidden.
- Debris and bubbles may obscure visualization.
- Diagnostic technique only, endoscopy, and/or surgery still required for biopsy and intervention.

Numerous VCs are now commercially available, many with subsequent generations with technology advances with each iteration (see Fig. 18.1). Variations include the number of cameras, rates of imaging, methods of data storage/transmission, battery power, and intended use (esophageal, small bowel, or colon). Each VC has at least one camera as an imager with either a charge-coupled device (CCD), which converts light and charge in every single pixel to voltage and has a higher electric output, with the advantage of stability with change in illumination, and lower optical noise, or a complementary metal oxide semiconductor (CMOS) chip, which uses an array of pixels requiring amplification, with the advantage of lower space usage and power consumption,

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Fig. 18.1 Comparison of different video capsules. *Front view* (**a**) and *top view* (**b**) of the capsules, with corresponding X-ray image (**c**). *Left to right*: Agile patency capsule, PillCam SB2, EndoCapsule, CapsoCam, MiroCam, OMOM capsule, PillCam ES02, PillCam Colon 2. Adapted from Kurniawan and Keuchel. [4,5] With permission of Springer Nature.

Table 18.1 Technical specifications of VCs

	PillCam SB2	SB3	MiroCam	EndoCapsule EC1	EC-S10	CapsoCam SV1	OMOM Capsule	PillCam ESO 2	PillCam COLON2
Length (mm)	26	26	24	26	26	31	28	26	31.5
Diameter (mm)	11	11	11	11	11	11	13	11	11
Weight (g)	2.9	1.9	3.4	3.8	3.3	4	<6	2.9	2.9
Cameras (n)	1	1	1	1	1	4	1	2	2
Frame rate (frames/s)	2	2/6	3	2	2	12/20	0.5/1/2	18	0.1/4/35
Image sensor	CMOS	CMOS	CMOS	CCD	CMOS	CMOS	CMOS	CMOS	CMOS
Viewing angle	156°	156°	150°	145°	160°	4x90°	140°	2 × 169°	2 × 172°
Minimal recording time (h)	11	11	11	8	12	15	8 ± 1	0.33	10

Adapted from Kurniawan and Keuchel [4]
CCD charge-coupled device, *CMOS* complementary metal oxide semiconductor

allowing for longer capacity and allowing for additional cameras (see Table 18.1).

Light-emitting diodes (LEDs) serve as a light source for the camera, which flash every time an image is captured. The energy source consists of silver oxide button batteries. Depending on the

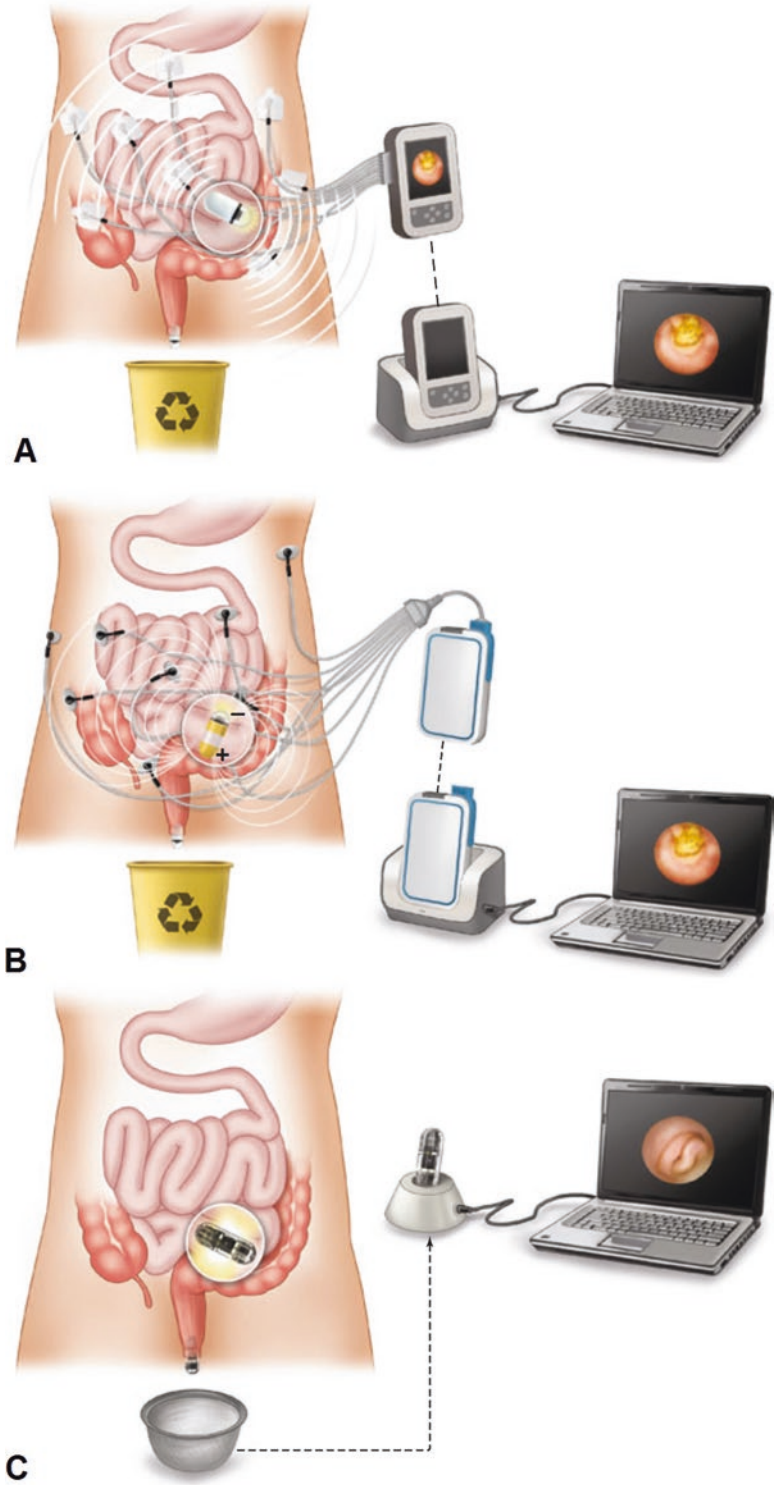

Fig. 18.2 Schematic diagrams for VCE data transmission. (**a**) Radio-frequency transmission. (**b**) Human body communication. (**c**) Integrated data storage. Adapted from Kurniawan and Keuchel [4]. With permission of Springer Nature

VC, the images are processed by radio-frequency (RF) transmission, human body communication, or integrated data storage. Only the integrated data storage method requires collection of the VC at the completion of the study (see Fig. 18.2).

Practical Considerations: Data Transmission

- VCE integrated data storage systems require collection of the video capsule from patient's stool.

Contraindications, Complications, and Challenges

Contraindications to VCE

Absolute

- Known/suspected obstruction (unless surgery is warranted and/or patency in confirmed)
- Pseudo-obstruction
- Pregnancy

Relative

- Cardiac pacemaker and/or defibrillator (implanted electrical devices)
- Gastroparesis
- Swallowing difficulty/dysphagia
- Age less than 10 years

Because the contraindications, complications, and challenges are common to all fields of application of VCE, we will review these issues before the specific modalities. With increasing experience with the application of VCE, many contraindications have been put into perspective and should be cautiously considered [5]. Absolute contraindications to VCE include known/suspected obstruction (unless surgery is warranted and/or patency in confirmed), pseudo-obstruction, and pregnancy [6]. Relative contraindications include swallowing difficulty/dysphagia, gastroparesis, cardiac pacemaker and/or defibrillator (implanted electrical devices), and age less than 10 years [7]. The age limit has been studied and is center dependent based on local expertise and training. Fritscher-Ravens et al. report safely performing VCE in 20 children, one as young as 1.5 years [8]. In special restricted circumstances, VCE in pregnancy has been performed when the diagnosis cannot be postponed after delivery, and single cases of patients incidentally undergoing MRI with an incorporated capsule have been reported, with artifacts but no signs of clinical harm [5].

The RF transmission of the VC has the potential to interfere with cardiac pacemaker function, and cardiac pacemakers also have the potential to inactivate VCs. Our general experience and reported literature suggests that use of VCE in pacemaker patients is likely safe and remains a relative contraindication and can be considered cautiously in those patients for whom it is deemed medically necessary [9, 10]. This is supported by recent clinical practice guidelines [3].

Up to 30% of patients will have incomplete VCE examinations of the small bowel, in which the VC does not reach the cecum during the recording, thus limiting the value of the study [11, 12], which may be due to primary small bowel motility issues, patient immobility, previous small bowel surgery, hospitalization, poor bowel cleansing, opiate use, advanced age, and hypothyroidism [11–13]. As a result, unless it is being done for urgent GI bleeding evaluation, VCE should ideally be avoided in hospitalized patients, or these patients should have their studies done with a prokinetic agent or direct placement (see below). This may also help if patient has a known or suspected delay in gastric transit time (GTT) [14]. The examinations are best performed when the patient is ambulatory in the outpatient setting to increase the likelihood of a complete small bowel examination [12]. Options when faced with an incomplete VCE study include repeating the study with a prokinetic agent (if not already done), endoscopically placing the VCE

Practical Considerations: Contraindications

- Don't forget potential solutions to contraindications.
- Suspected obstruction/risk for capsule retention: Patency capsule.
- Swallowing disorders: Direct placement of capsule.
- Gastroparesis: Direct placement or prokinetic agent.
- Younger age: Center-dependent experience in age ~2 years and older.
- Cardiac pacemaker/defibrillator: Discuss general safety with patient.
- Pregnancy: Avoid as contraindication because no safety data exists, but may consider in very strict circumstances.

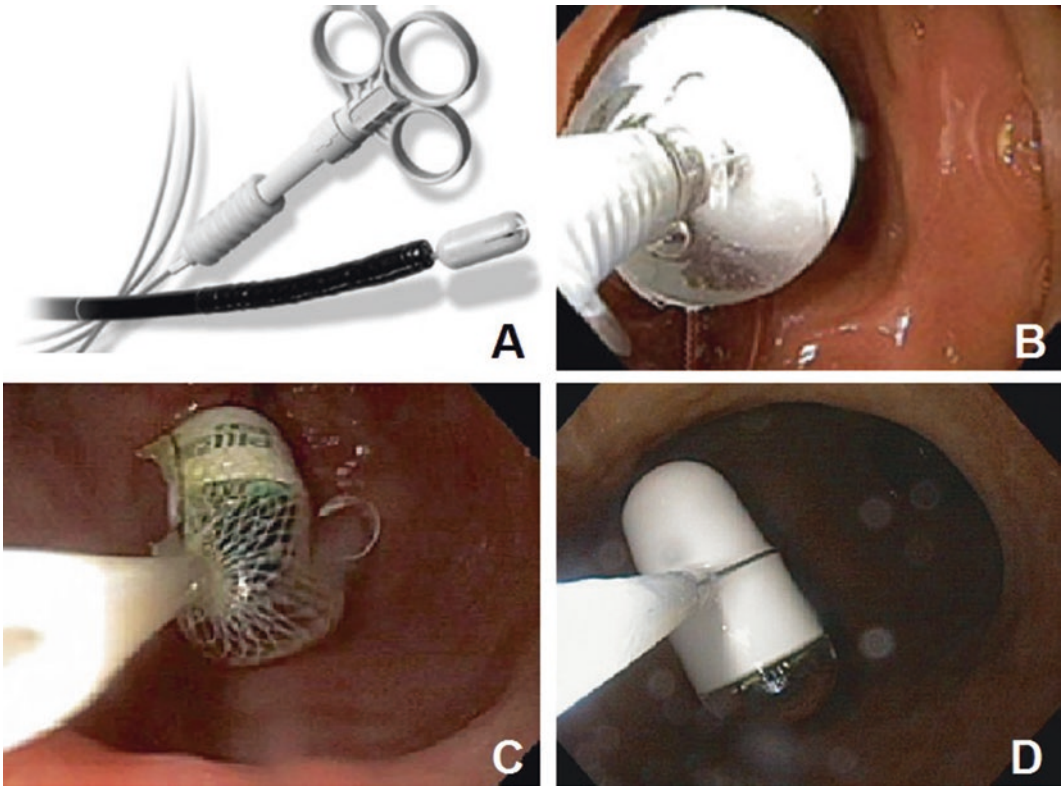

Fig. 18.3 Direct video capsule placement. (**a**) AdvanCE system (US endoscopy). (**b**) AdvanCE VC deployment. (**c**) Roth Net VC deployment. (**d**) Snare VC deployment (Adapted from Bandorski et al. [18] With permission of Springer Nature.)

capsule into the small bowel, or using an alternative technique for SB examination such as CT enterography. Although there are no consensus guidelines for the use of prokinetics to prevent or resolve delayed GTT in SBCE, there is evidence that prokinetics for capsule ingestion can improve completion rates [15].

Practical Considerations: Direct VCE Placement

- If AdvanCE delivery system is not available, a Roth Net may be more secure than a snare; however, you may encounter difficulty releasing the capsule into the small bowel.

In patients who have a history of dysphagia or swallowing disorder, who are likely unable to swallow the VC safely, and in patients with known or suspected delay in GTT, VCE can be pursued by deploying the VC under direct vision [16, 17] (see Fig. 18.3). This can be done using a retrieval net, retrieval basket, or retrieval snare. A Roth Net may be more secure; however, it may be somewhat difficult opening the net and releasing the capsule in the small bowel. Additionally, the AdvanCE capsule delivery system (US endoscopy) was released in 2005 for the endoscopic delivery of the VC into the small bowels of patients with known risk factors which could inhibit normal VC passage. Holden et al. reported a series of 16 consecutive patients with dysphagia, gastroparesis, and abnormal upper GI anatomy who underwent successful VC delivery with the use of the AdvanCE system [19].

Risk Factors for Video Capsule Retention

- Crohn's disease
- Chronic NSAID use
- Prior abdominopelvic irradiation
- Prior small bowel resection

Regardless of the field of application and type of VC used, the primary complication of VCE is capsule retention potentially requiring surgical intervention. Capsule retention risk factors include Crohn's disease, chronic nonsteroidal anti-inflammatory drug (NSAID) use, prior abdominal surgery (small bowel resection), and prior radiation to the abdominopelvic region.

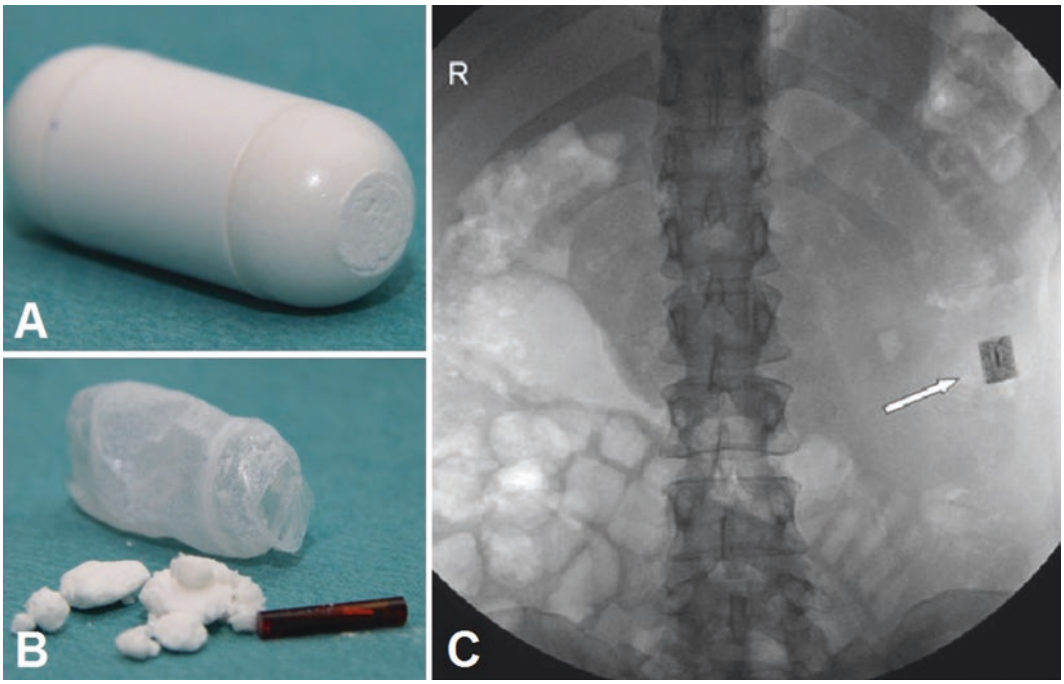

Fig. 18.4 PillCam patency capsule (Medtronic). (**a**) Intact. (**b**) Dissolved. (**c**) Retained on radiograph (Adapted from Costamagna et al. [28] With permission of Springer Nature.)

Complications can also occur related to swallowing the capsule and can potentially result in aspiration of the VC into the airway. Generally, this would be diagnosed clinically with coughing and expectoration and, however, if not expectorated spontaneously, may require bronchoscopic removal. In rare instances, asymptomatic tracheal aspiration has been diagnosed with real-time viewing [20]. Chiefetz et al. found a 1.6% capsule retention rate in patients with suspected Crohn's disease and a 13% capsule retention rate in those with known Crohn's disease [21]. The retention rate has been found to be similar in patients being investigated for suspected Crohn's disease and obscure GI bleeding [22–24]. Most patients will remain asymptomatic after capsule retention with the diagnosis only made when the physician fails to see the capsule enter the cecum on VCE images. However, cases of obstruction up to 6 years after ingestion [25] as well as perforation and capsule fragmentation have been reported [26].

Practical Considerations: Patients at Risk for VC Retention

- Pursue patency capsule to help guide decision to pursue VCE.
- A retained VC may be considered diagnostic but may prompt intervention.

Diagnosis of capsule retention then must be confirmed radiographically as most patients will fail to see the capsule in their stool even with its normal passage. Retained capsules have been removed surgically or with double-balloon enteroscopy.

In patients with an elevated risk for VC retention, the PillCam patency capsule (Medtronic) was developed (previously known as the Agile patency capsule) and FDA approved for patients with known or suspected small bowel obstructing lesions to assess the ability of the VCE capsule to traverse the small bowel prior to performing an actual VCE [27] (see Fig. 18.4). Its use is recommended in patients with known or suspected strictures of the small bowel before VCE to minimize the risk of capsule retention [3]. The patency capsule is composed of lactose with barium, two-sided timer plugs with exposed windows, and a RF identification (RFID) tag with an accompanying scanner. It remains intact for a minimum of 30 h and then disintegrates. If the patient observes excretion of the intact patency capsule or the scanner does not detect the RFID tag after at or before 30 h, then it is safe to proceed with VCE. If the patient has a cardiac pacemaker, then a plain X-ray or fluoroscopy can also be used to detect the barium capsule or the RFID tag. A multicentered trial using the Agile patency capsule in patients with known small bowel strictures prior to VCE found no cases of VCE capsule retention after appropriate passage of the patency capsule prior to the VCE studies [23].

Equipment and Accessories

Equipment for Video Capsule Endoscopy Procedure

- Video capsule
- Fully charged data recorder with real-time viewer
- Sensor belt or sensor array with adhesive sleeves and sensor location guide
- Recorder pouch with shoulder or waist strap
- Installed software system
- Glass of water
- Simethicone

Although there will be specific procedural differences for all fields of application of VCE, the equipment and accessory requirements will be generally common to all the modalities. The requirements of VCE include the VC itself, which will vary depending on the intended indication for the study. The VC will be sealed in a small box and marked with a unique identification number as well as an expiration date. It is activated upon opening the box and has a minimum battery life. For most systems, to receive and store data, a battery-operated data recorder is worn by the patient throughout the study, and the recorder is worn in a pouch held in place by a waist/shoulder strap, either a wearable sensor belt or a sensor array composed of leads secured by adhesive sleeves. While the sensor array may be more uncomfortable, it enables an estimated tracking system and may be more practical for obese patients. The battery of the data recorder is charged in a cradle system connected to a computer with the commercial software system installed, where patient- and study-specific information will be entered and reviewed. A glass of water will

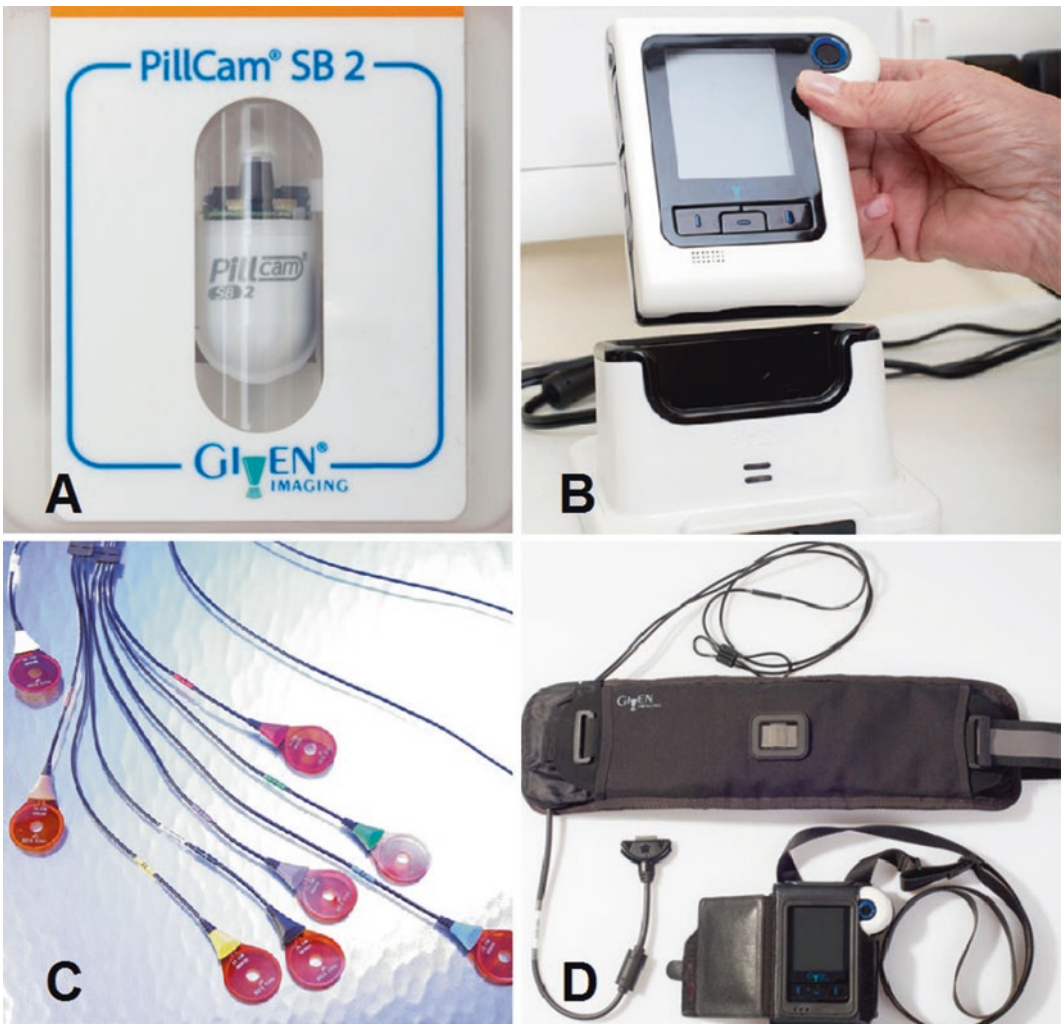

Fig. 18.5 Standard equipment for VCE. (**a**) PillCam SB2. (**b**) Data recorder in cradle. (**c**) Sensor array system. (**d**) Sensor belt with recorder pouch (Adapted from Davison et al. [29] With permission of Springer Nature.)

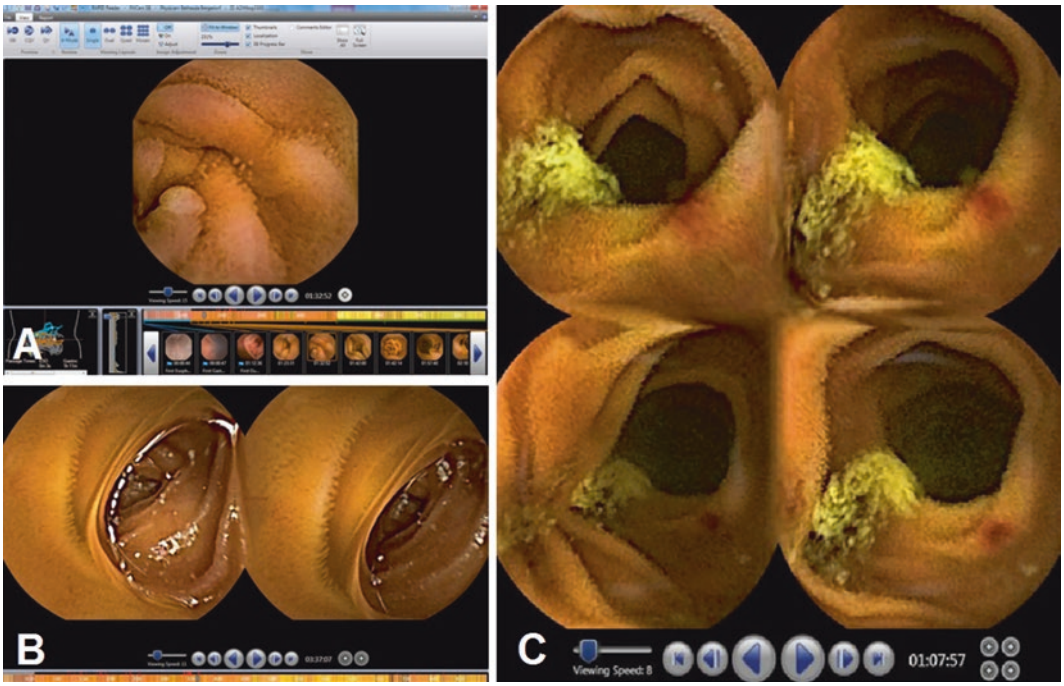

Fig. 18.6 VCE study interpretation. (**a**) Single view. (**b**) Dual view. (**c**) Quad view (Adapted from Lewis and Keuchel [30] With permission of Springer Nature.)

be needed for the patient to swallow the capsule, and simethicone is generally used to decrease intraluminal [29] (Figs. 18.5 and 18.6).

VCE technology continues to evolve and is improving with each subsequent generation and will continue to change as the fields of application also evolve. See Table 18.1 for specific details regarding the different VC technologies. The earlier CCE systems were designed to transmit images for 3 min after starting the examination followed by a dormant "sleep" mode for 1 h 45 min designed to save battery power, with the intent to reactivate the VC in the terminal ileum for the completion of the colon examination. Of note, the PillCam Colon 2 is the second-generation CCE and includes design improvements intended to improve the sensitivity of CCE. Upgrades include a wider field of view with an angle of 172°, allowing almost 360° visualization from both angles and a variable/adaptive frame rate of up to 35 frames per second while in motion and 4 frames per second while stationary. Additionally, the data recorder buzzes, vibrates, and instructs the patient during the day of the procedure, which helps with the potentially complex protocol involved in CCE (see below.)

The Procedure

VCE Procedure Checklist (Varies with VC Application)

- Review indications and patient history.
- Informed consent.
- Sufficient fasting time (8 h for SBCE) including bowel preparation.
- Enter patient information and fit patient with sensor array/belt and recorder.
- Confirm charged recorder and sensor array/sensor belt connection.
- Activate VC and confirm electronic pairing of VC.
- Observe ingestion, simethicone, ± prokinetic agent, and 30–60 cc water.
- Wait for sufficient time post-ingestion (8 h for SBCE) then collect sensor array/belt and data recorder, and download study to workstation.
- Capsule passes with bowel movement (evaluate passage on study).

Practical Considerations: Informed Consent for VCE

- Review the indications and contraindications.
- Beware of the swallowing issues (Zenker's diverticulum).
- If increased risk for capsule retention, make sure patency capsule has been performed.
- Advise 0% risk of capsule retention in a normal small bowel.
- Advise no MRIs until capsule clearance is confirmed.
- Risks including a failed procedure, capsule retention, and missed lesions should be part of the discussion.
- Emphasize the study is intended for a specific field of application, e.g., SBCE, ECE, and CCE.

The VCE procedure will be generally similar with all the fields of VCE application and will be reviewed here. Most of our discussion will focus on SBCE, the most common application; however, we will highlight specific details related to ECE and CCE as well. Depending on the specific modality, there will be protocol differences, which may also evolve as technology improves and as experience increases with time.

Informed Consent

The clinician should have a thorough understanding of the patient's clinical history, indications, and risk for complications, including those related to swallowing the VC (as reviewed above). In patients with increased risk for capsule retention, make sure a patency capsule has been performed. Risks including a failed procedure, capsule retention, and missed lesions should be part of the discussion [3]. The risks should be reviewed with the patient, and informed and written consent should be obtained. The patient should be advised that the risk of VC retention in a normal small bowel is negligible. The patient should also be advised that magnetic resonance imaging (MRI) is contraindicated until capsule passage is confirmed. Depending on the field of application for the study (SBCE, ECE, CCE), it should be emphasized that the study is not designed to detect lesions in separate fields of application.

Bowel Preparation

Preparation of the bowel in advance of VCE is important to optimize cleanliness and image quality, much like in standard endoscopy, and is recommended by current clinical practice guidelines, although there is insufficient evidence to recommend a specific type of preparation [3]. Oral iron, as well as antacids, bismuth subsalicylate (Pepto-Bismol), and sucralfate (Carafate), which can coat small bowel and discolor stool, should be stopped preferably 5–7 days and at least 3 days before the procedure. The day before the procedure, the patient should undergo a 10–12 h fast, and if bowel preparations are used, they should be done after the fasting period. Bowel cleansing has been shown to increase diagnostic yield and enhance mucosal visualization better than fasting alone [31]. Polyethylene glycol (PEG)-based regimens are commonly used; however, they are not standardized. We use a clear liquid diet and one bottle of magnesium citrate or 2 L of PEG the day before the procedure. Some protocols have used sodium phosphate preparations for cleansing [32].

Ingestion

Once the patient has been checked in for the procedure, identifying information is entered into the system, the recorder is confirmed as being fully charged, and the sensor array/sensor belt is attached. Patients fitted with a sensor array have leads attached to their abdomen at appropriate locations. The VC should be opened and activated, and electronic pairing of the VC should be confirmed. The VC is then removed from its magnet containing packaging thus activating the VC. Appropriate sensor array placement can be confirmed by running the VC over all the attached sensor array leads, which illuminates the recorder via RF. The VC ingestion should be observed and monitored for complications. Simethicone 80 mg is commonly given as part of the VC ingestion protocol to reduce intraluminal gas bubbles which could interfere with mucosal viewing. The capsule is then swallowed with 30–60 cc of water.

Practical Considerations: Poor GI Motility and Chronic Narcotic Use

- At 1 h, consider using real-time imaging to confirm VC entry into small bowel.
- If small bowel entry is not achieved, consider water and/or prokinetic agent.
- Continue study for the full duration of the study (SBCE, CCE).

After the VCE capsule is ingested, the patient leaves the endoscopy unit or office and remains nil per os for 2 h, followed by clear liquids only for the next 2 h. The recorder should be worn on the belt throughout the 8 h VCE study

time. The patient returns to the endoscopy unit or the office after 8 h with the VC battery life having expired. The sensor array and recorder are then removed from the patient and the recorder placed in the computer workstation receiver, and the VCE images are then downloaded into the computer workstation. If applicable to the field of application and oral ingestion, recent clinical practice guidelines recommend that patients with poor GI motility or chronic narcotic use have used real-time imaging to confirm VC entry into the small bowel within 1 h, pursuing interventions (water ingestion and/or prokinetic agent) if needed, and completion of the study to the full extent of the battery life of the VC [3].

Esophageal CE

The ingestion protocol is slightly different if ECE is being performed. The patient should be fasting for 1 h, and the sensor array is applied to the patient, and the recorder is connected. Gralnek et al. developed a simplified ingestion protocol (SIP) to better enhance viewing of the gastroesophageal (GE) junction [33]. The patient swallows 100 cc of water while standing, followed by the ingestion of the esophageal capsule in the supine right lateral decubitus position. While remaining in this position, the patient then drinks 15 cc sips of water every 30 s for 7 min. The patient then sits upright for 20 min. The SIP protocol extended the esophageal transit time by 3 min 45 s and improved visualization of the GE junction.

Colon CE

The protocol requirements for CCE have been more stringent due to the need for a medical supervision to supervise administration of laxative boosters when the VC enters the small bowel. This requirement is evolving as the technology has improved and is able to give automated queues. A more aggressive bowel preparation regimen is needed, which generally includes 4 L of split-dose PEG as well laxative boosters which need to be given when the VC has entered the small bowel, which are necessary to accelerate the VC transit through the small bowel while keeping the colon clean for adequate examination (see Table 18.2). Depending on the CCE technology used, the device may have the ability to give automated prompts to guide the protocol [34].

Table 18.2 Bowel preparation regimen for CCE

Day prior to procedure	Clear liquid diet only
Evening prior to procedure	2 1 of PEG
7 am day of procedure	2 1 of PEG
Ingestion of Colon Capsule 2	
Booster 1	Na phosphate or SUPREP
Booster 2 (if necessary)	Na phosphate or SUPREP
Suppository (if necessary)	Bisacodyl 10 mg
PEG polyethylene glycol	

Adapted from Adler et al. [34] With permission of Springer Nature.

Interpretation

After the VCE study is downloaded, we read and interpret the video using the available software features. The video can be read in a single, dual (2 × 1), and quad (2 × 2) format at speeds of 5–40 frames per second. A previous consensus conference in 2002 suggested 15 frames per second is the fastest acceptable rate of review; however, currently there is no definitive reading time to minimize missing lesions, [30] and the speed and view should be adjusted to accommodate viewer comfort. We generally read using the dual or quad format at the rate of 18–24 frames per second with an average of 20–45 min for the completion of the study.

VCE Study Interpretation: Tips for Concentration

- Review indications and patient history (again).
- Darkened lighting.
- Comfortable environment.
- Stimulation (caffeine, soft music).
- Limit session time (avoid long sessions, especially >1 h).
- Breaks as needed to maintain concentration.

VCE study interpretation can be tedious and time-consuming, therefore it is important to maintain vigilance and focus when perfoming this task. Reviewing the patient's study indication and medical history can be helpful. Simple measures to promote concentration may also be helpful and include darkened lighting, comfort, caffeine, auditory stimulation, limited session time, and breaks as needed. Maintaining a systematic approach to VCE study interpretation can also be helpful. Generally, viewing the end of the study to ensure the colon has been entered (for SBCE) is an important first step. If this has not been achieved, it can be useful to determine whether the VC has entered the small bowel. Setting landmarks can be helpful, including the first gastric image, first duodenal image, and first cecal image. In the case of SBCE, the small bowel images should be carefully reviewed. Thumbnails should be created for abnormalities.

VCE Study Interpretation: Tips for Reviewing Images

- Review images at the end of study to confirm colon entry.
- Review images at the start of study to confirm small bowel entry.
- Set landmarks for first gastric, duodenal, and cecal image.
- Review small bowel images carefully (SBCE).
- Use a comfortable frame reading rate and viewing mode.
- Consider using an atlas and the suspected blood indicator.

Practical Considerations: VCE Interpretation

- Temporarily setting the first duodenal image to the beginning of the SBCE study can utilize the suspected blood indicator (SBI) in the esophagogastric region.
- Due to high false-positive results and the possibility of missed non-bleeding lesions, the SBI should not be substituted for a careful review of the entire study.
- Based on prior consensus, 15 frames per second would be an appropriate starting reading time with single or dual view. Faster frame rates and quad views may be utilized based on personal comfort levels.

There is a suspected blood indicator (SBI) tool which can also be used, although this may be limited by false-positive results. This identifies images suspected of bleeding. However, this has been shown to be of little utility due to a high number of false-positive results [35]. Some reading platforms are equipped with an atlas feature that allows the viewer to match selected images with a standard VCE image atlas to facilitate interpretation. Another helpful software feature is the video time bar, which allows the provider to move quickly throughout the images on the VCE video. The time bar also contains a color bar, which averages the image color through each section of video to facilitate rapid locations of anatomic transitions in the GI tract. Estimating the localization of lesions found in the small bowel can be helpful for formulating recommendations. Lesions found within 30 min of small bowel entry and/or in the left abdomen are within reach of a 2.5 m push enteroscope. By calculating the time of small bowel entry (first duodenal image time) and exit (first cecal image time), the bowel transit can be divided into thirds. If device-assisted enteroscopy (DAE) such as single or double-balloon enteroscopy is needed, an anterograde/oral insertion approach can be recommended in the proximal 2/3 of the bowel, and a retrograde/anal insertion approach can be recommended for the distal 1/3.

Indications and Findings

Normal Study Findings

Although the views, resolution, and magnification will vary, operator experience with standard GI endoscopy is helpful in the recognition of normal and abnormal findings with VCE. At the onset of ingestion, if the VC was swallowed and not deployed, the landmarks for a normal esophagus, including the Z-line, will be visualized before entry into the stomach. There will be a noticeable increase in lumen size, and apart from the oscillating movement of the capsule, common landmarks will be seen, including the gastric angle/incisura and the antrum and pylorus.

Upon entry into the duodenum, a change in the mucosal pattern will be observed, with the characteristic villous appearance of the small bowel mucosa. Depending on the view, a retrograde appearance of the pyloric sphincter may be seen which may have a rosette pattern in the duodenal bulb (see Fig. 18.7).

The typical villous pattern of the small bowel will continue, and it is expected to see white-appearing lines, venous patterns, and occasionally a mucosal blush caused by the VC window pressing against the mucosal lining. Lymphangiectasias are not uncommon and may be seen. If they are numerous or very large, they could be a sign of disease, however. Otherwise, as the VC enters the cecum/colon, there will be noticeable increase in the diameter of the lumen, with pooling of fluid, which may have a dark bilious appearance, which is dependent on the type of bowel prep and is dependent on the intended field of application of the study. This movement of the capsule in the colon may have the appearance of movement similar to a washing machine (see Fig. 18.8). We will now review the different fields of application (SBCE, ECE, CCE), in respect to their indications together with their potential findings.

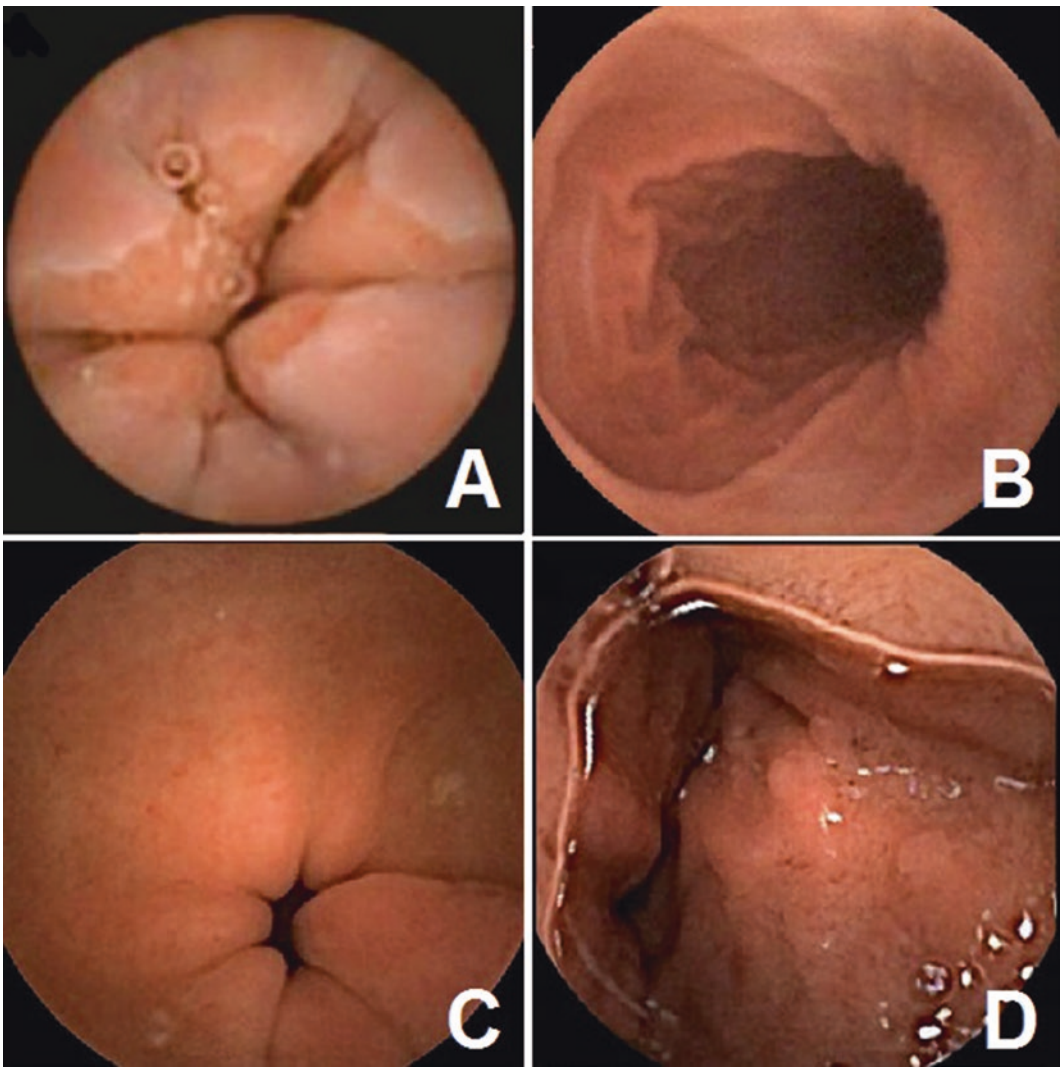

Fig. 18.7 VCE normal esophagus, stomach, duodenum. (**a**) Normal Z-line. (**b**) Gastric body. (**c**) Antrum. (**d**) Normal duodenum (with benign gastric heteropia) (Adapted from Eliakim and Sharma [36], Nakamura et al. [37] With permission of Springer Nature.)

Small Bowel Capsule Endoscopy: Indications and Findings

Indications for Small Bowel Capsule Endoscopy

- Obscure gastrointestinal/small bowel bleeding
- Crohn's disease
- Celiac disease
- Intestinal polyposis syndromes
- Small bowel tumors
- Miscellaneous

SBCE is the most common application of VCE, and indications include the evaluation of obscure GI bleeding/small bowel bleeding, suspected/active Crohn's disease, celiac disease, and suspected small bowel tumors. The yield of clinically important findings on VCE is greater in patients with obscure-overt than obscure-occult GI bleeding. Carey et al. studied 260 consecutive patients who had undergone VCE, and the most common findings included small bowel angioectasia (61%), small bowel ulcer (17%), and small bowel mass (10%) [41] (see Fig. 18.9).

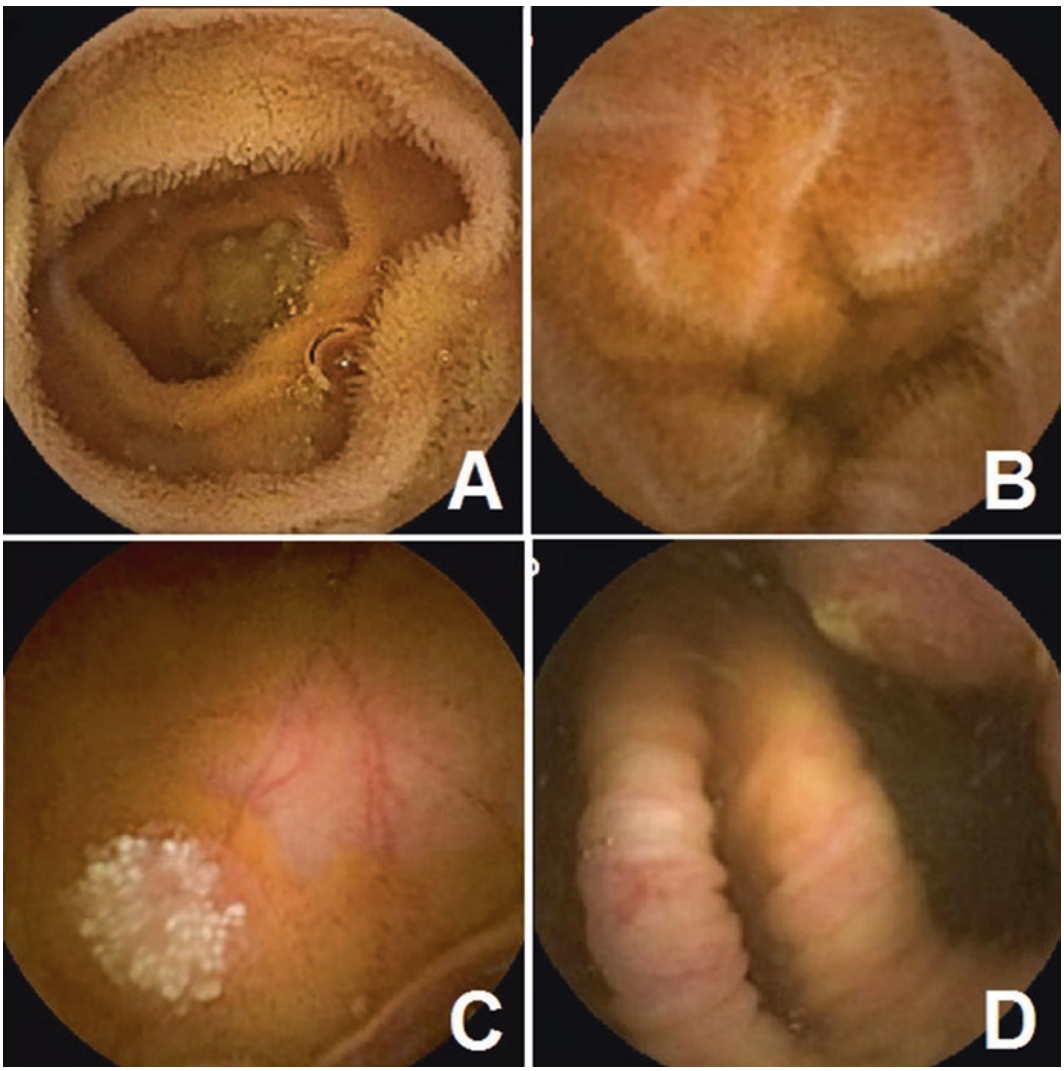

Fig. 18.8 VCE normal small bowel. (**a**) Normal small bowel villous pattern. (**b**) White lines are a normal finding. (**c**) Focal lymphangiectasia, benign lesion. (**d**) Colonic Haustra for Comparison. (Adapted from Steinbruck et al. [38], Toth et al. [39], Lewis and Keuchel [30], Appleyard et al. [40] With permission of Springer Nature.)

Obscure GI/Small Bowel Bleeding

Obscure GI bleeding, also known as small bowel bleeding, is the most common indication for SBCE and accounts for 5–10% of all patients with GI bleeding [42]. The term is generally used after esophagogastroduodenoscopy (EGD) and colonoscopy have not revealed a cause for the GI bleeding. It is considered overt when presenting with melena or hematochezia and occult, when presenting with anemia alone. Recent clinical practice guidelines specifically recommend VCE in patients with overt GI bleeding (excluding hematemesis) and negative findings on high-quality EGD and colonoscopy (overt OGIB), and it should be done as soon as possible to increase the yield. It is also recommended that in patients with a previously negative VCE who have recurrent OGIB, repeat EGD, colonoscopy, and/or VCE should be done, as well as in selected patients with suspected OGIB and unexplained iron-deficiency anemia (occult OGIB) [3]. The American College of Gastroenterology (ACG) has proposed that OGIB be reclassified with the more appropriate term small bowel bleeding because newer imaging modalities, including VCE, deep enteroscopy/DAE, and advanced radiographic imaging, have enabled the identification of the specific cause of small bowel bleeding in the majority of patients. The current 2015 ACG clinical guideline for the diagnosis and management of small bowel bleeding recommends VCE in the evaluation of occult or overt suspected small bowel bleeding, after a second-look EGD/colonoscopy is negative, and there is no concern/evidence for obstruction. It is also included in the evaluation of suspected subacute ongoing small bowel bleeding after stabilization of the patient, but not in brisk/massive suspected small bowel bleeding [43] (see Figs. 18.10 and 18.11).

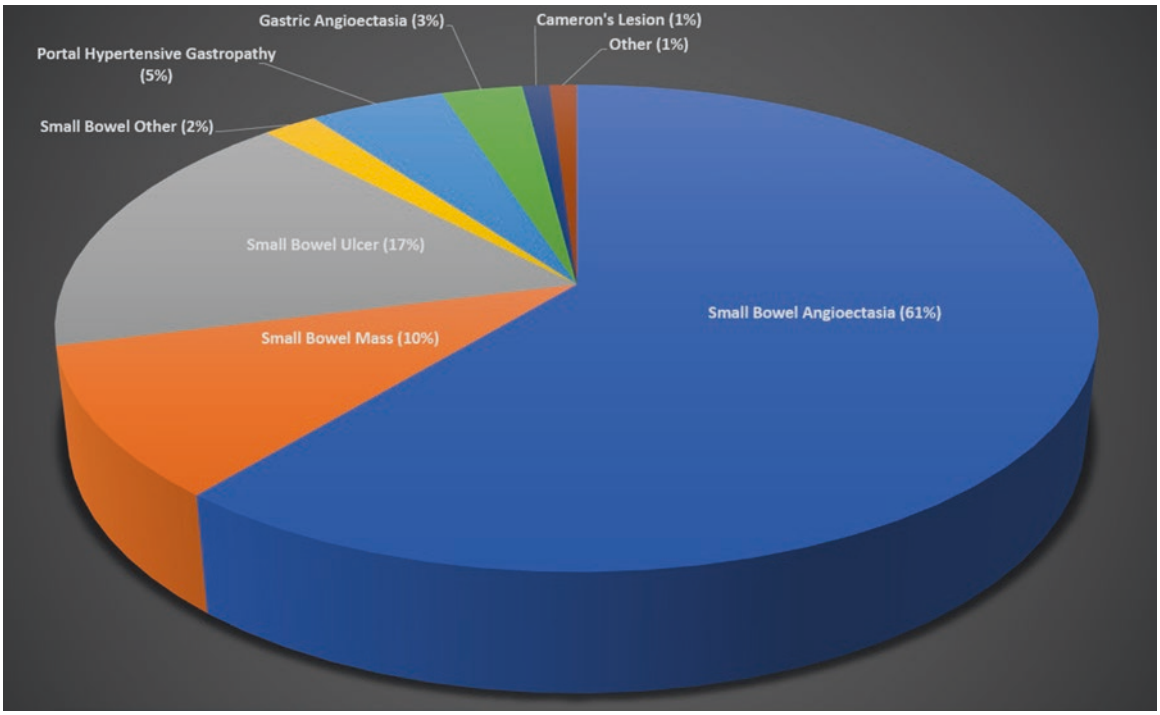

Fig. 18.9 Common VCE findings (Adapted from Carey et al. [41] With permission of Springer Nature.)

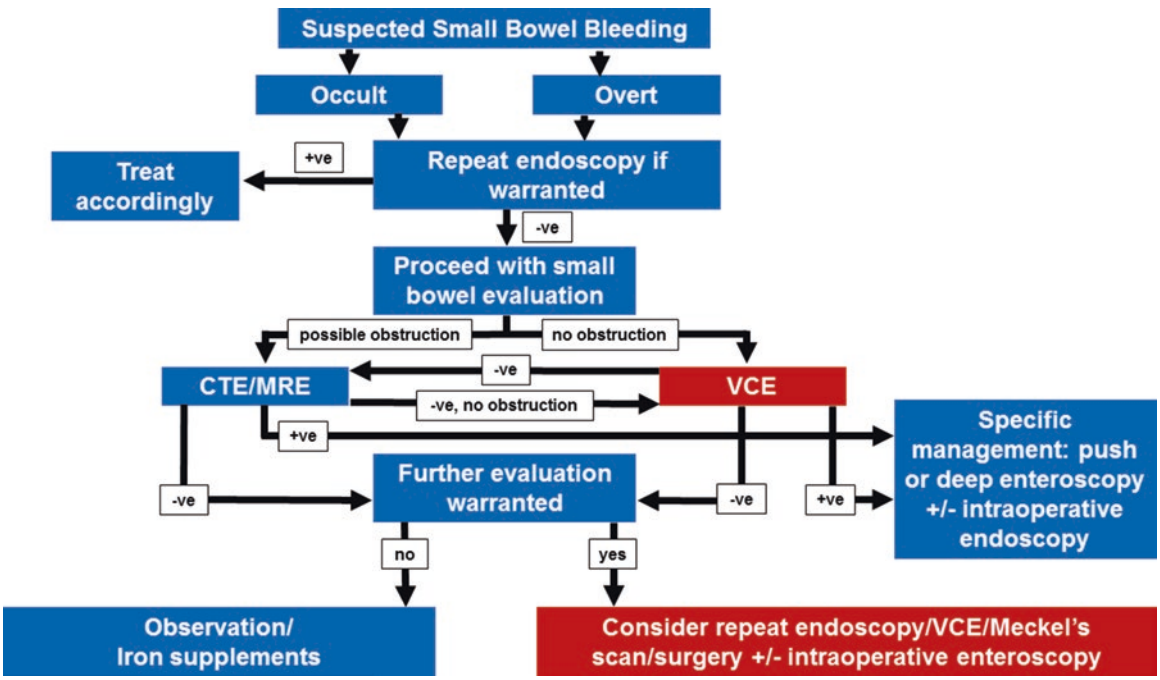

Fig. 18.10 Algorithm for suspected small bowel bleeding. *CTE* CT enterography, *MRE* MR enterography, *VCE* video capsule endoscopy (Adapted from Gerson et al. [43] With permission of Springer Nature.)

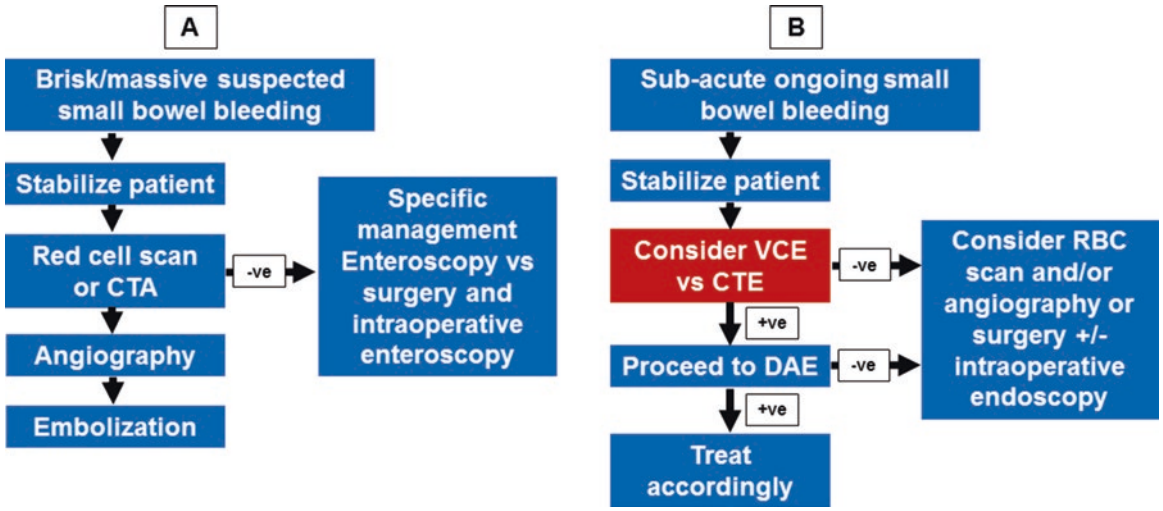

Fig. 18.11 (**a**) Algorithm for brisk or massive suspected small bowel bleeding. (**b**) Algorithm for subacute ongoing suspected small bowel bleeding. *CTA* CT angiography, *CTE* CT enterography, *RBC* red blood cell, *VCE* video capsule endoscopy (Adapted from Gerson et al. [43] With permission of Springer Nature.)

SBCE is considered a first-line noninterventional modality for evaluation of small bowel bleeding, with a diagnostic yield of 42–60% [44, 45], which is comparable to DAE and can help target the interventional management appropriately [46]. The diagnostic yield of VCE is improved during or close to the episode of bleeding [47], with repeat VCE having a higher yield of up to 75% [48]. The comparatively higher sensitivity for SBCE in small bowel bleeding is due to the fact that the most common lesions identified are angioectasias (also referred to as arteriovenous malformations, angiodysplasia, or telangiectasia), which are flat vascular mucosal lesions (see Fig. 18.12).

Nonspecific red spots are also common lesions, and it is important to become familiar with the appearance of red blood, blood clot, and hematin. Because dark bile may be confused with blood, it can be helpful to look for the appearance of hematin/melena downstream of a suspected bleeding lesion (see Fig. 18.13).

Crohn's Disease

SBCE can be used to monitor Crohn's disease activity or to make a new diagnosis in a patient with suspected active Crohn's disease. A meta-analysis by Triester et al. found VCE was significantly more accurate than both small bowel radiography (63% vs. 23%) and colonoscopy with ileoscopy (61% vs. 46%) in the diagnosis of non-stricturing small bowel Crohn's disease [51]. Recent clinical practice guidelines recommend VCE to evaluate patients with suspected Crohn's disease but with negative ileocolonoscopy and imaging studies, as well as patients with established Crohn's disease with clinical features unexplained by ileocolonoscopy or imaging studies, as well as patients with Crohn's disease when assessment of small bowel mucosal healing is needed but beyond the reach of ileocolonoscopy, and in patients with suspected small bowel recurrence of Crohn's disease after colectomy, undiagnosed by ileocolonoscopy. It is not recommended in patients with chronic abdominal pain and/or diarrhea, with negative inflammatory/biomarkers associated with Crohn's disease [3]. VCE may also be useful in typing patients with unclassified IBD [52]. Common VCE Crohn's findings include mucosal breaks, focal villous denudation, erosions and frank ulceration, and stricture formation [53]. VCE study findings are not specific and thus not sufficient for the diagnosis of Crohn's disease. Abnormal findings such as mucosal breaks and minor lesions may be seen in up to 13% of normal patients [54]. The Lewis score is a standardized VCE scoring index that may be used for monitoring Crohn's disease activity, with a score of 135 as a suggested cutoff between normal and active disease, although it is not meant to be used in making the diagnosis of Crohn's disease and its role is still evolving [55, 56]. Crohn's disease must be diagnosed on the basis of a constellation of clinical, histologic, radiologic, and biochemical patient findings (see Fig. 18.14).

Celiac Disease

There has been a growing interest in the use of VCE in the diagnosis and management of celiac disease. This is due to the high magnification of the VC camera and the ability to visualize villous atrophy, scalloping, layered/stacked folds, and a mosaic mucosal appearance. A meta-analysis by Rokkas and Niv showed a pooled VCE sensitivity of 89% and specificity of 95% in the diagnosis of celiac disease [60], although Petroniene et al. found that while investigators with

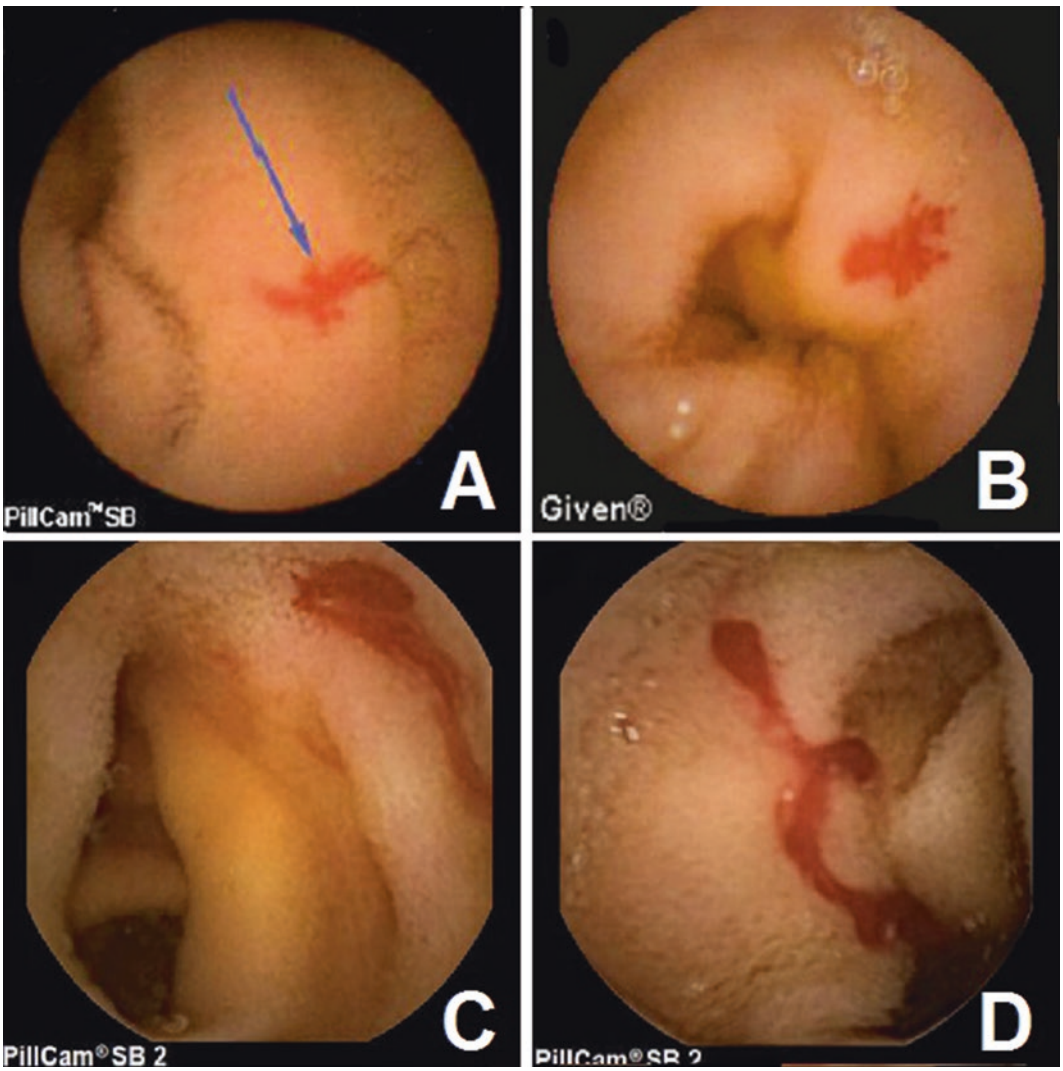

Fig. 18.12 VCE in angioectasia. (**a**, **b**) Small bowel angioectasia. (**c**, **d**) Active small bowel bleeding from angioectasia (Adapted from Pennazio et al. [49] With permission of Springer Nature.)

prestudy VCE experience had perfect interobserver agreement in celiac disease, those with limited VCE experience had poor interobserver agreement [61]. VCE has been employed in patients suspected of celiac disease, with positive celiac serology, but who have a negative EGD and proximal small bowel biopsies or in those who decline to undergo EGD. However, because endoscopic biopsies would still be required to confirm the diagnosis of celiac disease, recent clinical practice guidelines recommend against the routine use of VCE for making a diagnosis of celiac disease; however, it is recommended in evaluating patients with celiac disease who have unexplained symptoms despite treatment and appropriate investigations [3]. VCE may be considered for evaluating complications such as chronic ulcerative jejunoileitis, small bowel lymphoma, and adenocarcinoma. VCE may also be clinically helpful in special circumstances, such as in patients with seronegative villous atrophy, to help obtain further evidence to support or exclude the diagnosis of celiac disease, including the exclusion of Crohn's disease. VCE findings of patients with complicated or refractory celiac disease include ulcerations, ulcerated nodular mucosa, small bowel cancer and polyps, strictures, and submucosal masses [62] (see Fig. 18.15).

Other small bowel pathologic processes can appear similar to Crohn's disease on VCE and include celiac disease (discussed above), NSAID, and other drug-induced enteropathies. NSAID enteropathy can create diaphragms, webs, and strictures that may be indistinguishable from findings in Crohn's disease. VCE for celiac disease may also appear similar to Behçet's disease and ulcerated small bowel tumors. Other ulcerating lesions include immune disease, like Henoch-Schonlein purpura and sarcoidosis (see Fig. 18.16).

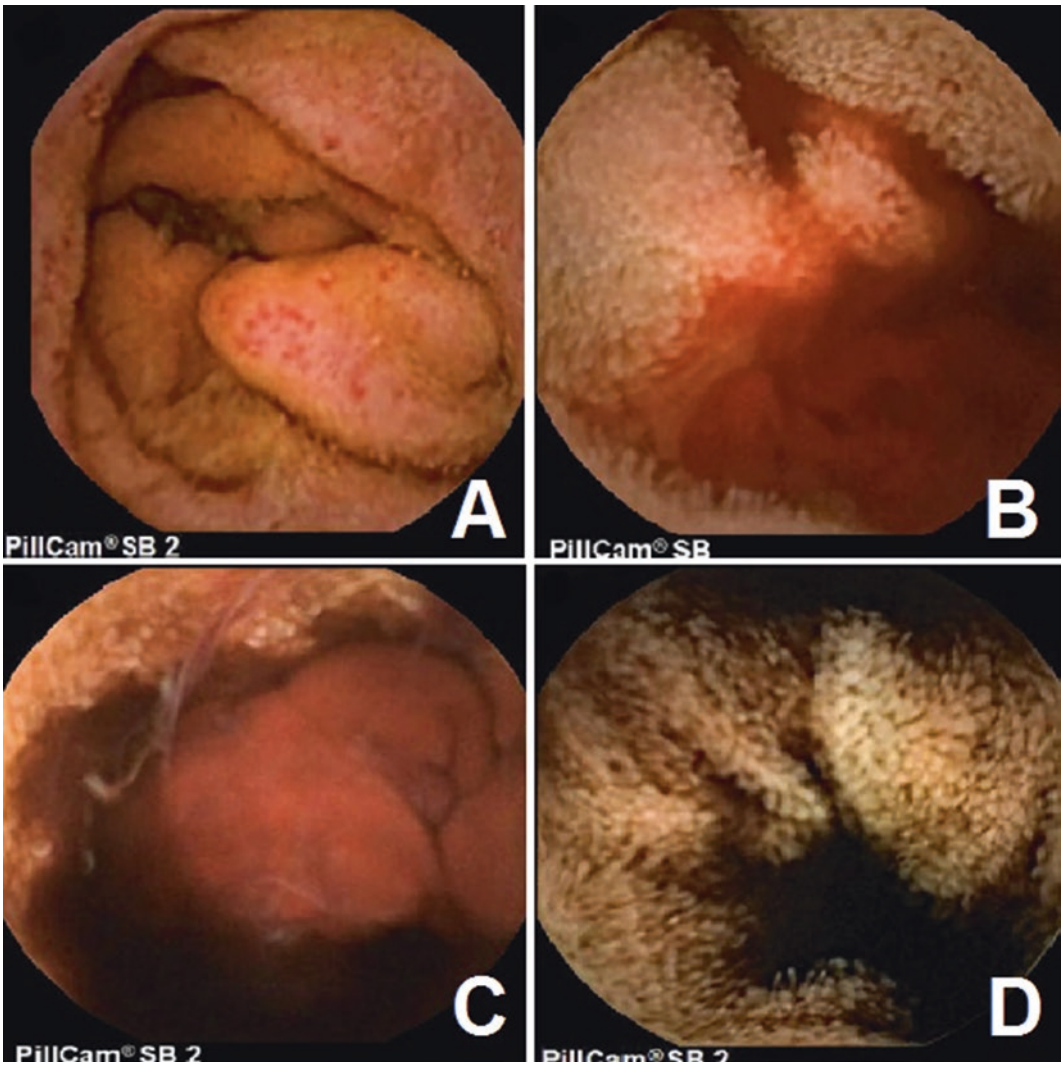

Fig. 18.13 VCE in GI bleeding. (**a**) Nonspecific red spots. (**b**) Red blood. (**c**) Blood clot. (**d**) Hematin (Adapted from Delvaux et al. [50] With permission of Springer Nature.)

Intestinal Polyposis Syndromes

Intestinal polyposis syndromes are rare and include the categories of familial adenomatous polyposis (FAP), hamartomatous polyposis syndromes, and other rare syndromes. The hamartomatous syndromes include Peutz-Jeghers syndrome (PJS), PTEN-associated hamartomatous syndromes, familial juvenile polyposis, and Cronkhite-Canada syndrome [66, 67]. Small bowel polyps occur in more than 75% of FAP and PJS patients, and the likelihood of jejunal/ileal polyps is higher in those who have duodenal polyps, and although endoscopy has been shown to be superior for duodenal polyps, the yield of VCE is better for more distal small bowel polyps and comparable to radiography including MR enterography, although larger polyps could be missed [68, 69], with similar detection rates compared to DAE [70]. Because of this, recent clinical practice guidelines have recommended VCE as a form of ongoing surveillance in patients with intestinal polyposis syndromes who require small bowel studies [3] (see Fig. 18.17).

Small Bowel Tumors

Cancer of the small intestine is uncommon, and the four main histological subtypes include adenocarcinoma, carcinoid, lymphoma, and sarcoma. An increased risk is noted with Crohn's disease, celiac disease, adenoma, FAP, and PJS [71]. Small bowel tumors account for 1–3% of all gastrointestinal neoplasms. The frequency of tumor detection is highest with VCE than other radiographic modalities. Patients younger than age 50 with small bowel bleeding have an increased risk of small bowel tumors as a bleeding source, whereas those older than 50 are significantly more likely to have angioectasias as their small bowel bleeding source [72]. Rondonotti et al. conducted a multicenter study from Europe

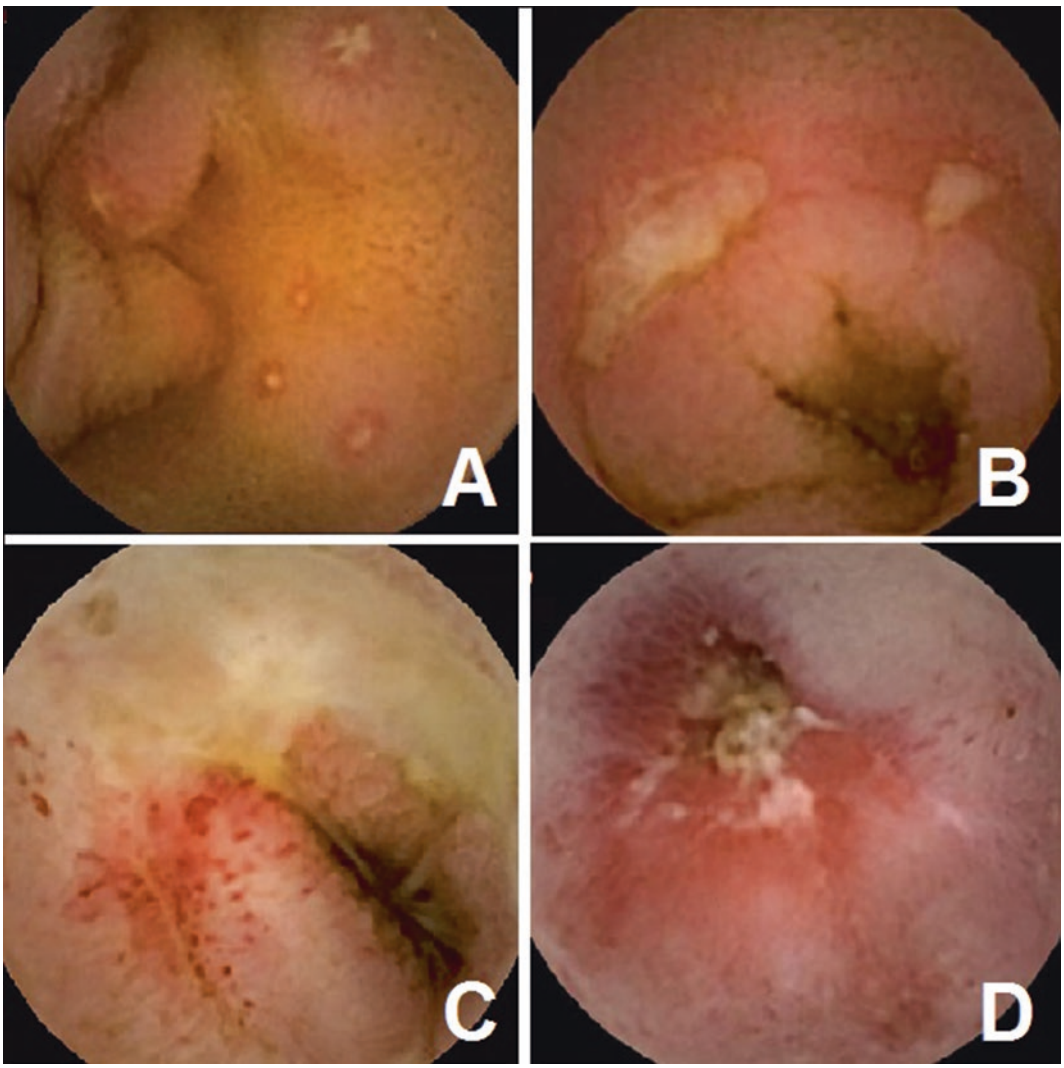

Fig. 18.14 VCE in Crohn's disease. (**a**) Aphthous ulcers. (**b**) Deep linear ulcers. (**c**) Extensive ulceration and multiple petechiae. (**d**) Ileal stricture (Adapted from Voderholzer et al. [57], Leighton et al. [58], and McAlindon et al. [59] With permission of Springer Nature.)

reporting results from 5129 patients who underwent VCE, with 124 diagnosed with small bowel tumors, and found the main tumor type was gastrointestinal stromal tumor (GIST) (32%), adenocarcinoma (20%), and carcinoid (15%), with 66% of secondary small bowel tumors being melanoma. Of the tumors identified, 80.6% were diagnosed solely by VCE, with other modalities failing to make the diagnosis. Capsule retention occurred in 9.8% of the patients with small bowel tumors [73] (see Fig. 18.18).

Esophageal Capsule Endoscopy: Indications and Findings

ECE may be considered as an alternative to standard endoscopy for the evaluation of Barrett's esophagus, esophageal varices, and reflux esophagitis. It has been shown to

Indications for Esophageal Capsule Endoscopy

- Barrett's esophagus detection
- Esophageal variceal screening
- Esophagitis screening

Practical Considerations

- ECE is not a first-line screening test for Barrett's esophagus.
- Consider esophageal capsule endoscopy as an alternative form of esophageal evaluation and screening in patients.

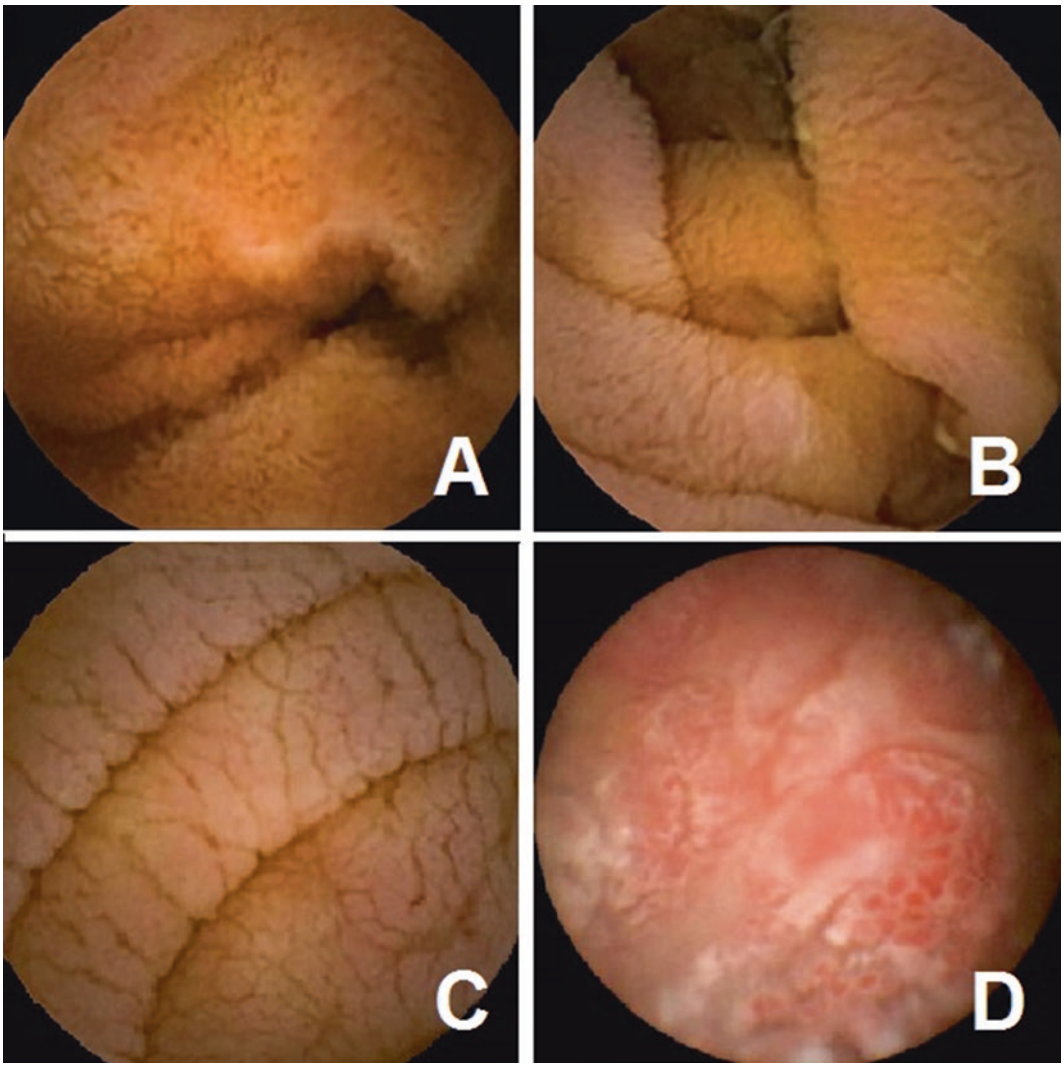

Fig. 18.15 VCE in celiac disease (**a**) Normal villi. (**b**) Mild villous atrophy. (**c**) Subtotal villous atrophy. (**d**) Enteropathy-associated T-cell lymphoma complicating celiac disease (Adapted from Schuppan et al. [63] and McAlindon et al. [59] With permission of Springer Nature.)

demonstrate good visualization, with high rates of detection for Barrett's esophagus, esophagitis, esophageal varices, as well as portal hypertensive gastropathy [74, 75]. The general limitations and complications are common to VCE in general. The advantages of ECE include the ability to be administered without sedation and better patient tolerance; [76] however, due to limited accuracy, it is not a first-line form of screening for Barrett's esophagus [77]. Similarly, it is a secondary form of evaluation/screening for esophageal varices and may be useful for patients who decline or have contraindications to EGD [78, 79] (see Fig. 18.19).

Colon Capsule Endoscopy: Indications and Findings

Indications for Colon Capsule Endoscopy

- Colon cancer/polyp screening
- Inflammatory bowel disease

Practical Considerations

- CCE is not a substitute for optical colonoscopy for colon cancer screening or assessing severity of colonic disease in inflammatory bowel disease.
- Useful in incomplete colonoscopy.
- May be considered in patients who decline optical colonoscopy.

Similar to the advantages of other VCE, CCE allows the evaluation of the colon without sedation, radiation, or insufflation. In 2014, the FDA approved the use of PillCam Colon for use in patients who had an incomplete optical colonoscopy. Large multicenter studies have shown sensitivities up to 88% and specificities up to 95% for the detection of polyps [80, 81]. These results are comparable to studies on tandem colonoscopy and CT colonography [82, 83]. Cost-effectiveness of CCE has been found to be associated with a moderate cost increase compared to CT colonography but continues to be studied [84]. Other indications for CCE may include patients who have contraindications for optical colonoscopy and patients who decline optical colonoscopy. Recent clinical practice guidelines recommend against the substitution of CCE for optical colonoscopy and against the substitution of CCE for assessing the extent and severity of IBD in situations where optical colonoscopy would be ideal (ulcerative colitis or Crohn's colitis) [3]. Conventional/optical colonoscopy is still established as the gold standard in colorectal cancer screening, particularly because it is the only method with the ability to remove detected polyps and obtain biopsy specimens. However, VCE still seems to be an adequate alternative for patients reluctant to undergo the standard testing, and it continues to be studied [85, 86] (see Fig. 18.20).

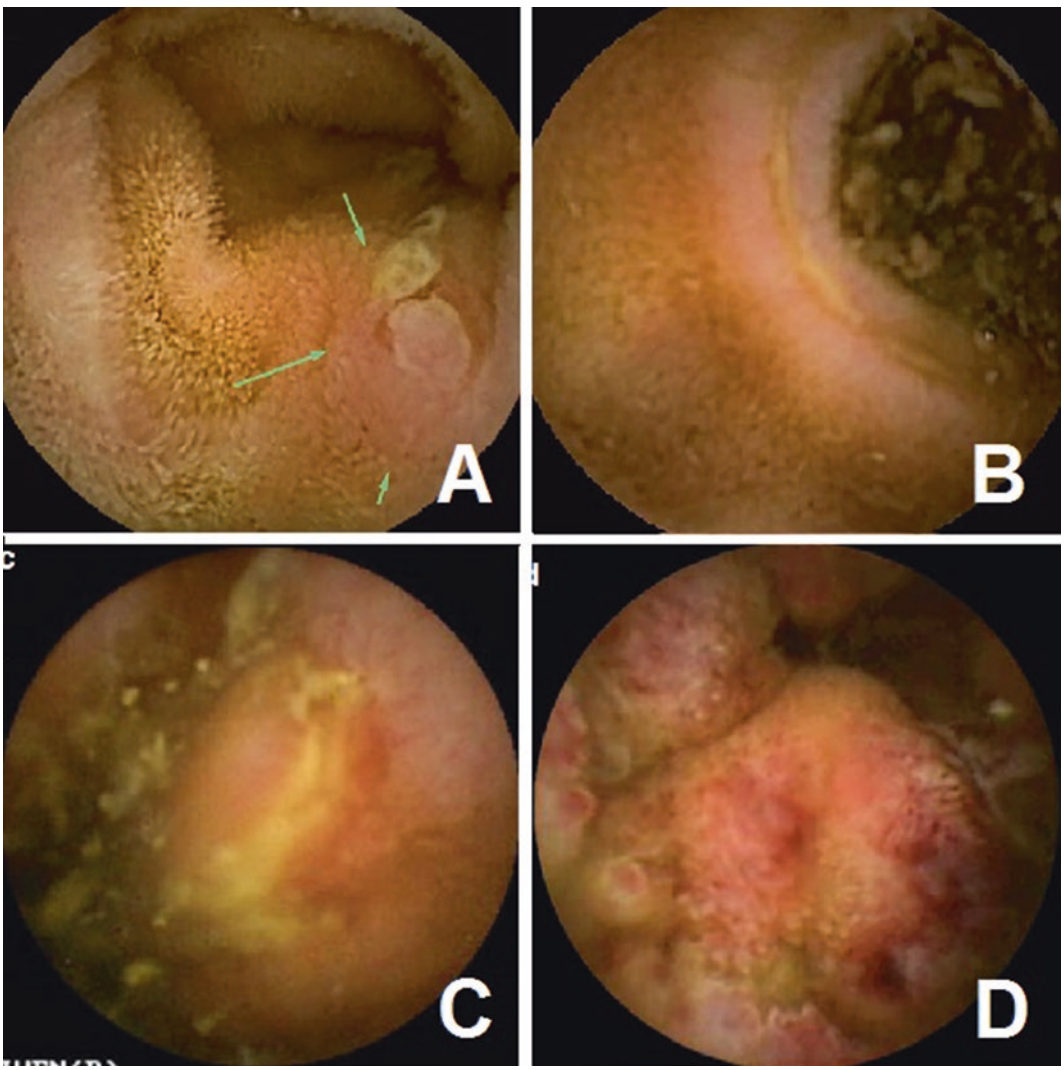

Fig. 18.16 VCE ulcerated lesions. (**a**) Denuded area with loss of villi and a central/erosion ulcer after short-term NSAID use. (**b**) Linear, circular NSAID-induced ulcer sitting on a fold. (**c**) Aphthous ulcer in the ileum in Behcet's syndrome. (**d**) Large ulcerated, hemorrhagic small bowel in Henoch-Schonlein purpura (Adapted from Bjarnason et al. [64] and Safatle-Ribeiro et al. [65] With permission of Springer Nature.)

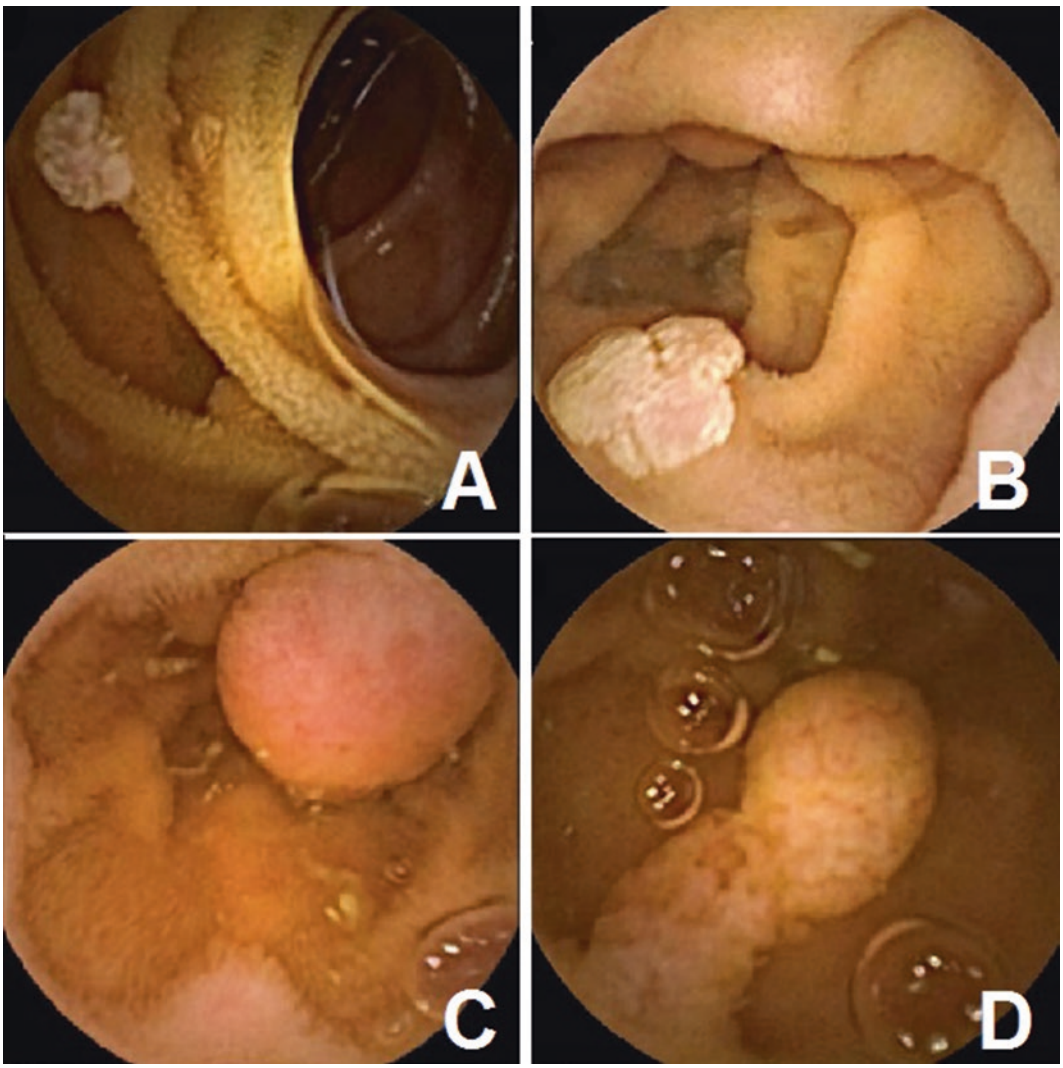

Fig. 18.17 VCE small bowel polyps. (**a**) Small polyp. (**b**) Sessile polyp. (**c**) Medium polyp. (**d**) Pedunculated polyp (Adapted from Delvaux et al. [50] With permission of Springer Nature.)

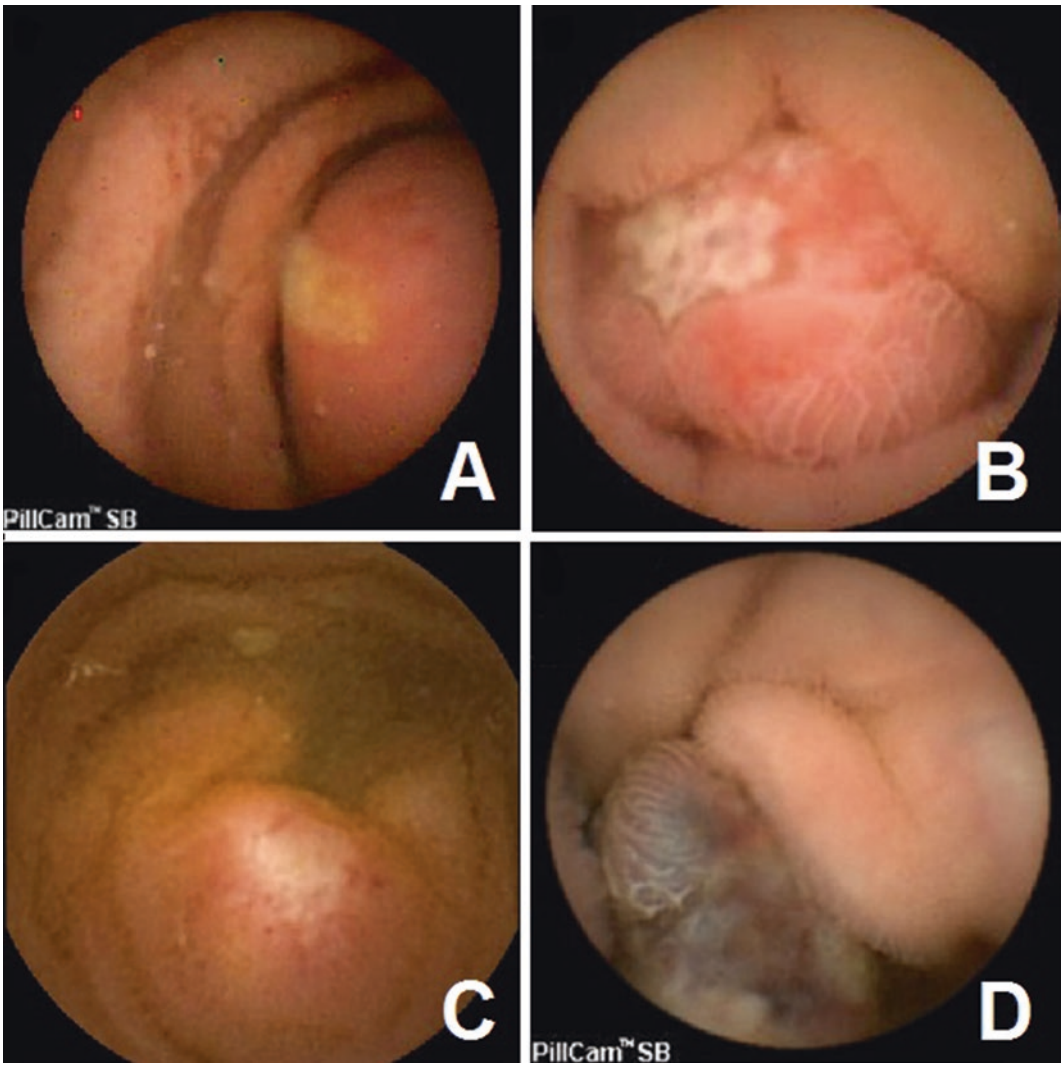

Fig. 18.18 VCE small bowel tumors. (**a**) Submucosal jejunal mass, confirmed as GIST. (**b**) Protruding jejunal lesion with central ulceration, confirmed as adenocarcinoma. (**c**) Submucosal tumor with umbilication, discoloration, and bridging folds confirmed as carcinoid. (**d**) Large metastasis of malignant melanoma (Adapted from Lewis et al. [30] With permission of Springer Nature.)

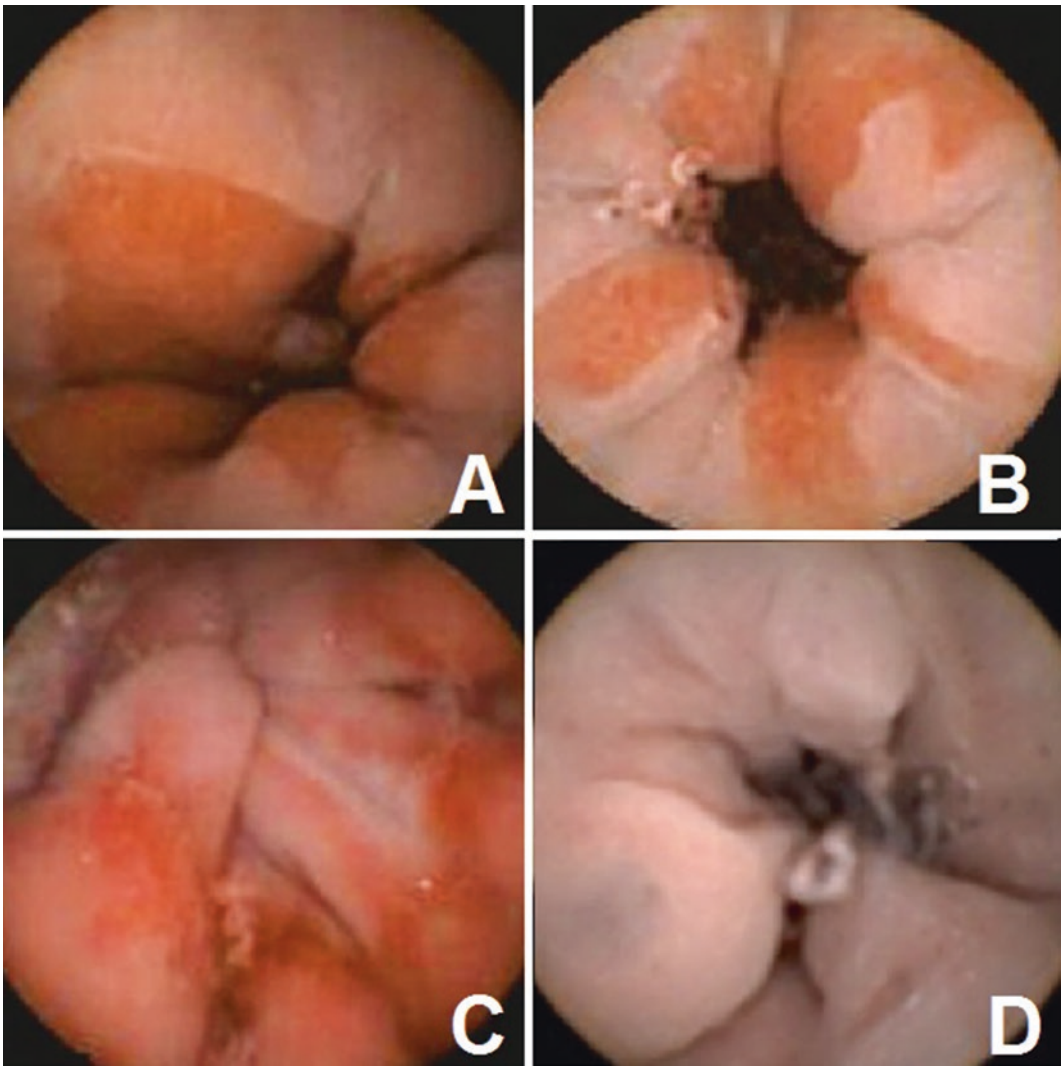

Fig. 18.19 VCE esophageal findings. (**a**) Normal Z-line. (**b**) Barrett's esophagus. (**c**) Esophagitis. (**d**) Esophageal varices (Adapted from Eliakim and Sharma [36] With permission of Springer Nature.)

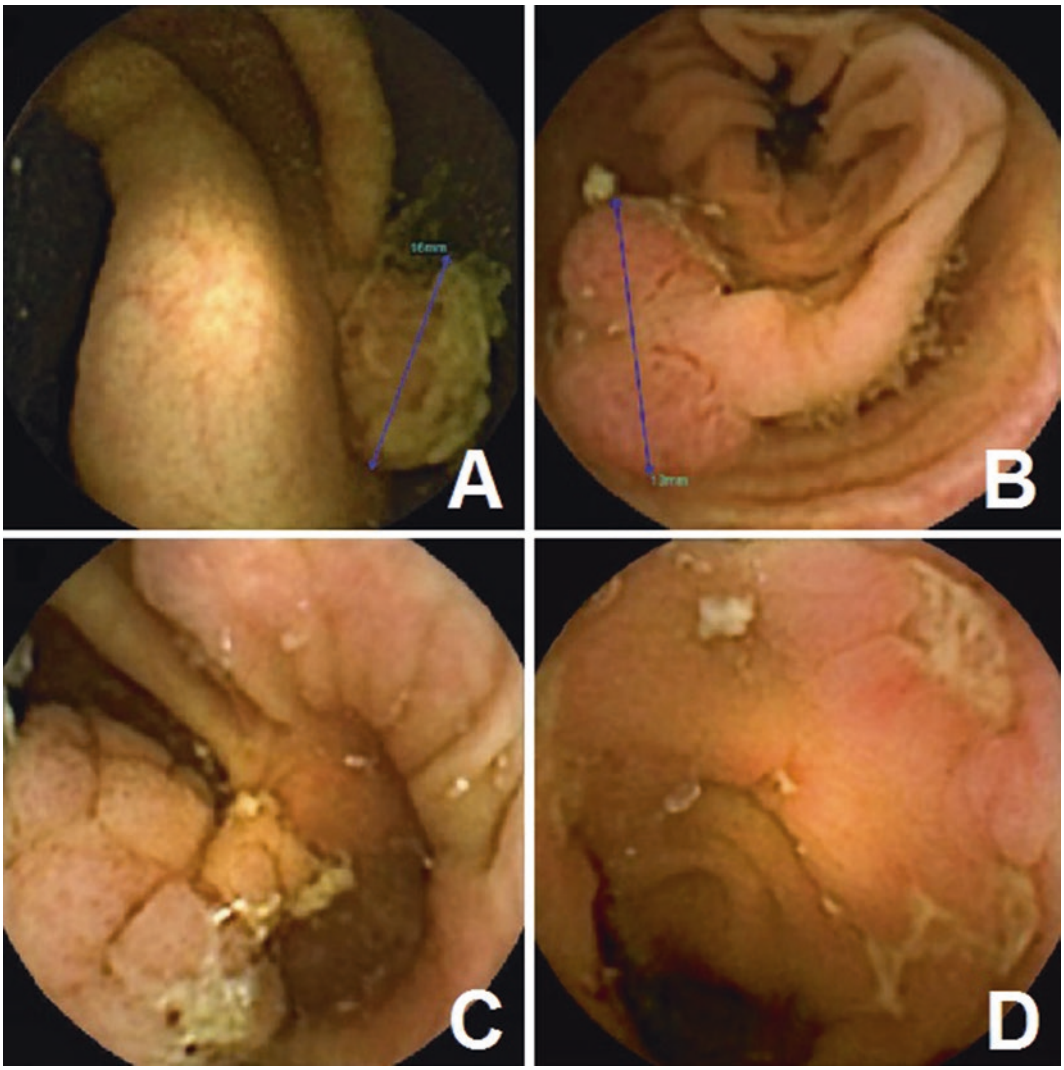

Fig. 18.20 VCE colon findings. (**a**) Sessile polyp in the ascending colon. (**b**) Pedunculated polyp in the descending colon. (**c**) Large laterally spreading polyp at the ileocecal valve. (**d**) Deep serpiginous ulcers from Crohn's colitis (Adapted from Aihara et al. [87] McAlindon et al. [59] With permission of Springer Nature.)

Documentation of Findings

Sample Documentation of VCE Examination

- Patient information
- Date and examiner
- Indication for exam
- Limitations
- Complications
- Description of findings
- Localization
- Diagnosis
- Recommendations

The VCE examination report should follow the general Minimal Standard Terminology (MST) created by the collaboration of international endoscopy societies, the World Endoscopy Organization (WEO) [50]. Localization of the described lesions can be done using localization software (if applicable), organ/anatomic landmarks, and time.

Practical Considerations

- Bowel transit time from small bowel entry (first duodenal image time) and exit (first cecal image time), divided into thirds, the first 2/3, anterograde DAE, and the last 1/3, retrograde DAE

Conclusions

VCE has advanced significantly from its introduction in 2001 and has progressed from a novel innovation in the management of GI bleeding in the small bowel and has continued to expand its technological applications to various applications in the GI tract, including the esophagus and colon. As VCE technology continues to advance, so will its role in the management of patients with GI disorders. As experience continues to grow, knowledge will continue to expand in this field, and the standardization of criteria, training, and applications will be forthcoming.

References

1. Iddan GJ, Swain CP. History and development of capsule endoscopy. Gastrointest Endosc Clin N Am. 2004;14:1–9.
2. Appleyard M, Glukhovsky A, Swain P. Wireless-capsule diagnostic endoscopy for recurrent small-bowel bleeding. N Engl J Med. 2001;344:232–3.
3. Enns RA, Hookey L, Armstrong D, Bernstein CN, Heitman SJ, Teshima C, Leontiadis GI, TSE F, Sadowski D. Clinical practice guidelines for the use of video capsule endoscopy. Gastroenterology. 2017;152(3):497–514.
4. Kurniawan N, Keuchel M. Technology. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
5. Bandorski D, Kurniawan N, Baltes P, Hoeltgen R, Hecker M, Stunder D, Keuchel M. Contraindications for video capsule endoscopy. World J Gastroenterol. 2016;22:9898–908.
6. Storch I, Barkin JS. Contraindications to capsule endoscopy: do any still exist? Gastrointest Endosc Clin N Am. 2006;16:329–36.
7. Mishkin DS, Chuttani R, Croffie J, Disario J, Liu J, Shah R, Somogyi L, Tierney W, Song LM, Petersen BT, Technology Assessment Committee, A. S. F. G. E. ASGE technology status evaluation report: wireless capsule endoscopy. Gastrointest Endosc. 2006;63:539–45.
8. Fritscher-Ravens A, Scherbakov P, Bufler P, Torroni F, Ruuska T, Nuutinen H, Thomson M, Tabbers M, Milla P. The feasibility of wireless capsule endoscopy in detecting small intestinal pathology in children under the age of 8 years: a multicentre European study. Gut. 2009;58:1467–72.
9. Dirks MH, Costea F, Seidman EG. Successful video capsule endoscopy in patients with an abdominal cardiac pacemaker. Endoscopy. 2008;40:73–5.
10. Stanich PP, Kleinman B, Betkerur K, Mehta Oza N, Porter K, Meyer MM. Video capsule endoscopy is successful and effective in outpatients with implantable cardiac devices. Dig Endosc. 2014;26:726–30.
11. Westerhof J, Weersma RK, Koornstra JJ. Risk factors for incomplete small-bowel capsule endoscopy. Gastrointest Endosc. 2009;69:74–80.
12. Yazici C, Losurdo J, Brown MD, Oosterveen S, Rahimi R, Keshavarzian A, Bozorgnia L, Mutlu E. Inpatient capsule endoscopy leads to frequent incomplete small bowel examinations. World J Gastroenterol. 2012;18:5051–7.
13. Lee MM, Jacques A, Lam E, Kwok R, Lakzadeh P, Sandhar A, Segal B, Svarta S, Law J, Enns R. Factors associated with incomplete small bowel capsule endoscopy studies. World J Gastroenterol. 2010;16:5329–33.
14. Ben-Soussan E, Savoye G, Antonietti M, Ramirez S, Lerebours E, Ducrotte P. Factors that affect gastric passage of video capsule. Gastrointest Endosc. 2005;62:785–90.
15. Koulaouzidis A, Giannakou A, Yung DE, Dabos KJ, Plevris JN. Do prokinetics influence the completion rate in small-bowel capsule endoscopy? A systematic review and meta-analysis. Curr Med Res Opin. 2013;29:1171–85.
16. Carey EJ, Heigh RI, Fleischer DE. Endoscopic capsule endoscope delivery for patients with dysphagia, anatomical abnormalities, or gastroparesis. Gastrointest Endosc. 2004;59:423–6.
17. Seidman EG, Sant'Anna AM, Dirks MH. Potential applications of wireless capsule endoscopy in the pediatric age group. Gastrointest Endosc Clin N Am. 2004;14:207–17.
18. Bandorski D, Dirks MH, Seidman EG, Keuchel M. Swallowing and motility disorders, pacemakers and obesity. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
19. Holden JP, Dureja P, Pfau PR, Schwartz DC, Reichelderfer M, Judd RH, Danko I, Iyer LV, Gopal DV. Endoscopic placement of the small-bowel video capsule by using a capsule endoscope delivery device. Gastrointest Endosc. 2007;65:842–7.
20. Despott EJ, O'Rourke A, Anikin V, Davison C, Panter S, Bromley J, Plaice J, Corbett M, Fraser C. Tracheal aspiration of capsule endoscopes: detection, management, and susceptibility. Dig Dis Sci. 2012;57:1973–4.
21. Cheifetz AS, Kornbluth AA, Legnani P, Schmelkin I, Brown A, Lichtiger S, Lewis BS. The risk of retention of the capsule endoscope in patients with known or suspected Crohn's disease. Am J Gastroenterol. 2006;101:2218–22.
22. Caunedo-Alvarez A, Romero-Vazquez J, Herrerias-Gutierrez JM. Patency and agile capsules. World J Gastroenterol. 2008;14:5269–73.
23. Herrerias JM, Leighton JA, Costamagna G, Infantolino A, Eliakim R, Fischer D, Rubin DT, Manten HD, Scapa E, Morgan DR, Bergwerk AJ, Koslowsky B, Adler SN. Agile patency system eliminates risk of capsule retention in patients with known intestinal strictures who undergo capsule endoscopy. Gastrointest Endosc. 2008;67:902–9.
24. Ladas SD, Triantafyllou K, Spada C, Riccioni ME, Rey JF, Niv Y, Delvaux M, De Franchis R, Costamagna G, Committee ECG. European Society of Gastrointestinal Endoscopy (ESGE): recommendations (2009) on clinical use of video capsule endoscopy to investigate small-bowel, esophageal and colonic diseases. Endoscopy. 2010;42:220–7.
25. Lipka S, Vacchio A, Katz S, Ginzburg L. Retained capsule extraction 6 years after wireless bowel capsule endoscopy: the importance of follow up. J Crohns Colitis. 2013;7:e271–2.
26. De Magalhaes Costa MH, da Luz Moreira A, Zaltman C. Wireless capsule endoscopy fragmentation in a patient with Crohn's disease. Clin Gastroenterol Hepatol. 2011;9:e116–7.
27. Spada C, Spera G, Riccioni M, Biancone L, Petruzziello L, Tringali A, Familiari P, Marchese M, Onder G, Mutignani M, Perri V, Petruzziello C, Pallone F, Costamagna G. A novel diagnostic tool for detecting functional patency of the small bowel: the given patency capsule. Endoscopy. 2005;37:793–800.
28. Costamagna G, Riccioni ME, Urgesi R, Keuchel M, Steinbruck I. Patency capsule. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
29. Davison C, de Franchis R, Iannuzzi F. Procedure for small bowel video capsule endoscopy. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
30. Lewis BS, Keuchel M, Wiedbrauck F, Caselitz J, Kakugawa Y, Saito Y. Malignant tumors. In: Martin Keuchel FH, Tajiri H, editors. Video capsule endoscopy: a reference guide and Atlas. Berlin/Heidelberg: Springer-Verlag; 2014.

31. Rokkas T, Papaxoinis K, Triantafyllou K, Pistiolas D, Ladas SD. Does purgative preparation influence the diagnostic yield of small bowel video capsule endoscopy?: a meta-analysis. Am J Gastroenterol. 2009;104:219–27.
32. Niv Y, Niv G. Capsule endoscopy: role of bowel preparation in successful visualization. Scand J Gastroenterol. 2004;39:1005–9.
33. Gralnek IM, Rabinovitz R, Afik D, Eliakim R. A simplified ingestion procedure for esophageal capsule endoscopy: initial evaluation in healthy volunteers. Endoscopy. 2006;38:913–8.
34. Adler SN, Spada C, Eliakim R. Colon capsule endoscopy: procedure and evaluation. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
35. Buscaglia JM, Giday SA, Kantsevoy SV, Clarke JO, Magno P, Yong E, Mullin GE. Performance characteristics of the suspected blood indicator feature in capsule endoscopy according to indication for study. Clin Gastroenterol Hepatol. 2008;6:298–301.
36. Eliakim R, Sharma VK. Esophageal capsule endoscopy. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
37. Nakamura T, Delvaux M, Hagenmuller F. Stomach and duodenum. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
38. Steinbruck I, Keuchel M, Hagenmuller F, Von Herbay A. Normal small intestine. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
39. Toth E, Wiedbrauck F, Riemann JF. Intestinal lymphangiectasia. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
40. Appleyard MN, Keuchel M, Hagenmuller F. Findings in the colon. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
41. Carey EJ, Leighton JA, Heigh RI, Shiff AD, Sharma VK, Post JK, Fleischer DE. A single-center experience of 260 consecutive patients undergoing capsule endoscopy for obscure gastrointestinal bleeding. Am J Gastroenterol. 2007;102:89–95.
42. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1997;92:419–24.
43. Gerson LB, Fidler JL, Cave DR, Leighton JA. ACG clinical guideline: diagnosis and management of small bowel bleeding. Am J Gastroenterol. 2015;110:1265–87. quiz 1288
44. Liao Z, Gao R, Xu C, Li ZS. Indications and detection, completion, and retention rates of small-bowel capsule endoscopy: a systematic review. Gastrointest Endosc. 2010;71:280–6.
45. Sidhu R, McAlindon ME, Drew K, Hardcastle S, Cameron IC, Sanders DS. Evaluating the role of small-bowel endoscopy in clinical practice: the largest single-centre experience. Eur J Gastroenterol Hepatol. 2012;24:513–9.
46. Pasha SF, Leighton JA, Das A, Harrison ME, Decker GA, Fleischer DE, Sharma VK. Double-balloon enteroscopy and capsule endoscopy have comparable diagnostic yield in small-bowel disease: a meta-analysis. Clin Gastroenterol Hepatol. 2008;6:671–6.
47. Apostolopoulos P, Liatsos C, Gralnek IM, Kalantzis C, Giannakoulopoulou E, Alexandrakis G, Tsibouris P, Kalafatis E, Kalantzis N. Evaluation of capsule endoscopy in active, mild-to-moderate, overt, obscure GI bleeding. Gastrointest Endosc. 2007;66:1174–81.
48. Jones BH, Fleischer DE, Sharma VK, Heigh RI, Shiff AD, Hernandez JL, Leighton JA. Yield of repeat wireless video capsule endoscopy in patients with obscure gastrointestinal bleeding. Am J Gastroenterol. 2005;100:1058–64.
49. Pennazio M, Keuchel M, Jensen DM, Dulai GS. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
50. Delvaux M, Korman LY, Keuchel M. Terminology. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
51. Triester SL, Leighton JA, Leontiadis GI, Gurudu SR, Fleischer DE, Hara AK, Heigh RI, Shiff AD, Sharma VK. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. Am J Gastroenterol. 2006;101:954–64.
52. Lopes S, Figueiredo P, Portela F, Freire P, Almeida N, Lerias C, Gouveia H, Leitao MC. Capsule endoscopy in inflammatory bowel disease type unclassified and indeterminate colitis serologically negative. Inflamm Bowel Dis. 2010;16:1663–8.
53. Kornbluth A, Colombel JF, Leighton JA, Loftus E, ICCE. ICCE consensus for inflammatory bowel disease. Endoscopy. 2005;37:1051–4.
54. Goldstein JL, Eisen GM, Lewis B, Gralnek IM, Zlotnick S, Fort JG, Investigators. Video capsule endoscopy to prospectively assess small bowel injury with celecoxib, naproxen plus omeprazole, and placebo. Clin Gastroenterol Hepatol. 2005;3:133–41.
55. Efthymiou A, Viazis N, Mantzaris G, Papadimitriou N, Tzourmakliotis D, Raptis S, Karamanolis DG. Does clinical response correlate with mucosal healing in patients with Crohn's disease of the small bowel? A prospective, case-series study using wireless capsule endoscopy. Inflamm Bowel Dis. 2008;14:1542–7.
56. Rosa B, Moreira MJ, Rebelo A, Cotter J. Lewis score: a useful clinical tool for patients with suspected Crohn's disease submitted to capsule endoscopy. J Crohns Colitis. 2012;6:692–7.
57. Voderholzer WA, Kornbluth A, Legnani PE. Established Crohn's disease. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
58. Leighton JA, Watanabe K, Arguelles-Arias F, Gutierrez JMH. Video capsule endoscopy in suspected Crohn's disease. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
59. McAlindon ME, Hagenmüller F, Fleischer DE. Fields of application. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
60. Rokkas T, Niv Y. The role of video capsule endoscopy in the diagnosis of celiac disease: a meta-analysis. Eur J Gastroenterol Hepatol. 2012;24:303–8.
61. Petroniene R, Dubcenco E, Baker JP, Ottaway CA, Tang SJ, Zanati SA, Streutker CJ, Gardiner GW, Warren RE, Jeejeebhoy KN. Given capsule endoscopy in celiac disease: evaluation of diagnostic accuracy and interobserver agreement. Am J Gastroenterol. 2005;100:685–94.
62. Culliford A, Daly J, Diamond B, RUBIN M, GREEN PH. The value of wireless capsule endoscopy in patients with complicated celiac disease. Gastrointest Endosc. 2005;62:55–61.
63. Schuppan D, Mulder CJ, Collin P, Murray JA. Villous atrophy. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
64. Bjarnason I, Adler SN, Sakamoto C. Physical-chemical small intestinal injury. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
65. Safatle-Ribeiro A, Gay G, Barth E, Keuchel M. Involvement of the small intestine in systemic diseases. In: Keuchel M, Hagenmüller

F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.
66. Burke CA, Santisi J, Church J, Levinthal G. The utility of capsule endoscopy small bowel surveillance in patients with polyposis. Am J Gastroenterol. 2005;100:1498–502.
67. Schulmann K, Hollerbach S, Kraus K, Willert J, Vogel T, Moslein G, Pox C, Reiser M, Reinacher-Schick A, Schmiegel W. Feasibility and diagnostic utility of video capsule endoscopy for the detection of small bowel polyps in patients with hereditary polyposis syndromes. Am J Gastroenterol. 2005;100:27–37.
68. Gupta A, Postgate AJ, Burling D, Ilangovan R, Marshall M, Phillips RK, Clark SK, Fraser CH. A prospective study of MR enterography versus capsule endoscopy for the surveillance of adult patients with Peutz-Jeghers syndrome. AJR Am J Roentgenol. 2010;195:108–16.
69. Tescher P, Macrae FA, Speer T, Stella D, Gibson R, Tye-Din JA, Srivatsa G, Jones IT, Marion K. Surveillance of FAP: a prospective blinded comparison of capsule endoscopy and other GI imaging to detect small bowel polyps. Hered Cancer Clin Pract. 2010;8:3.
70. Ohmiya N, Nakamura M, TAKENAKA H, Morishima K, Yamamura T, Ishihara M, Miyahara R, Kawashima H, Itoh A, Hirooka Y, Watanabe O, Ando T, Goto H. Management of small-bowel polyps in Peutz-Jeghers syndrome by using enteroclysis, double-balloon enteroscopy, and video capsule endoscopy. Gastrointest Endosc. 2010;72:1209–16.
71. Pan SY, Morrison H. Epidemiology of cancer of the small intestine. World J Gastrointest Oncol. 2011;3:33–42.
72. Cobrin GM, Pittman RH, LEWIS BS. Increased diagnostic yield of small bowel tumors with capsule endoscopy. Cancer. 2006;107:22–7.
73. Rondonotti E, Pennazio M, Toth E, Menchen P, Riccioni ME, De Palma GD, Scotto F, De Looze D, Pachofsky T, Tacheci I, Havelund T, Couto G, Trifan A, Kofokotsios A, Cannizzaro R, Perez-Quadrado E, De Franchis R, European Capsule Endoscopy, G., Italian Club for Capsule, E. & Iberian Group for Capsule, E. Small-bowel neoplasms in patients undergoing video capsule endoscopy: a multicenter European study. Endoscopy. 2008;40:488–95.
74. Eisen GM, Eliakim R, Zaman A, Schwartz J, Faigel D, Rondonotti E, Villa F, Weizman E, Yassin K, Defranchis R. The accuracy of PillCam ESO capsule endoscopy versus conventional upper endoscopy for the diagnosis of esophageal varices: a prospective three-center pilot study. Endoscopy. 2006;38:31–5.
75. Gralnek IM, Adler SN, Yassin K, Koslowsky B, Metzger Y, Eliakim R. Detecting esophageal disease with second-generation capsule endoscopy: initial evaluation of the PillCam ESO 2. Endoscopy. 2008;40:275–9.
76. Di Pietro M, Fitzgerald RC. Screening and risk stratification for Barrett's esophagus: how to limit the clinical impact of the increasing incidence of esophageal adenocarcinoma. Gastroenterol Clin N Am. 2013;42:155–73.
77. Shaheen NJ, Falk GW, Iyer PG, Gerson LB, American College OF, G. ACG clinical guideline: diagnosis and management of Barrett's esophagus. Am J Gastroenterol. 2016;111:30–50. quiz 51
78. Krok KL, Wagennar RR, Kantsevoy SV, Thuluvath PJ. Esophageal capsule endoscopy is not the optimal technique to determine the need for primary prophylaxis in patients with cirrhosis. Arch Med Sci. 2016;12:365–71.
79. Mccarty TR, Afinogenova Y, Njei B. Use of wireless capsule endoscopy for the diagnosis and grading of esophageal varices in patients with portal hypertension: a systematic review and meta-analysis. J Clin Gastroenterol. 2017;51:174–82.
80. Eliakim R, Yassin K, Niv Y, Metzger Y, Lachter J, Gal E, Sapoznikov B, Konikoff F, Leichtmann G, Fireman Z, Kopelman Y, Adler SN. Prospective multicenter performance evaluation of the second-generation colon capsule compared with colonoscopy. Endoscopy. 2009;41:1026–31.
81. Spada C, Hassan C, Munoz-Navas M, Neuhaus H, Deviere J, Fockens P, Coron E, Gay G, Toth E, Riccioni ME, Carretero C, Charton JP, Van Gossum A, Wientjes CA, Sacher-HUVELIN S, Delvaux M, Nemeth A, Petruzziello L, De Frias CP, Mayershofer R, Amininejad L, Dekker E, Galmiche JP, Frederic M, Johansson GW, Cesaro P, Costamagna G. Second-generation colon capsule endoscopy compared with colonoscopy. Gastrointest Endosc. 2011;74:581–589.e1.
82. Heresbach D, Barrioz T, Lapalus MG, Coumaros D, Bauret P, Potier P, Sautereau D, Boustiere C, Grimaud JC, Barthelemy C, See J, Serraj I, D'Halluin PN, Branger B, Ponchon T. Miss rate for colorectal neoplastic polyps: a prospective multicenter study of back-to-back video colonoscopies. Endoscopy. 2008;40:284–90.
83. Johnson CD, Chen MH, Toledano AY, Heiken JP, Dachman A, Kuo MD, Menias CO, Siewert B, Cheema JI, Obregon RG, Fidler JL, Zimmerman P, Horton KM, Coakley K, Iyer RB, Hara AK, Halvorsen RA Jr, Casola G, Yee J, Herman BA, Burgart LJ, Limburg PJ. Accuracy of CT colonography for detection of large adenomas and cancers. N Engl J Med. 2008;359:1207–17.
84. Palimaka S, Blackhouse G, Goeree R. Colon capsule endoscopy for the detection of colorectal polyps: an economic analysis. Ont Health Technol Assess Ser. 2015;15:1–43.
85. Morgan DR, Malik PR, Romeo DP, Rex DK. Initial US evaluation of second-generation capsule colonoscopy for detecting colon polyps. BMJ Open Gastroenterol. 2016;3:e000089.
86. Sieg A. Colon capsule endoscopy compared with conventional colonoscopy for the detection of colorectal neoplasms. Expert Rev Med Devices. 2011;8:257–61.
87. Aihara H, Tajiri H, Schneider M, Charton J-P, Neuhaus H. Colon capsule endoscopy in screening and surveillance for polyps and cancers. In: Keuchel M, Hagenmüller F, Tajiri H, editors. Video capsule endoscopy: a reference guide and atlas. Berlin/Heidelberg: Springer; 2014.

Device-Assisted Enteroscopy

19

Arthur Kaffes and Mathew J. Keegan

Introduction

Since the first published experience of capsule endoscopy in 2000, there have been exciting changes in the diagnostic and therapeutic rolls for endoscopy in small bowel disease [26]. The first description of a double-balloon enteroscope (DBE) was published by Yamamoto in 2001 [78] and was subsequently developed by Fujinon Corporation [79]. This technique offered reproducible deep bowel intubation with clinically useful success rates [30, 77] and has since allowed adaptation of a variety of therapeutic modalities to the previously out-of-reach small bowel [29].

Additional methods for device-assisted enteroscopy (DAE) have since been described. In 2008 Tsujikawa and colleagues described a method employing a single balloon on an overtube, in conjunction with tip deflection, to achieve deep small intestinal intubation. They described their technique as an easy to perform adjunct to DBE and reported six cases of successful total enteroscopy (from 24 attempts) [72]. Later the same year, another group reported on a product (Discovery Small Bowel spiral overtube) which could be used with either an Olympus or Fujinon enteroscope and, by a spiralling mechanism, pleat the small bowel over the shaft of the scope. Again effective anterograde deep bowel intubation was reported, with a suggestion of potentially favourable insertion times with spiral enteroscopy [1].

This chapter aims to describe the various DAE techniques and explore the current state of their clinical use.

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Indications and Common Findings

Practical Considerations

- Video capsule endoscopy is important to DAE clinical practice, both as an important source of referral and as a minimally invasive means to assess many small bowel presentations.
- In developed countries, most small bowel diagnostic needs are met by capsule endoscopy and other less invasive modalities (when tissue acquisition is not needed).
- The majority of therapeutic procedures are for obscure GI bleeding.
- The role for DAE in altered anatomy is important; the most widely reported of these indications are for ERCP in Roux-en-Y anatomy and for failed colonoscopy.

By far the most common indication for both SBE and DBE is OGIB, which accounts for 60–97% of referrals for these procedures [15, 57, 75]. Following OGIB, Crohn's disease is the next most frequently quoted indication for DAE, ranging

Indications

Diagnosis

- Obscure GI bleeding (OGIB)
- Abnormality on capsule endoscopy or enterography/cross-sectional imaging
- Small bowel stricturing disease
- Evaluation of small bowel tumours and surveillance of polyposis syndromes
- Tissue or microbiological sampling – particularly segmental processes beyond the duodenum

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- Chronic diarrhoea
- Crohn's disease

Therapeutic

- Haemostasis for obscure GI bleeding
- Retained foreign bodies, including video capsules
- Luminal stenting
- Polypectomy and resection of small bowel masses – e.g. Peutz-Jeghers syndrome, small bowel adenomas
- Dilatation of small bowel stricturing disease, particularly Crohn's

Salvage Therapy

- Foregut examination in gastric bypass patients
- ERCP with post-Roux-en-Y anatomy
- PEG placement with post-gastric bypass anatomy
- Failed colonoscopy

from 11% to 22% in large databases [24, 57]. Despite this it is seldom the first-line investigation in Crohn's disease.

Other reported indications and findings include surveillance of polyposis syndromes (such as Peutz-Jeghers [see Fig. 19.1] and small bowel involvement in familial adenomatous polyposis [FAP]) and small bowel masses including neuroendocrine tumours (NET), gastrointestinal stromal tumours (GIST) and small bowel lymphoma [5, 16, 36]; NSAID-related small bowel lesions [22]; investigation of cause of small bowel obstruction; and abnormalities in other imaging modalities, distal coeliac disease and other rarer conditions [59, 75]. Figure 19.2 shows a jejunal adenocarcinoma which presented with intussusception.

The original clinical series for DAE showed a predominance of diagnostic procedures, reporting a therapeutic intervention rate of only 18% [77]. There appears to be a trend toward a higher proportion of therapeutic DAE procedures in subsequent reports (42% in more recent series) [14, 45].

As already stated the most common indication for DAE is OGIB [43]. Xin and colleagues in their systemic review of the first decade of DAE practice noted a separation in the most commonly found cause of small bowel bleeding with inflammatory lesions (37.6%) in Eastern countries and vascular lesions (65.9%) in Western countries [75]. Knowing this, argon plasma coagulation (APC), and haemostatic clips for pulsatile lesions, can be made ready by routine. Dulic-Lakovic and colleagues have reported on a series of ten patients with small Dieulafoy lesions treated during DAE with successful initial haemostasis from a variety of modalities – APC in three, haemostatic clips in three, injection therapy alone in one, injection with haemostatic clips in two and injection combined with APC in one [9].

DAE is invasive and certainly not the only tool for investigating an OGIB. Careful upper and lower GI endoscopy should be performed first, with adequate visualisation and findings which do not account for the clinical presentation. Once this point is satisfied, the choice between DAE, VCE and other modalities (such as CT angiography) is influenced by rapidity of bleeding and patient stability. In stable patients performing an initial VCE for OGIB not only allows for a diagnosis by less invasive means in many patients; it also helps plan the most appropriate route of insertion and equipment likely to be required [18, 38]. In stable patients with active bleeding (>0.5 mL/min), CT angiography can also be used to locate the cause of blood loss. In unstable patients with active bleeding, the options include proceeding directly to DAE if available or conventional angiography [20]. Figure 19.3 shows a lesion which was found to be the source of an obscure gastrointestinal bleed presentation referred to our centre.

Other reported therapeutic DAE procedures include polypectomy (both traditional snare and EMR), stenting and dilatation. The role of polypectomy in DAE is hugely important for patients with Peutz-Jeghers syndrome, many of whom may otherwise face surgery from a young age [29, 59]. After Crohn's disease, other causes of small bowel stricturing requiring DAE-directed therapy include NSAID usage, previous radiotherapy, small bowel surgery and enteric ischemia. While NSAID enteropathy can be extensive enough to require surgical excision [23], most cases are amenable to definitive endoscopic therapy [7, 58, 60]. Figure 19.4 shows a Crohn's stricture in the ileum which is dilated under endoscopic view.

DAE has been used as a salvage procedure. DAE with a retrograde approach is a useful tool for failed colonoscopy. The reasons for failed colonoscopy were largely related to adhesions or looping [17, 55]. A randomised trial comparing SBE and DBE in 21 patients whom had failed colonoscopy did not show any difference in caecal intubation or polyp detection [76]. To date the same results have not been shown for SE; however, the ability to perform SE in the retrograde direction has been established [35].

The role of all three DAE modalities for the performance of ERCP in patients with surgically altered anatomy has been well established. Factors contributing to the difficulty in performing conventional ERCP in these patients can include an excessively long reconstructed proximal intestine relative to the endoscope, surgical adhesions, the approach angle of the afferent limb and difficulties identifying the correct limb. While DAE devices greatly improve the success rate in reaching the blind end, there are often restrictions imposed on which conventional ERCP equipment can be used owing to the smaller accessory channel size in many enteroscopes and

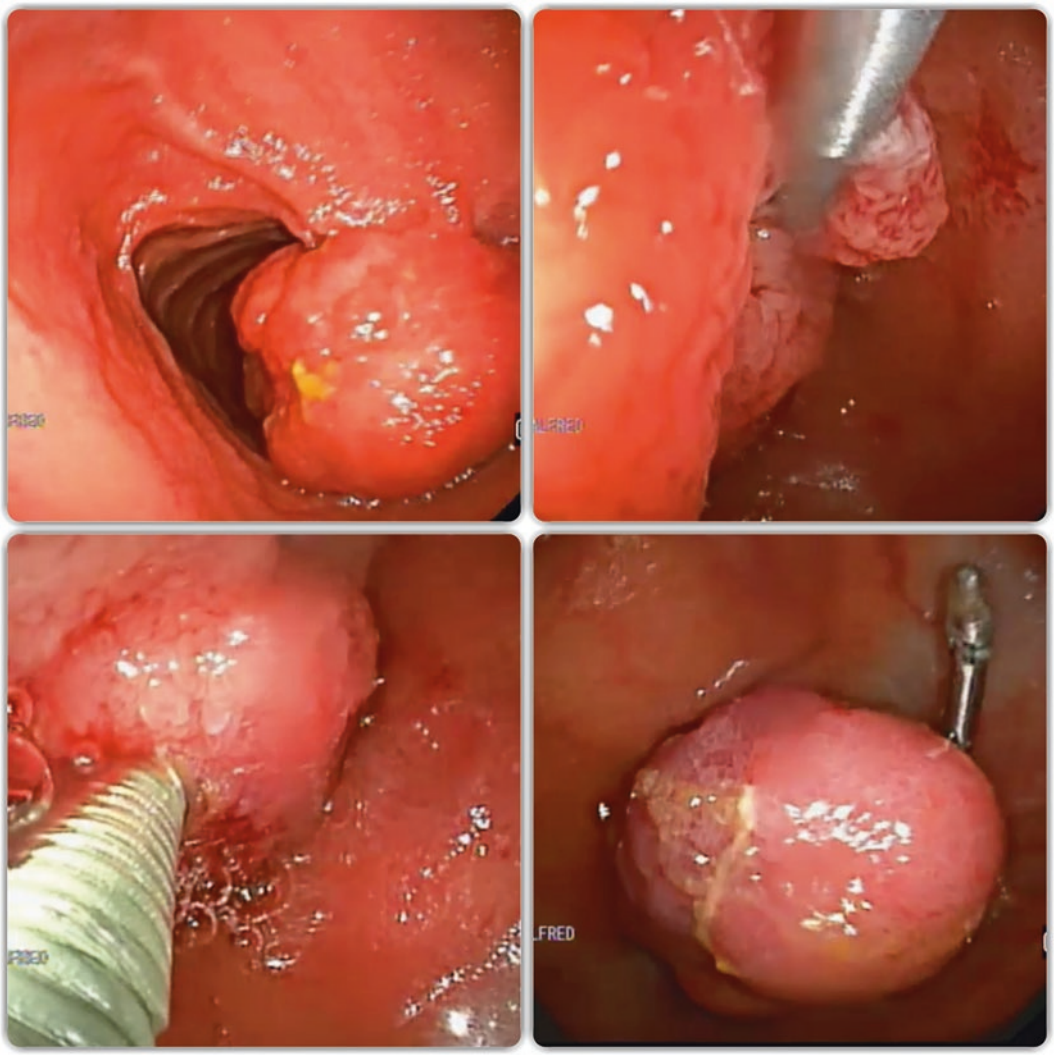

Fig. 19.1 Removal of Peutz-Jeghers polyp, including clipping of polyp stalk, injection of adrenaline solution into stalk and snare polypectomy

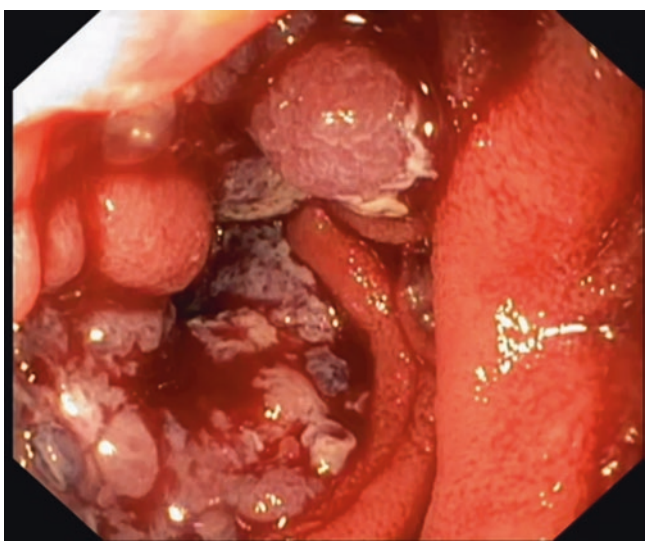

Fig. 19.2 Jejunal adenocarcinoma which presented with an intussusception

the greater length of enteroscopes relative to duodenoscopes. Some of these difficulties have been overcome with the recent introduction of short-type DBE (EI-530B, Fujifilm, Osaka, Japan) and SBE (SIF-Y0004, SIF-Y0004-V01, Olympus Medical Systems, Tokyo, Japan) [27, 68, 80, 81]. A large multicentre US trial comparing 180 SBE, DBE and SE-assisted ERCP procedures in 129 patients with altered anatomy reported a success rate of 63% which was not different between the three modalities [67]. Figure 19.5 shows a patient who has presented with cholangitis due to a stenosed hepaticojejunostomy after liver transplantation. A double-balloon ERCP is performed where the stenosis is dilated before sweep with a balloon to remove pus and debris.

DAE has been used to insert percutaneous feeding tubes in gastric bypass anatomy patients [64], as well as more distally inserted percutaneous jejunostomy tubes with both the DBE and SBE systems [4, 6].

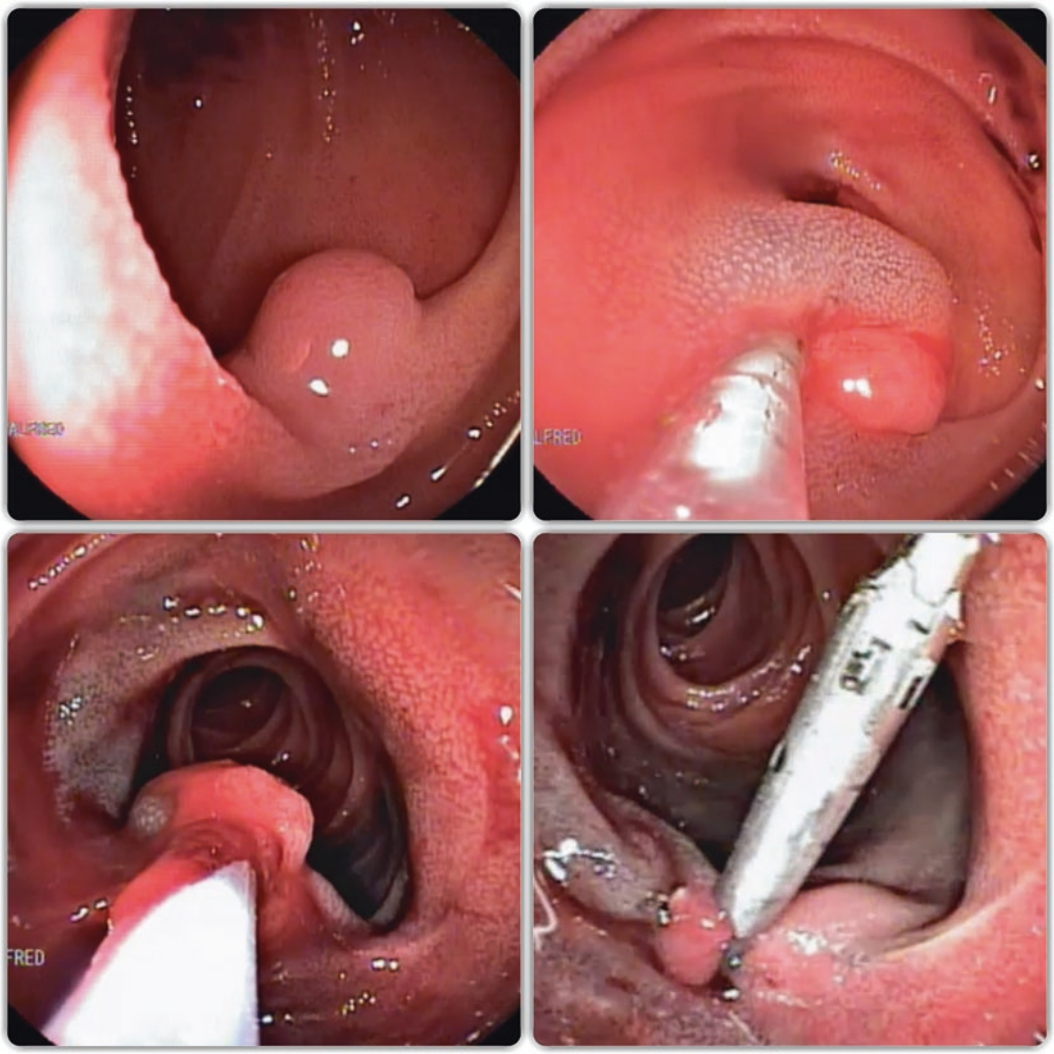

Fig. 19.3 Identification of a small bleeding lesion in the ileum. Submucosal injection is performed prior to polypectomy. A haemostatic clip is placed. Both a haemostatic clip and tattoo are used to facilitate identification at angiography or surgery in case of ongoing bleeding

Contraindications

Practical Considerations

- Intra-abdominal adhesions may prolong the procedure and hamper the depth of insertion, but do not contraindicate enteroscopy.

Contraindications

- Existing perforation
- Weakened intestinal wall
- High-grade obstruction
- Significant bleeding tendency
- Inability to tolerate prolonged anaesthetic
- Latex allergy (DBE)

As a starting point, DAE carries contraindications common to other endoscopy including, but not limited to, untreated haemodynamic instability, existing perforation, fulminant colitis and factors which would contraindicated an aesthetic time longer than most other endoscopic procedures [66].

Given the nature of the push-pull technique for BAE, or torqueing in the case of SE, the concern regarding susceptibility to perforation is well grounded, and these should be considered. Factors encountered in patients undergoing DAE, which may predispose to enteric perforation, thus may be considered as a relative contraindication, included recent formation of enteric anastomosis, severe small bowel ulceration, small bowel lymphoma with recent chemotherapy and connective tissue diseases such as Ehlers-Danlos syndrome. Bleed tendencies have been associated with haemorrhage or intramural haematoma. Severe inflammatory states, be it from Crohn's or otherwise, also increases the risk of perforation [39, 50, 66, 77].

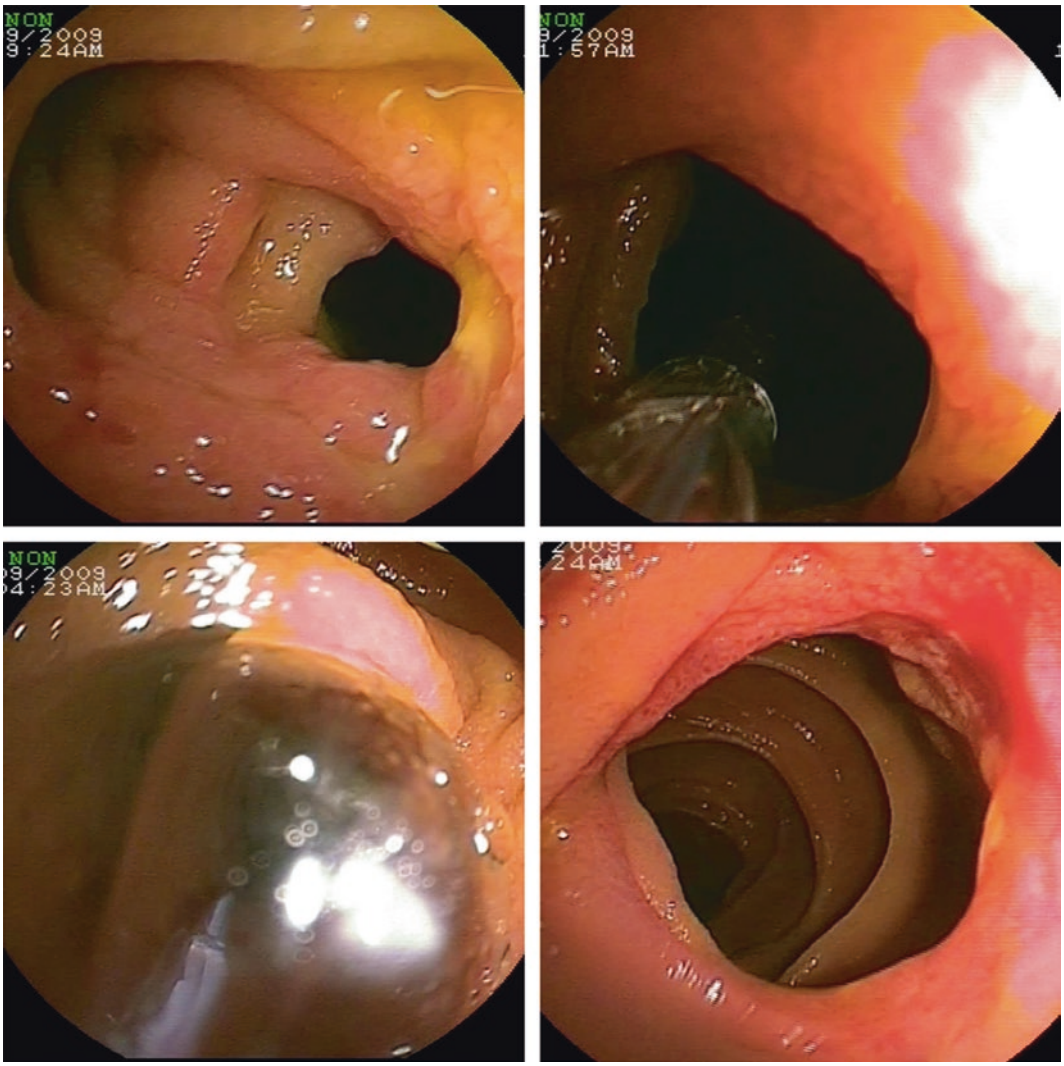

Fig. 19.4 Ileal Crohn's stricture (*top left*) dilated with through the scope balloon (*top right*, *bottom left*). The image in the *bottom right* shows the dilated stricture which we were able to traverse

Both the overtubes and balloons for the Fujinon double-balloon enteroscopy contain latex, and thus severe allergy to latex is a contraindication. Significant oesophageal or rectal varices are also a contraindication if they involve the intended route of approach.

Instruments and Accessories

There are three DAE systems, which need to be described separately. All three systems have an enteroscope (and related equipment including light source and processor) and an overtube. In the case of the SBE and DBE systems, there is also a balloon control unit, whereas the SE overtube has no balloons and the shaft is instead manually rotated to advance the enteroscope.

Practical Considerations

- The DBE system is the only one to contain latex.
- The working channel diameter is an important consideration when choosing an enteroscope for a therapeutic procedure.
- The inner working tube diameter relative to outer endoscope diameter is essential to review when choosing a compatible endoscope for spiral enteroscopy.

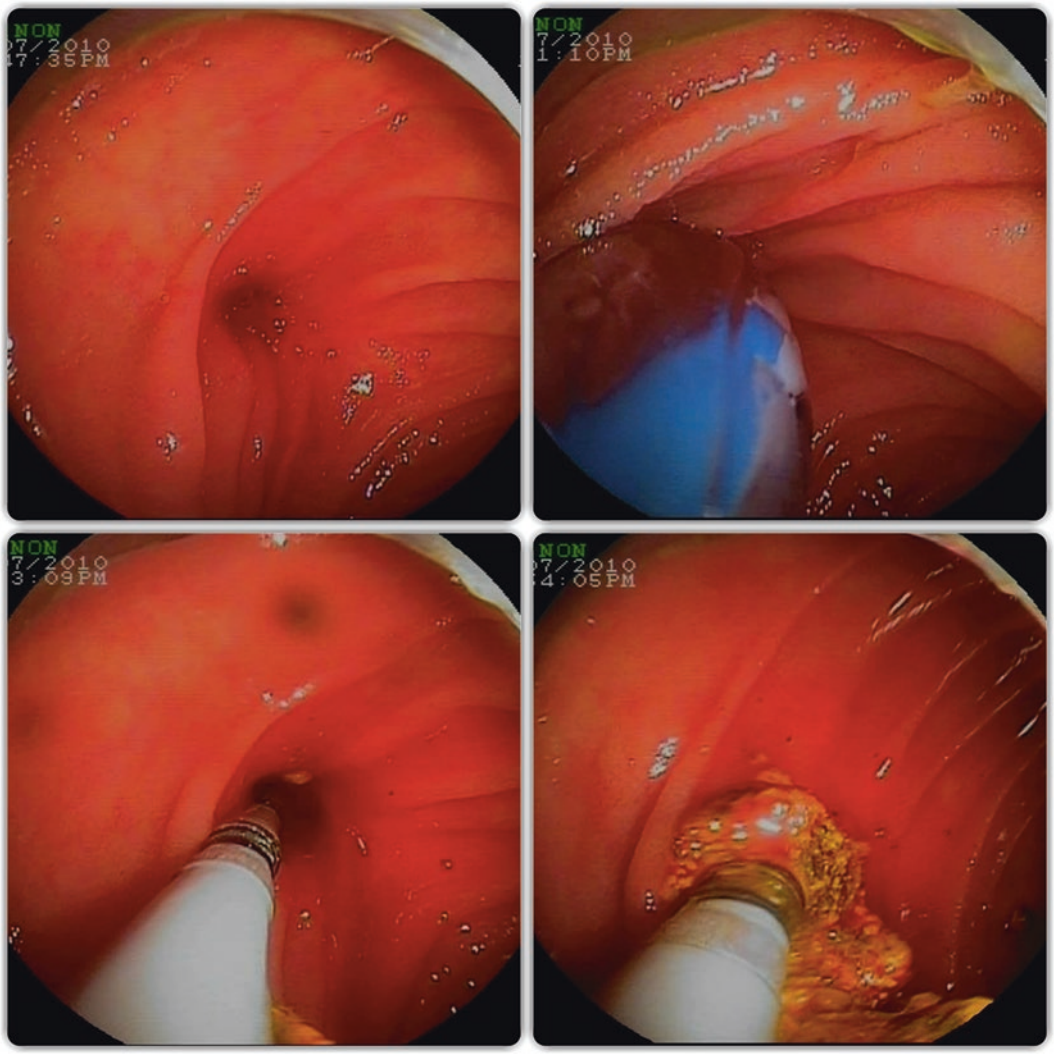

Fig. 19.5 Double-balloon ERCP. A stenosed hepaticojejunostomy (*top left*) is dilated (*top right*) prior to balloon trawling (*bottom left* and *right*)

Instruments and Accessories

Double-Balloon Enteroscopy

- Fujinon enteroscope
- DBE overtube
- Enteroscope balloon
- Balloon pump controller
- Setting tool
- Processor and light source

Single-Balloon Enteroscopy

- Olympus enteroscope
- SBE splinting tube with balloon
- Balloon controller unit
- Processor and light source

Spiral Enteroscopy

- Endo-Ease overtube
- Compatible enteroscope or colonoscope and equipment

Double-Balloon Enteroscopy

DBE employs one of three coupled enteroscopes with accompanied overtube, both of which have distally mounted latex balloons. The balloons serve to anchor their corresponding component within the small bowel and via the balloon control apparatus, may be inflated or deflated singularly or in unison. This allows one component to be advanced while the other anchors the bowel or for both to be withdrawn in unison to concertina the small bowel and straighten

Table 19.1 Features of the various enteroscopes

	Olympus	Fujinon		
Model	SIF-Q180	EN-450P5/20	EN-450T5	EC-450BI5
Type	SBE	DBE, diagnostic	DBE, therapeutic	DBE, short
Field of view	140°	120°	140°	140°
Outer diameter	9.2 mm	8.5 mm	9.4 mm	9.4 mm
Bending capability				
Up	180°	180°	180°	180°
Down	180°	180°	180°	180°
Left	160°	160°	160°	160°
Right	160°	160°	160°	160°
Working channel diameter	2.8 mm	2.2 mm	2.8 mm	2.8 mm
Working length	2000 mm	2000 mm	2000 mm	1520 mm
Total length	2345 mm	2300 mm	2300 mm	1820 mm

Table 19.2 Overtube specifications

Manufacturer	Olympus	Fujinon			Spirus medical		
Overtube model	ST-SB1	TS-12140	TS-13140	TS-13101	Endo-ease discovery, standard profile	Endo-ease discovery, low profile	Endo-ease vista, retrograde
Type	SBE overtube	DBE overtube	DBE overtube	DBE overtube	Spiral enteroscopy	Spiral enteroscopy	Spiral enteroscopy
Compatible with	SIF-Q180	EN-450P5/20	EN-450T5 EN-450T5/W	EC-450BI5	SIF-Q180	SIF-Q180	Pediatric colonoscope
					EM-450T5	EN-450T5	
					EN-450T5/W	EN-450T5/W	
					EN-450P5/20	EN-450P5/20	
					EC-450BI5	EC-4S0BI5	
Outer diameter	13.2 mm	12.2 mm	13.2 mm	13.2 mm	14.5 mm	14.5 mm	17.4 mm
Inner diameter	11 mm	10 mm	10.8 mm	10.8 mm	9.8 mm	9.8 mm	13 mm
Balloon diameter or spiral height	40 mm	40 mm	40 mm	40 mm	5.5 mm	4.5 mm	5 mm
Working length	1320 mm	1350 mm	1350 mm	950 mm			
Total length	1400 mm	1450 mm	1450 mm	1050 mm	1180 mm	1180 mm	1000 mm
Material	Silicone	Latex	Latex	Latex	Polyvinyl chloride	Polyvinyl chloride	Polyvinyl chloride

the lumen ahead of the enteroscope both to minimise looping and increase depth of insertion.

There currently exist three DBE systems: a diagnostic (EN-450P) and therapeutic (EN-450T) in the standard length (2300 mm) and a shorter system (EC-450B15) for performing procedures such as ERCP in patient with surgically altered anatomy as well as completing ileocolonoscopy in patients who have failed standard colonoscopy. The standard length enteroscope with 2.8 mm working channel (EN-450T; Fujinon, Saitama, Japan) is used for most procedures in adults and allows passage of commonly used enteroscopic accessories. The EN-450P (Fujinon) is intended for diagnostic procedures, and the shorter enteroscope, with 2.8 mm working channel, is designed for ERCP and other therapeutic work in patients with postsurgical altered anatomy. The specifications are detailed in Table 19.1.

Each of the three enteroscope models has a corresponding, disposable, latex overtube with balloon at its distal extent. The overtube for EN-450T is 145 cm long and 13.2 mm in outer diameter. There is both a narrower and shorter overtube available for the EN-450P and EC-450BI, respectively, and these are detailed in Table 19.2. The overtubes have an irrigation lumen through which water is flushed to lubricate the space between the enteroscope and the overtube.

Both the enteroscope and overtube balloons are controlled by a balloon pump controller (PB-20; Fujinon), which regulates the internal pressure to 5.6 kPa. Each balloon can be

operated individually. An alarm signals if balloon pressure is excessive.

Single-Balloon Enteroscopy

The Olympus system introduced in 2007 uses a single dedicated enteroscope (SIF-Q180; Olympus America Inc., Central Valley, Pa) and with a disposable silicone overtube (ST-SB1; Olympus). The latex-free, silicone overtube, like the Fujinon system, has an inflatable balloon at its distal end, which is controlled by an overtube balloon control unit (OBCU) with a regulated pressure (5.4 kPa). The OBCU can be operated both by a front panel and remote control.

The working length of the enteroscope is 200 cm, with an outer diameter of 9.2 mm and working channel diameter, which matches the commonly used version of DBE (2.8 mm). The overtube is 140 cm in length, with an outer diameter of 13.2 mm. It has a hydrophilic inner lining and like the DBE system is water lubricated.

Spiral Enteroscopy

The spiral enteroscopy system from Spirus Medical Inc. (Stoughton, Mass) differs the most in design from these three DAE systems. Rather than balloons, it employs a disposable overtube with an elevated spiral ridge which pleats the small bowel over the device by rotation of the tube shaft. The overtube is 118 cm in length with either 4.5 mm or 5.5 mm raised spiral at the distal end. Unlike the SBE and DBE systems, the Spirus Medical system does not have a proprietary enteroscope. The antegrade SE overtubes (Endo-Ease Discovery, standard and low profile) are compatible with 200 cm enteroscopes between 9.1 and 9.5 mm in external diameter. The retrograde overtube (Endo-Ease Vista) is 100 cm in length and works with a standard paediatric colonoscope. On insertion the overtube is coupled to the enteroscope so as to allow rotation but not longitudinal movement. It can be uncoupled to allow insertion and withdrawal independent of the overtube.

The Procedure

Several authors have shown that the use of CO_2, when compared to air insufflation, improves both the depth of insertion and patient comfort [25, 74]. The antegrade route is advised for lesions in the proximal two thirds of small bowel as measured by VCE transit [18]. While these factors are common across all three modalities presented here, some other aspects differ greatly enough that they need to be discussed separately.

At a practical level, there appear to be differences in both the mean procedure times and depth of insertion between the different systems. The mean publish procedure times for SE are the shortest, at 40 min for the oral route and 46 min for the rectal route. SBE and DBE follow at 60 and 70 min and 69 and 89 min for the oral and rectal routes, respectively [37]. Several cohort and randomised control studies have shown no difference in depth of insertion between SBE and DBE [8, 11, 62]; however, DBE has been shown to have a significantly greater depth of insertion when compared with SE [44, 52]. Overall the mean depth of insertion appears to decrease from DBE to SBE to SE with reported mean ranges of 240–360 cm [12, 21, 37, 45, 47, 48, 50], 133–256 cm [34, 63, 73] and 176–250 cm [1, 34, 56] in the antegrade direction, respectively. DBE has a clear advantage in complete enteroscopy rate [8, 11, 37, 42, 69].

Depth of insertion can be difficult to establish from landmarks. One described method is to correlate each 5 cm of overtube insertion with 40 cm of small bowel visualisation [28, 45, 48], while other authors have described a reproducible correlation between small bowel fold count and depth of insertion [11]. Overall factors shown to correlate with procedure time include operator expertise, previous surgical history, adhesions and obesity [28]. Lastly, while once considered a necessity for DAE, fluoroscopy has been shown not to affect technical success (depth of insertion) and has fallen out of favour [40].

Double-Balloon Enteroscopy

Before the enteroscope balloon can be attached, the overtube must first be loaded over the enteroscope. The balloon is pulled onto the cardboard applicator and loaded over the distal tip of the enteroscope. Correct positioning should be verified by inflation and deflation of the balloon before the band applicator is used to apply the latex bands to secure each end of the balloon. If the balloon does not inflate, run dry air through the inflation channel, as water in this channel after processing is a common reason for failure of balloon inflation. Next, connect the balloon inflation tubing to the respective input for the overtube and enteroscope balloons, and confirm correct orientation of the tubing with the enteroscope and overtube balloon inflation buttons on the balloon control device prior to commencement of the procedure.

For antegrade procedures, the enteroscope and overtube are inserted with both balloons deflated until the operator is confidently distal to the second part of the duodenum, and the overtube balloon is then inflated. It is important to be beyond the major papilla before the first balloon inflation, as inflating the balloon in the second part of the duodenum is thought to be associated with a greater risk of pancreatitis [61]. The overtube balloon is inflated to secure the position, and the enteroscope is

advanced before inflating the enteroscope balloon. The overtube balloon must be deflated before advancing, and care must be taken not to advance beyond the thick white mark on the enteroscope so as to avoid dislodging the enteroscope balloon. Once this is done, both balloons are simultaneously inflated, and the enteroscope and overtube are slowly retracted together to pleat the small bowel onto the overtube and straighten the lumen ahead of the advancing enteroscope as this process is repeated. It is important to take time for mucosal inspection during insertion, as subtle lesions may be difficult to differentiate from minor trauma during withdrawal.

While insertion technique is a prerequisite for adequate depth of insertion and an acceptable procedure time, ensuring all withdrawal is done in a careful controlled manner is essential to mucosal inspection. This is done by reversing the technique for insertion; first, the enteroscope balloon is kept inflated while the overtube balloon is deflated and then withdrawn, before inflating the overtube and bringing the enteroscope back to meet it [49, 54]. This is repeated until the duodenojejunal junction at which point balloon inflation is avoided as on insertion.

For the retrograde DBE procedure, the colon is prepared as per colonoscopy. Depending on patient factors and endoscopist preference, the enteroscope can either be inserted to the caecum directly or in the push-pull manner described for the antegrade approach. Once the caecum is intubated, the overtube balloon is inflated to hold this position, the ileocaecal valve is intubated, and the enteroscope is advanced into the terminal ileum. Once the enteroscope balloon is inflated, the overtube can be deflated and advanced into the ileum; from this point, one proceeds as per the push-pull method described previously. It is possible to perform total enteroscopy by one route; however, this usually isn't achievable, and a submucosal tattoo is a useful means to confirm complete enteroscopy when the proceduralist arrives at this mark by the other route [13, 33, 75].

There is no clear agreement regarding the learning curve for DBE. While some authors have stated there is not a distinct learning curve [53, 70], Mehdizadeh and colleagues showed an improvement in visualisation and procedure time that continued beyond 10–15 cases [50].

Single-Balloon Enteroscopy

The SBE system has many similarities to DBE including the overtube back loaded over the enteroscope and the balloon control buttons, with the exception of there being no enteroscope balloon. The procedure starts as per the method described for DBE, with intubation to the distal duodenum prior to the use of the overtube balloon; however, rather than using a balloon to anchor the enteroscope, the endoscopist angulates the distal tip of the enteroscope (with or without mucosal suctioning) when deflating the balloon to advance the overtube or when pulling both back in unison to shorten the small bowel [31, 32, 73]. This process is repeated to advance the enteroscope.

For retrograde procedures, a colonoscopy preparation is again needed. Like with DBE, the device can be inserted directly to the caecum as per a colonoscopy technique, or in difficult colons, a push-pull technique as describe for antegrade SBE can be employed. The overtube is used to anchor the device in the caecum and allow for a controlled position while attempting intubation of the ileocaecal valve. The tip angulation technique, with or without mucosal suctioning, is employed to stabilise the enteroscope position, while the overtube is advanced into the ileum.

Similar to the situation with DBE, it appears that ongoing improvement in mucosal visualisation and procedure time are seen beyond 10–15 procedures [10].

Spiral Enteroscopy

This final technique is the most dissimilar. Again this is a two-person procedure requiring both an endoscopist and an assistant to operate the overtube. Prior to being back-fed onto a compatible enteroscope, the overtube needs to be lined with the supplied Endo-Ease lubricant. With the distal 20 cm of enteroscope beyond the overtube, the device is advanced by a clockwise rotation of the overtube performed by the assistant. Conversely, counterclockwise rotation withdraws the enteroscope.

Excessive insufflation (even with CO_2) can reduce the efficacy of the overtube coupling with the small bowel mucosa. Ensuring this is the case, another cause for failure to advance is looping within the stomach. The technique for gastric loop reduction is to continue slow clockwise rotation of the overtube while applying gentle traction on the enteroscope. Concurrent abdominal pressure can aid insertion. Once maximal insertion is reached, the enteroscope can be uncoupled from the overtube and maximally advanced. For controlled withdrawal, the overtube is recoupled and rotated in a counterclockwise manner. After a colonoscopy bowel preparation, the same technique can be used for the retrograde examination.

While advocates of SE claim a shorter procedure time, the rate of total enteroscopy is significantly lower than either balloon-assisted technique [52].

Complications

The types of complications encountered in DAE have significant overlap across the three modalities, some difference in incidence and a few particular concerns. Generally speaking the procedures are safe; and reported risks include bleeding, perforation, mucosa damage, pancreatitis and risks associ-

ated with an extended anaesthesia time are proportionate to many other endoscopic procedures.

The majority of available data in this area are for DBE and include three large databases comprising over 8000 patients, which reflect an adverse event rate close to 1% [19, 51, 57]. This rises to 3–4% when therapeutic procedures are considered in isolation [46, 51]. Of the major adverse events, the rates of pancreatitis (antegrade procedures) and perforation have been reported at close to 0.3% [19, 51, 57]. One case of pancreatitis has been reported by the rectal route [19]. In the German registry, there was one death reported from 3894 procedures performed [53].

The adverse events encountered in SBE are similar to those seen in DBE, and in line with DBE, the overall adverse event rate is 1% [41]. It is thought that hooking of the enteroscope tip during advancement of the overtube may lead to a higher rate of mucosal injury and perforation, which may be mitigated by using the mucosal suctioning technique previously described [31, 32, 63, 71, 72].

Like the other modalities, the most commonly reported adverse events after SE are minor, such as sore throat and mucosal injury [2]. The incidence of significant adverse events does no different from DBE and SBE [34, 52], for example, the rate of perforation is again 0.3% [3].

Follow-Up

The aforementioned adverse events drive an important component of follow-up. After being appropriately informed prior to the procedure, patients should be encouraged to report concerning symptoms, which may give rise to the diagnosis of one of the above adverse events.

For many patients, the follow-up is tailored to the underlying condition for which the DAE was indicated. An important example is that of obscure gastrointestinal blood loss related to angioectatic lesions. This is a common indication for DAE, and while initial treatment response is very high, close to 50% of patients represent, often within the first few years [43, 65]. For therapeutic procedures such as luminal stenting or DAE ERCP, then these therapeutic procedures and implanted hardware are the main driver of follow-up.

Conclusion

The last 15 years has seen the advent of three main DAE techniques, which have opened up diagnostic and therapeutic options for previously difficult to reach regions of the small bowel. The majority of DAE procedures are still being performed for occult and overt obscure gastrointestinal bleeding; in stable patients, this is primarily after lesion diagnosis with video capsule endoscopy, but in patients with ongoing bleeding, this may be done as a primary intervention. The experience in, and range of, broader indications continues to develop, both as a salvage procedure in patients with altered anatomy, as well as for the delivery of therapy to sites long from the reach of conventional endoscopic techniques.

In the large series reviewing DAE practice, discussed above, the complication rates have been low. These have been primarily related to pancreatitis and perforation. The current limitations relate to the need for two staff members and long procedure times. Due to the long procedure times, anaesthetic support is often required; however, the use of fluoroscopy has diminished since the early days with DBE. The costs to a department vary and depend in part if the DAE system is one of the two that use a dedicated enteroscope and if so if it is of the same manufacturer as the rest of the department endoscopes.

To date the majority of data pertains to DBE. There exists room for further comparative studies contrasting DBE and the two newer modalities, and we are also likely to see more studies emerge on the more recent "on-demand" enteroscopy which uses a through the scope balloon.

References

1. Akerman P, et al. Spiral enteroscopy with the new DSB overtube: a novel technique for deep peroral small-bowel intubation. Endoscopy. 2008;40(12):974–8.
2. Akerman P, et al. Spiral enteroscopy- a novel method of enteroscopy by using the Endo-Ease Discovery SB overtube and a pediatric colonoscope. Gastrointest Endosc. 2009;69(2):327–32.
3. Akerman PA, Cantero D. Severe complications of spiral Enteroscopy in the first 1750 patients. Gastrointest Endosc. 2009;69(5):AB127.
4. Aktas H, et al. Single-balloon enteroscopy-assisted direct percutaneous endoscopic jejunostomy. Endoscopy. 2012;44(2):210–2.
5. Cangemi D, et al. Small bowel tumours discovered during double-balloon enteroscopy: analysis of a large prospectively collected single-center database. J Clin Gastroenterol. 2013;47(9):769–72.
6. Despott EJ, et al. Enteral access by double-balloon enteroscopy: an alternative method of direct percutaneous endoscopic jejunostomy placement. Dig Dis Sci. 2011;56(2):494–8.
7. Despott EJ, et al. Effective dilation of small-bowel strictures by double-balloon enteroscopy in patients with symptomatic Crohn's disease (with video). Gastrointest Endosc. 2009;70(5):1030–6.
8. Domagk D, et al. Single- vs. double-balloon enteroscopy in small-bowel diagnostics: a randomized multicenter trial. Endoscopy. 2011;43(6):472–6.
9. Dulic-Lakovic E, et al. Bleeding Dieulafoy lesions of the small bowel: a systematic study on the epidemiology and efficacy of enteroscopic treatment. Gastrointest Endosc. 2011;74(3):573–80.
10. Dutta A, et al. Learning curve, diagnostic yield and safety of single balloon enteroscopy. Trop Gastroenterol. 2012;33(3):179–84.
11. Efthymiou M, et al. SINGLE-01: a randomized, controlled trial comparing the efficacy and depth of insertion of single- and double-balloon enteroscopy by using a novel method to determine insertion depth. Gastrointest Endosc. 2012;76(5):972–80.
12. Elena RM, et al. Current status of device-assisted enteroscopy: technical matters, indication, limits and complications. World J Gastrointest Endosc. 2012;4(10):453–61.
13. Ell C, May A. Mid-gastrointestinal bleeding: capsule endoscopy and push-and-pull enteroscopy give rise to a new medical term. Endoscopy. 2006;38(1):73–5.

14. Ell C, et al. Push-and-pull enteroscopy in the small bowel using the double-balloon technique: results of a prospective European multicenter study. Endoscopy. 2005;37(7):613–6.
15. Frantz DJ, et al. Single-balloon enteroscopy: results from an initial experience at a U.S. tertiary-care center. Gastrointest Endosc. 2010;72(2):422–6.
16. Fry LC, et al. Small bowel polyps and tumours: endoscopic detection and treatment by double-balloon enteroscopy. Aliment Pharmacol Ther. 2009;29(1):135–42.
17. Gay G, Delvaux M. Double-balloon colonoscopy after failed conventional colonoscopy: a pilot series with a new instrument. Endoscopy. 2007;39(9):788–92.
18. Gay G, et al. Outcome of capsule endoscopy in determining indication and route for push-and-pull enteroscopy. Endoscopy. 2006;38(1):49–58.
19. Gerson L, et al. Long-term outcomes after double-balloon enteroscopy for obscure gastrointestinal bleeding. Clin Gastroenterol Hepatol. 2009;7(6):664–9.
20. Gerson LB, et al. ACG clinical guideline: diagnosis and management of small bowel bleeding. Am J Gastroenterol. 2015;110(9):1265–87. quiz 1288
21. Gross SA, Stark ME. Initial experience with double-balloon enteroscopy at a U.S. center. Gastrointest Endosc. 2008;67(6):890–7.
22. Hayashi Y, et al. Non-steroidal anti-inflammatory drug-induced small bowel injuries identified by double-balloon endoscopy. World J Gastroenterol. 2005;11(31):4861–4.
23. Hayashi Y, et al. Nonsteroidal anti-inflammatory drug-induced small-bowel lesions identified by double-balloon endoscopy: endoscopic features of the lesions and endoscopic treatments for diaphragm disease. J Gastroenterol. 2009;44(Suppl 19):57–63.
24. Heine G, et al. Double-balloon enteroscopy: indications, diagnostic yield, and complications in a series of 275 patients with suspected small-bowel disease. Endoscopy. 2006;38(1):42–8.
25. Hirai F, et al. Carbon dioxide insufflation compared with air insufflation in double-balloon enteroscopy: a prospective, randomized, double-blind trial. Gastrointest Endosc. 2011;73(4):743–9.
26. Iddan G, et al. Wireless capsule endoscopy – the discomfort of internal gastrointestinal examination may soon be a thing of the past. Nature. 2000;405:417.
27. Iwai T, et al. Short-type and conventional single-balloon enteroscopes for endoscopic retrograde cholangiopancreatography in patients with surgically altered anatomy: single-center experience. Dig Endosc. 2014;26(Suppl 2):156–63.
28. Jeon SR, Kim JO. Deep enteroscopy: which technique will survive? Clin Endosc. 2013;46(5):480–5.
29. Kaffes A. Advances in modern enteroscopy therapeutics. Best Pract Res Clin Gastroenterol. 2012;26:235–46.
30. Kaffes AJ, et al. Double-balloon enteroscopy in the diagnosis and the management of small-bowel diseases: an initial experience in 40 patients. Gastrointest Endosc. 2006;63(1):81–6.
31. Kav T, et al. The power suction maneuver in single-balloon enteroscopy. Endoscopy. 2008;40(11):961–2.
32. Kawamura T, et al. Clinical evaluation of a newly developed single-balloon enteroscope. Gastrointest Endosc. 2008;68(6):1112–6.
33. Khashab M, Helper DJ, Johnson CS, Chiorean MV, et al. Predictors of depth of maximal insertion at double-balloon enteroscopy. Dig Dis Sci. 2010;55(5):1391–5.
34. Khashab MA, Lennon AM, Dunbar KB, et al. A comparative evaluation of single-balloon enteroscopy and spiral enteroscopy for patients with mid-gut disorders. Gastrointest Endosc. 2010;72(4):766–72.
35. Lara L, et al. Initial experience with retrograde overtube-assisted enteroscopy using a spiral tip overtube. Proc (Bayl Univ Med Cent). 2010;23(2):130–3.
36. Lee BI, et al. Clinical characteristics of small bowel tumors diagnosed by double-balloon endoscopy: KASID multi-center study. Dig Dis Sci. 2011;56(10):2920–7.
37. Lenz P, Domagk D. Double- vs. single-balloon vs. spiral enteroscopy. Best Pract Res Clin Gastroenterol. 2012;26(3):303–13.
38. Li X, et al. Predictive role of capsule endoscopy on the insertion route of double-balloon enteroscopy. Endoscopy. 2009;41(9):762–6.
39. Lo SK. Technical matters in double balloon enteroscopy. Gastrointest Endosc. 2007;66(3 Suppl):S15–8.
40. Manner H, et al. Impact of fluoroscopy on oral double-balloon enteroscopy: results of a randomized trial in 156 patients. Endoscopy. 2010;42(10):820–6.
41. May A. Modern imaging techniques: which – when – why? Dig Dis Sci. 2013;31:63–8.
42. May A, et al. Prospective multicenter trial comparing push-and-pull enteroscopy with the single- and double-balloon techniques in patients with small-bowel disorders. Am J Gastroenterol. 2010;105(3):575–81.
43. May A, Friesing-Sosnik T, Manner H, Pohl J, Ell C, et al. Long-term outcome after argon plasma coagulation of small-bowel lesions using double-balloon enteroscopy in patients with mid-gastrointestinal bleeding. Endoscopy. 2011;43(9):759–65.
44. May A, Manner H, Aschmoneit I, Ell C, et al. Prospective, crossover, single-center trial comparing oral double-balloon enteroscopy and oral spiral enteroscopy in patients with suspected small-bowel vascular malformations. Endoscopy. 2011;43(6):477–83.
45. May A, Nachbar L, Ell C, et al. Double-balloon enteroscopy (push-and-pull enteroscopy) of the small bowel- feasibility and diagnostic and therapeutic yield in patients with suspected small bowel disease. Gastrointest Endosc. 2005;62(1):62–70.
46. May A, et al. Endoscopic interventions in the small bowel using double balloon enteroscopy: feasibility and limitations. Am J Gastroenterol. 2007;102(3):527–35.
47. May A, et al. Prospective comparison of push enteroscopy and push-and-pull enteroscopy in patients with suspected small-bowel bleeding. Am J Gastroenterol. 2006;101(9):2016–24.
48. May A, Nachbar L, Schneider M, Neumann M, Ell C, et al. Push-and-pull enteroscopy using the double-balloon technique: method of assessing depth of insertion and training of the enteroscopy technique using the Erlangen endo-trainer. Endoscopy. 2005;37(1):66–70.
49. May A, et al. Double-balloon enteroscopy: preliminary experience in patients with obscure gastrointestinal bleeding or chronic abdominal pain. Endoscopy. 2003;35(12):985–91.
50. Mehdizadeh S, et al. What is the learning curve associated with double-balloon enteroscopy? Technical details and early experience in 6 U.S. tertiary care centers. Gastrointest Endosc. 2006;64(5):740–50.
51. Mensink P, et al. Complications of double balloon enteroscopy: a multicenter survey. Endoscopy. 2007;39(7):613–5.
52. Messer I, et al. Prospective, randomized, single-center trial comparing double-balloon enteroscopy and spiral enteroscopy in patients with suspected small-bowel disorders. Gastrointest Endosc. 2013;77(2):241–9.
53. Moeschler O, Mueller K. Deep enteroscopy – indications, diagnostic yield and complications. World J Gastroenterol. 2015;21(5):1385–93.
54. Mönkemüller K, et al. Diagnostic and therapeutic impact of double-balloon enteroscopy. Endoscopy. 2006;38(1):67–72.
55. Moreels T, Pelckmans P. Double-balloon endoscope for failed conventional colonoscopy. Clin Gastroenterol Hepatol. 2008;6(2):259.
56. Morgan D, et al. Spiral enteroscopy: prospective U.S. multicenter study in patients with small-bowel disorders. Gastrointest Endosc. 2010;72(5):992–8.
57. Möschler O, et al. Complications in and performance of double-balloon enteroscopy (DBE): results from a large prospective DBE database in Germany. Endoscopy. 2011;43(6):484–9.
58. Ohmiya N, et al. Small-bowel obstruction: diagnostic comparison between double-balloon endoscopy and fluoroscopic enteroclysis,

and the outcome of enteroscopic treatment. Gastrointest Endosc. 2009;69(1):84–93.
59. Parikh D, et al. Efficacy of single balloon enteroscopy- a 2 year Veterans Affairs medical center experience with a systematic review of the literature. J Interv Gastroenterol. 2013;3(4):116–21.
60. Pasha S, Leighton JA. Enteroscopy in the diagnosis and management of Crohn disease. Gastrointest Endosc Clin N Am. 2009;19(3):427–44.
61. Pata C, et al. Post-procedure elevated amylase and lipase levels after double-balloon enteroscopy: relations with the double-balloon technique. Dig Dis Sci. 2010;55(7):1982–8.
62. Rahmi G, et al. Multicenter comparison of double-balloon enteroscopy and spiral enteroscopy. J Gastroenterol Hepatol. 2013;28(6):992–8.
63. Ramchandani M, et al. Diagnostic yield and therapeutic impact of single-balloon enteroscopy: series of 106 cases. J Gastroenterol Hepatol. 2009;24(10):1631–8.
64. Sakai P, et al. Is it feasible to reach the bypassed stomach after Roux-en-Y gastric bypass for morbid obesity? The use of the double-balloon enteroscope. Endoscopy. 2005;37(6):566–9.
65. Samaha E, et al. Long-term outcome of patients treated with double balloon enteroscopy for small bowel vascular lesions. Am J Gastroenterol. 2012;107(2):240–6.
66. Saygili F, et al. Examining the whole bowel, DBE- indications, diagnostic yield and complications. World J Gastrointest Endosc. 2015;7(3):247–52.
67. Shah R, et al. Shah GIE A multicenter, U.S. experience of single-balloon, double-balloon, and rotational overtube-assisted enteroscopy ERCP in patients with surgically altered pancreaticobiliary anatomy (with video). Gastrointest Endosc. 2013;77(4):593–600.
68. Shimatani M, et al. Effective "short" double-balloon enteroscope for diagnostic and therapeutic ERCP in patients with altered gastrointestinal anatomy: a large case series. Endoscopy. 2009;41(10):849–54.
69. Takano N, et al. Single-balloon versus double-balloon endoscopy for achieving total enteroscopy: a randomized, controlled trial. Gastrointest Endosc. 2011;73(4):734–9.
70. Tee HP, et al. Learning curve for double-balloon enteroscopy: findings from an analysis of 282 procedures. World J Gastrointest Endosc. 2012;4(8):368–72.
71. Tominaga K, et al. Small intestinal perforation of endoscopically unrecognized lesions during peroral single-balloon enteroscopy. Endoscopy. 2008;40(suppl2):213–4.
72. Tsujikawa T, et al. Novel single-balloon enteroscopy for diagnosis and treatment of the small intestine: preliminary experience. Endoscopy. 2008;40(1):11–5.
73. Upchurch BR, et al. The clinical utility of single-balloon enteroscopy: a single-center experience of 172 procedures. Gastrointest Endosc. 2010;71(7):1218–23.
74. Wang WL, et al. Meta-analysis: the use of carbon dioxide insufflation vs. room air insufflation for gastrointestinal endoscopy. Aliment Pharmacol Ther. 2012;35(10):1145–54.
75. Xin L, et al. Indications, detectability, positive findings, total enteroscopy, and complications of diagnostic double-balloon endoscopy: a systematic review of data over the first decade of use. Gastrointest Endosc. 2011;74(3):563–70.
76. Yamada A, et al. Utility of single and double balloon endoscopy in patients with difficult colonoscopy: a randomized controlled trial. World J Gastroenterol. 2013;19(29):4732–6.
77. Yamamoto H, et al. Clinical outcomes of double-balloon enteroscopy for the diagnosis and treatment of small-intestinal diseases. Clin Gastroenterol Hepatol. 2004;2(11):1010–6.
78. Yamamoto H, et al. Total enteroscopy with nonsurgical steerable double-balloon method. Gastrointest Endosc. 2001;53(2):216–20.
79. Yamamoto H, et al. New system of double-balloon enteroscopy for diagnosis and treatment of small intestinal disorders. Gastroenterology. 2003;125:1556.
80. Yamauchi H, et al. Innovations and techniques for balloon-enteroscope- assisted endoscopic retrograde cholangiopancreatography in patients with altered gastrointestinal anatomy. World J Gastroenterol. 2015;21(21):6460–9.
81. Yamauchi H, et al. Short-type single balloon enteroscope for endoscopic retrograde cholangiopancreatography with altered gastrointestinal anatomy. World J Gastroenterol. 2013;19(11):1728–35.

Gastrointestinal Tract Stenting

20

Anthony A. Razzak, Andrew S. Ross,
and Richard A. Kozarek

Introduction

Enteral stent placement for disorders of the gastrointestinal tract has evolved significantly over the past decade. While the majority of enteral stent placement is performed to palliate malignant obstruction, advancements in technique and device technology have created suitable alternative endoscopic options for certain benign conditions. This chapter focuses on the indications, techniques, and currently available technologies for stent placement in the esophagus, small intestine, and colon.

Esophageal Stent Placement

Indications

The leading indications for esophageal stent placement are for palliation of complications related to esophageal and extraesophageal malignancies (Fig. 20.1). In the United States, rates of esophageal squamous cell carcinoma have declined, while the incidence and mortality rate of esophageal adenocarcinoma have increased [54]. The majority of patients with esophageal cancer will present with unresectable disease, and the overall 5-year survival rates remain poor at less than 20% [11, 46, 54, 57]. In this group of patients, the treatment goals are essentially directed toward improvement in quality of life: maintenance of esophageal luminal patency, reduction in dysphagia, optimization of nutrition, and reduction in the risk of aspiration (and resultant pneumonia) [11, 57]. These patients may be prone to malignant fistula formation from local radiation therapy or invasion of cancer into the respiratory tract and, less commonly, aorta, mediastinum, or pleural space [33, 49, 57, 58, 81]. Aside from dysphagia secondary to intrinsic malignant obstruction, extrinsic esophageal compression and dysphagia can be observed in patients with various forms of lung cancer, mediastinal lymphadenopathy, and mediastinal metastases [3, 53, 80]. While these indications rarely exist in isolation for any given patient, esophageal stent placement is appropriate and well suited for each.

Self-expandable stent placement has also been utilized for benign diseases of the esophagus, including perforation, anastomotic leaks, and treatment of refractory benign esophageal strictures [46, 56, 57] (Fig. 20.2). Esophageal perforation, which may occur as a result of iatrogenic injury related to endoscopic therapy or spontaneous rupture (Boerhaave syndrome), is often associated with significant morbidity when repaired surgically [46]. In addition, abscess formation and mediastinitis can occur if these are left untreated [84]. The placement of a self-expandable metal stent (SEMS) or self-expandable plastic stent (SEPS) has emerged as an alternative therapeutic option in these cases [48, 15–17, 56, 66, 68, 74]. Esophageal leaks following esophagectomy and anastomotic breakdown following bariatric or bypass surgery have also been reported to be successfully managed using SEMS or SEPS without the need for an operative intervention [48, 15, 16, 56, 66, 68, 74, 77].

Contraindications

There are very few contraindications to esophageal stent placement. Severe cardiorespiratory compromise, which may limit the safe performance of upper gastrointestinal endoscopy, is an absolute contraindication to the placement of an esophageal stent. Uncontrolled coagulopathy and esophageal varices are additional contraindications.

Tumors located in the mid- to upper esophagus raise important clinical issues with regard to compression of the tracheobronchial tree. The radial expansion force associated with SEMS placement across tumors in this location has the

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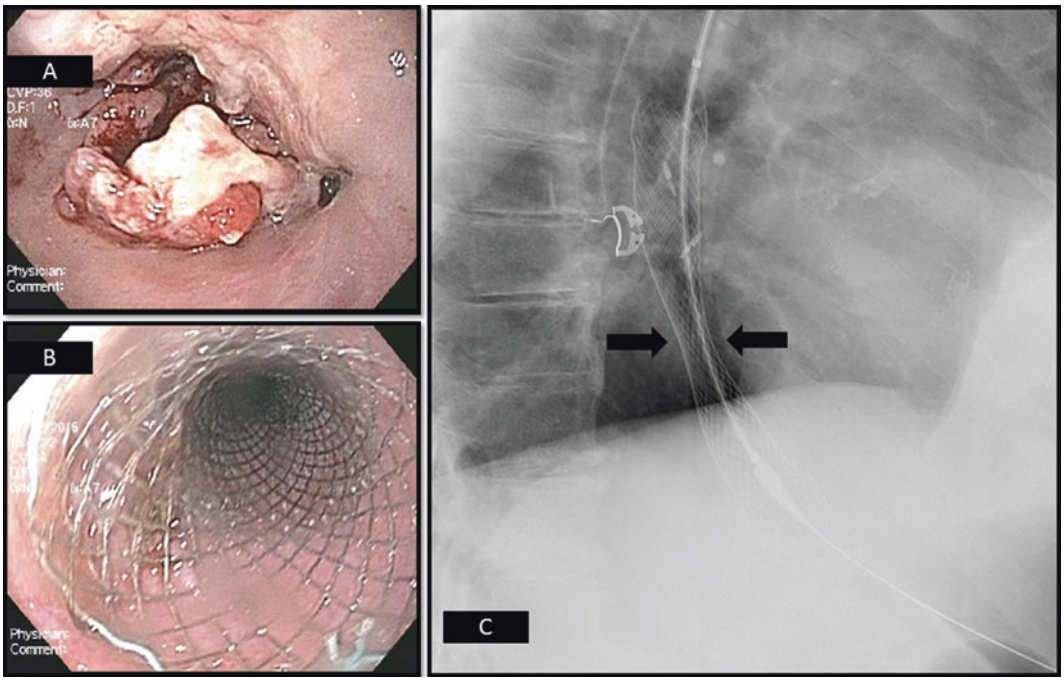

Fig. 20.1 Endoscopic (**a**) and (**b**) and radiographic views (**c**) of a partially covered SEMS for an esophageal adenocarcinoma (*arrows* highlight tumor preventing full stent expansion after deployment)

risk of causing iatrogenic airway obstruction [13, 31]. Although not a contraindication to esophageal stent placement, a chest CT scan should be obtained and reviewed with a thoracic surgeon prior to SEMS placement in patients with mid- to upper esophageal tumors. In some case, bronchoscopy with placement of a tracheal or bronchial stent may be indicated prior to, during, or immediately following esophageal stent placement [9, 45] (Fig. 20.3).

The risk of stent migration (see Complications) is typically lowest in patients with intrinsic strictures of the esophagus. Although not a contraindication, esophageal leaks or perforations where no intrinsic luminal narrowing is present should be stented with caution, with proper informed consent, and with the use of clips or endoscopic suturing (see Technique) to decrease the risk of stent migration.

The safety and efficacy of esophageal stent placement in patients who are undergoing chemotherapy and/or radiotherapy has been questioned [20, 41, 47, 60]. Concern exists from a surgical perspective with regard to the possibility of removing a SEMS at the time of surgery and the risk of esophageal perforation related to device insertion in those eligible for curative resection [59]. In addition, as tumors respond to therapy, stent migration may occur [41]. A recent retrospective study evaluating 55 individuals with locally advanced esophageal adenocarcinoma who underwent fully covered SEMS placement before neoadjuvant therapy revealed a statistically significant improvement in dysphagia, unchanged weight from baseline at 1-month follow-up, a 31% rate of stent migration, and successful stent extraction in all 8 patients who underwent eventual curative surgery [60]. Data from a multicenter European cohort of patients that underwent surgery for esophageal cancer with curative intent included 38 individuals who received a SEMS prior to surgery. The SEMS-related perforation rate was 5.3% (n = 2/38), and those with presurgical SEMS had a significantly lower 3-year survival rate (25% versus 44%, p = 0.023). Multivariate analysis independently identified SEMS as a predictor of poor prognosis (hazard ratio 1.6, p = 0.038) [38]. Given this controversy, the use of self-expandable stents prior to chemoradiotherapy is largely dictated by local practice bias.

Technique

The technique for endoscopic placement of esophageal stents, both plastic and metal, is relatively straightforward. Selection of appropriate candidates from the standpoint of medical stability and the ability to tolerate an endoscopic procedure is imperative. As for any endoscopic procedure, patients should be fasting for at least 6–8 h prior to the procedure. The choice of anesthetic is based on local practice bias. However, in our experience, the majority of procedures can be performed using conscious sedation with narcotic analgesics and a benzodiazepine. Patients being considered for esophageal stent placement due to a perforation or anastomotic breakdown following bariatric surgery should be

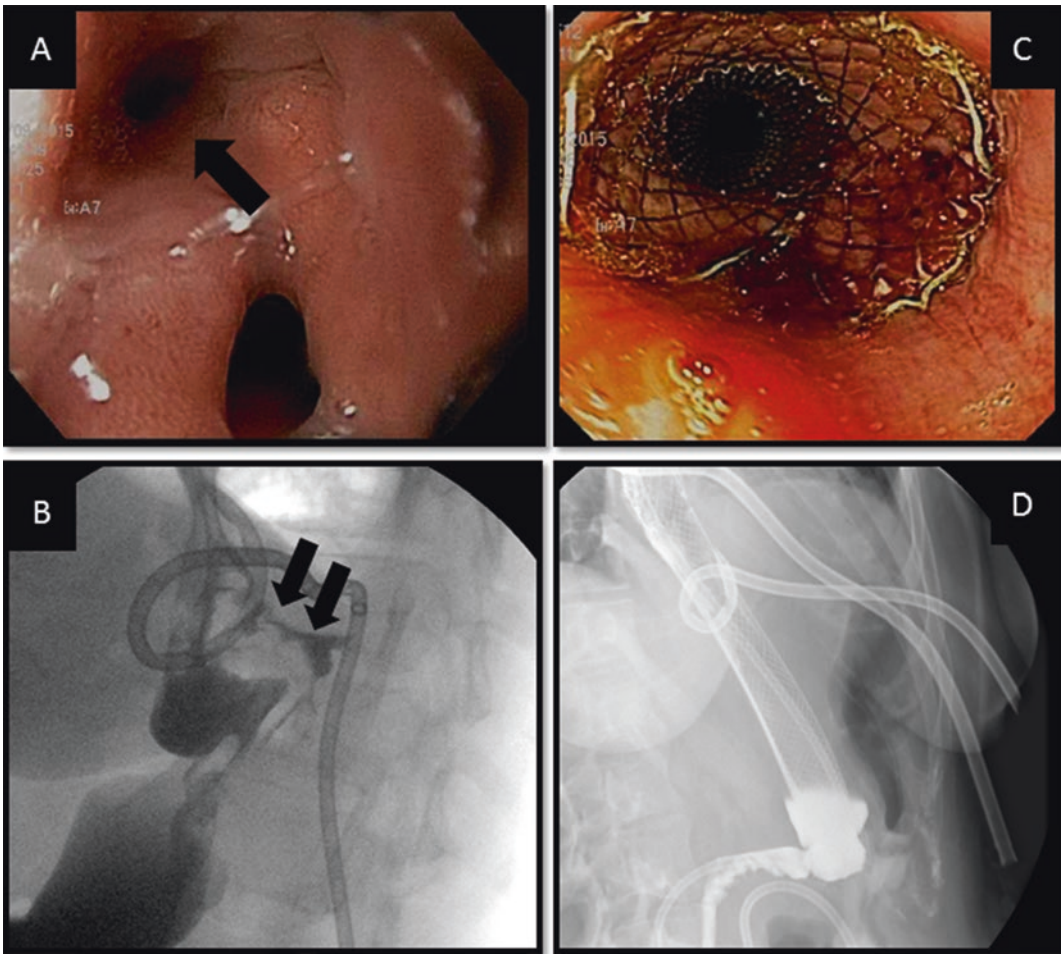

Fig. 20.2 Endoscopic view (**a**) of a gastric sleeve fistula and upper GI series (**b**) revealing leakage of water-soluble contrast into the thorax with a percutaneous drain in place. A partially covered SEMS (**c**) was placed and follow-up upper GI series (**d**) revealed no further contrast extravasation

approached with caution as these individuals are typically obese and have poor oral airways. In these individuals or others with multiple medical comorbidities, consultation with an anesthesiologist is recommended.

Practical Considerations

- Patients for stent placement due to a perforation or anastomotic breakdown following bariatric surgery should be approached with caution as these individuals are typically obese and have poor oral airways.

For patients with malignant disease, an upper endoscopy to define the proximal and distal margins of the tumor is the first step in esophageal stent placement. The total length of the stricture will help to determine the length of the desired stent. In the event that the upper endoscope cannot be passed beyond the esophageal stricture, careful esophageal dilation should be performed to allow passage of the endoscope beyond the tumor in order to obtain proper measurements. Although esophageal dilation techniques are beyond the scope of this chapter, controlled radial expansion balloon dilators may be preferable to bougies for this purpose as the former allow direct visualization of the stricture and a more "controlled" dilation. Fluoroscopy, while mandatory for esophageal stent placement, may be helpful when dilating malignant esophageal strictures.

The proximal and distal margins of the stricture can be marked using a variety of methods. Endoscopic clips can be applied or contrast dye can be injected into the submucosa. A less desirable (but cheaper) approach consists of marking the level of the endoscope externally using a radio-opaque object (such as a paper clip or hemostat). For malignant disorders, the stent should be deployed 2 cm above the proximal tumor margin to decrease the risk of distal stent migration. Once the tumor has been measured and the proximal and distal margins marked, a wire guide should be placed across the

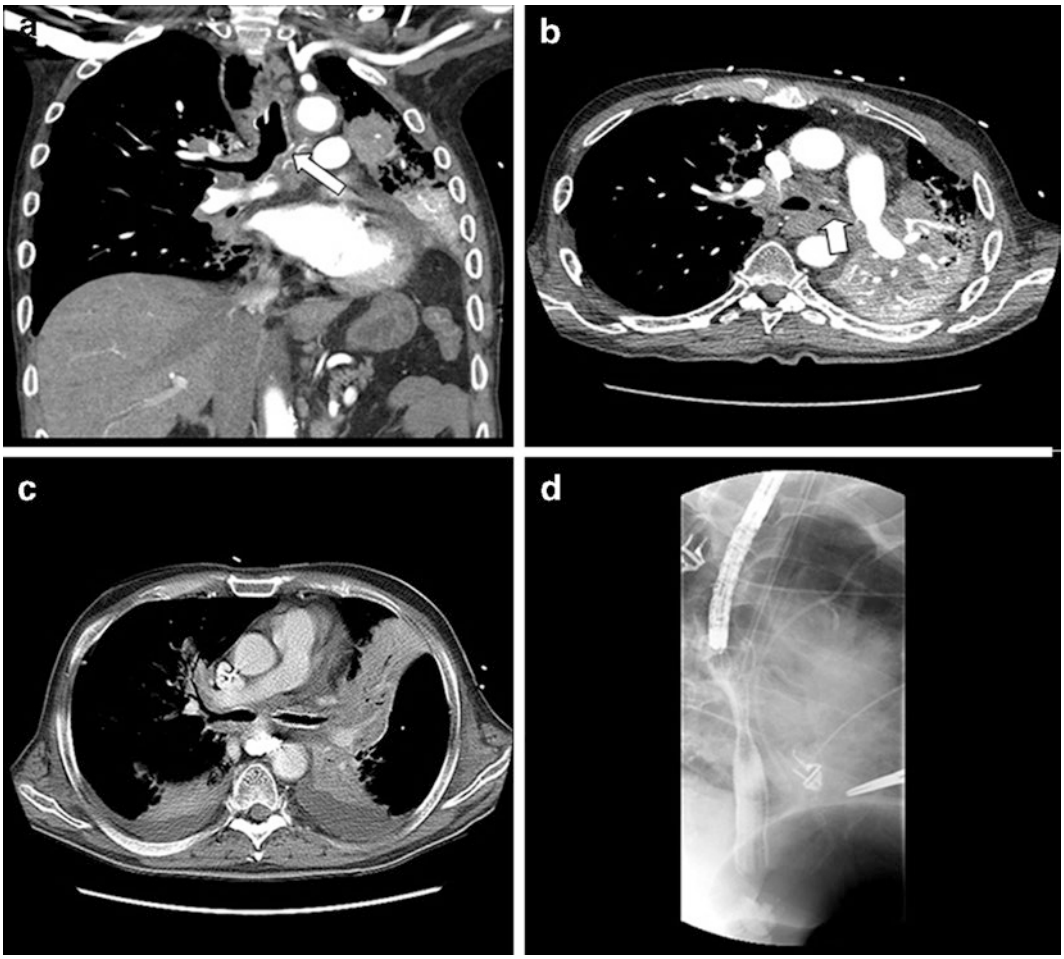

Fig. 20.3 Chest CT scan demonstrating left main stem bronchus (*arrows*) and proximal esophageal obstruction secondary to a squamous cell carcinoma of the lung (**a**) and (**b**). A bronchial stent was placed (**c**) following which a partially covered SEMS was successfully deployed (**d**) across the esophageal obstruction

stenosis into the stomach. The endoscope is then typically removed leaving the wire guide in place, unless a stent with through-the-scope deployment capabilities is being used at which point the endoscope remains in place and the stent is deployed under direct endoscopic visualization (Fig. 20.4) (see "Available Devices").

For malignant lesions, the type of stent utilized (i.e., fully covered (FC) versus partially covered (PC) SEMS, anti-reflux, length, and diameter) will depend on the lesion. In general, we prefer to place the stent with the largest diameter possible. A smaller stent diameter may be used for lesions within the cervical esophagus in order to decrease the possible "foreign body" sensation associated with stent placement in this location. Over the last two decades, the use of uncovered SEMS has fallen out of favor due to the high rate of obstructing tumor ingrowth, the recurrent dysphagia, and the need for repeated endoscopic interventions [72]. A partially or fully covered SEMS is preferable as the covered portion will prevent the tumor ingrowth and tissue hyperplasia. In addition, a covered SEMS should also be utilized for malignant tracheoesophageal fistulas with data revealing occlusion rates of 70–100% [57]. Studies on SEPS for malignant esophageal lesions reveal successful alleviation of dysphagia but high rates of complications, including stent migration [7]. For this reason, SEPS are not recommended for use in malignancy. With regard to length, stents should be long enough to cover the desired lesion. Because endoscopic measurements may be slightly inaccurate, it is best to err on the side of a longer (rather than shorter) stent in order to decrease the risk of failing to palliate the obstructing lesion.

For lesions in the distal esophagus where the stent may cross the gastroesophageal junction, patients almost invariably develop reflux of gastric contents into the proximal esophagus or oropharynx. A study comparing standard SEMS to specifically designed "anti-reflux" stents for the treatment of inoperable distal esophageal adenocarcinoma revealed a statistically significant reduction in reported reflux symptoms with those receiving the anti-reflux stent (96% versus 12%, $p < 0.001$) [35]. However, further data on their

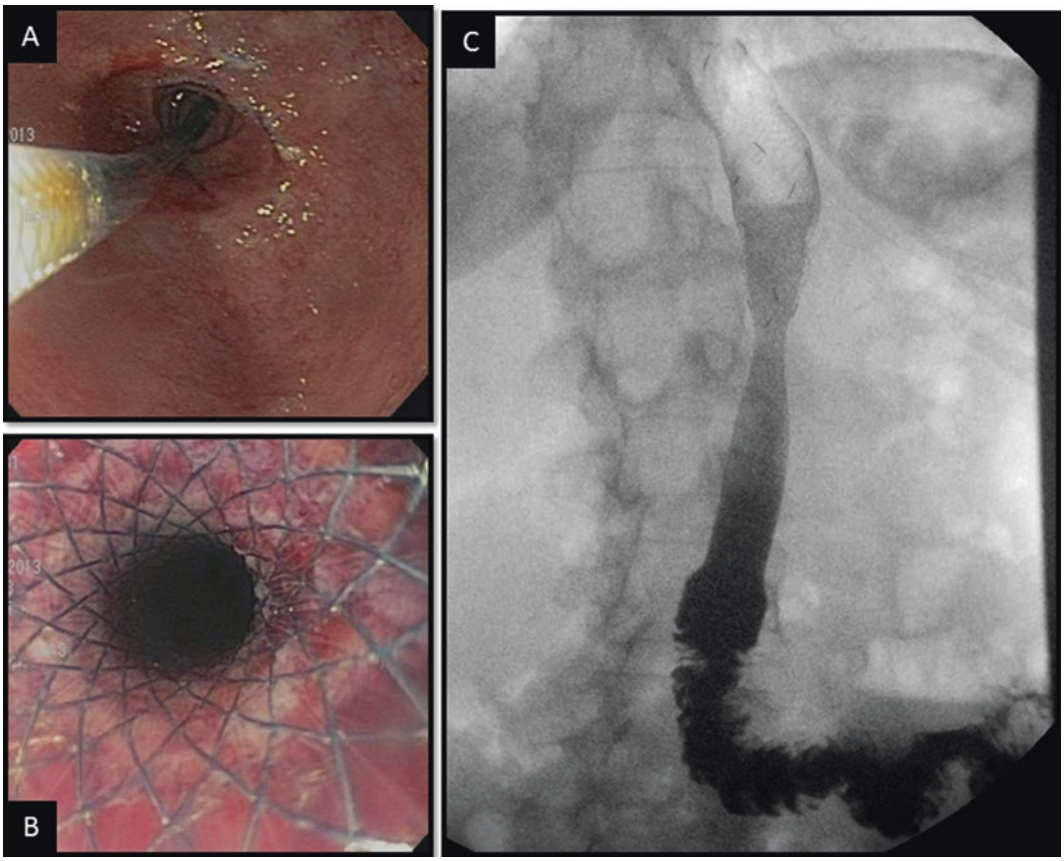

Fig. 20.4 Endoscopic view (**a**) and (**b**) of a through-the-stent deployment of an esophageal partially covered SEMS for a severe gastrojejunal anastomotic stricture in a patient with a prior subtotal gastrectomy presenting with dysphagia and PO intolerance. Follow-up upper GI series (**c**) reveals stent patency

efficacy is limited, and at the present time, anti-reflux stent availability in the United States is restricted.

Once the appropriate stent has been selected, deployment is straightforward. The stent is advanced over the wire guide, and the outer markings of the stent aligned with the proximal and distal margins of the stricture, recognizing that most SEMS foreshortens by 30–40% with deployment. Release of the stent (which varies by device) can then proceed under fluoroscopic control. Post-deployment endoscopy can be performed to ensure proper stent positioning; however, the endoscope should not be passed through a tight "waist" in the stent in order to decrease the risk of stent dislodgement. In the case of fully covered metal stents, proximal repositioning, using grasping forceps, can be accomplished with ease in most cases. Partially covered stents can be repositioned with some difficulty, in most cases, immediately after deployment, especially when the deployed stent is a distal release device [46].

As is the case for malignant indications, esophageal stent placement for benign indications is technically straightforward. Typically, a contrast-enhanced radiograph or CT scan is indicated prior to esophageal stent placement for benign indications. This will allow the endoscopist to identify the exact location and extent of the stricture, leak, or perforation. Upper endoscopy is then performed to further define the proximal and distal margins of the stricture or defect, which can be marked using any of the three methods outlined above. A wire guide is then placed into the stomach following which the endoscope is removed leaving the wire guide in place. For benign indications, a self-expanding plastic stent or fully covered metal stent should be selected in order to allow removal at a later date. In instances of severe strictures, use of a temporary small caliber covered biliary stent is a feasible means to bridge to a larger caliber esophageal stent, though the data on this technique is limited (Fig. 20.5). Deployment is performed under fluoroscopic control in most cases (see below).

The risk of migration is highest in patients with benign indications for esophageal stent placement [23, 46, 56, 68]. Refractory benign esophageal strictures have different characteristics in comparison to their malignant counterparts. Although occasionally problematic (i.e., stent occlusion), ingrowth of tumor into the stent helps to anchor it in position. In addition, malignant strictures tend to be longer than

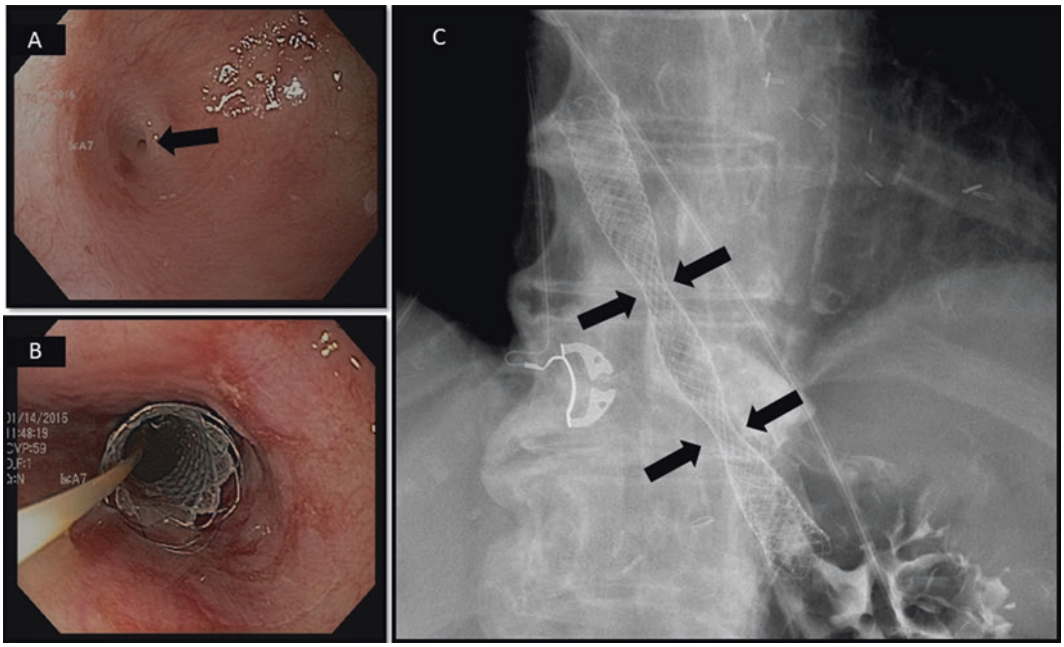

Fig. 20.5 A severe peptic stricture (**a**) with a pinpoint opening, treated with a covered biliary stent (**b**) as a bridge to a larger esophageal stent. Fluoroscopic images (**c**) after stent deployment revealed a multifocal process

most benign strictures. Finally, for perforations and anastomotic leaks, there is no stricture to hold a stent in place (and, therefore, this indication has the highest risk of migration). Several measures can be taken to reduce the risk of stent migration. First, the stent with the largest possible diameter should be selected. The length of the stent should be long enough to bridge the stenosis, leak, or perforation. For the latter two indications, we tend to select the longest stent available as an additional (potential) safeguard against stent migration. Endoscopic clips, including over-the-scope clips, can be applied to the proximal end of the stent in an attempt to maintain stent position [4, 25, 40]. Techniques to remove the over-the-scope clips include submucosal injection and submucosal electrocautery-assisted dissection [40]. The use of a PCSEMS has the added appeal of allowing tissue ingrowth at the uncovered portions of the stent to act in an anti-migration manner. Stent removal can be successfully and safely achieved with temporary placement of a FCSEMS within the PCSEMS ("stent-in-stent" technique) to facilitate pressure necrosis of the granulation tissue and subsequent extraction [8]. Lastly, fixation via application of interrupted or continuous sutures on the proximal aspect of a covered stent using an endoscopic suturing device has been reported with success [28].

Complications

Immediate and early procedure-related complications following esophageal stent placement occur in up to 10% of individuals [4, 46]. These include aspiration, airway compromise, malpositioning of the device, entrapment of the stent delivery system, dislodgement of the stent, hemorrhage, severe chest pain, nausea, and esophageal perforation [4, 57]. Careful intraprocedural airway management, including utilization of general anesthesia if necessary, can reduce the risk of aspiration. As discussed above, patients with stridor, wheezing, or mid- to upper esophageal tumors should undergo CT of the chest, prior to stent placement, to evaluate for airway compromise, which may be exacerbated by stent placement. As with all therapeutic endoscopic procedures, an INR of 1.5 or less is desired for elective esophageal stent placement to reduce the risk of bleeding.

Late (or delayed) complications occur in 30–50% of patients and include bleeding and fistula formation from stent erosion, severe gastroesophageal reflux, stent migration, and obstruction secondary to tissue ingrowth or food bolus impaction [4, 24, 41, 46, 57, 66, 74, 77]. Some malpositioned or migrated stents can be repositioned or removed, using grasping forceps, inflated balloon catheter, or a polypectomy snare. On occasion, migrated stents may be left in the stomach and a new stent placed [46]. The decision to remove a migrated stent should ideally be made based on the patient performance status as this is not without risk. But, leaving a migrated stent within the stomach is associated with a small (but definite) risk of migration into the small intestine with resultant perforation or obstruction. Stents that become occluded secondary to tumor ingrowth can be treated with argon plasma coagulation or placement of a second stent through the first (stent-within-stent design). Food bolus impaction can typically be treated endoscopically.

Practical Considerations

- For patients with malignant disease, an upper endoscopy to define the proximal and distal margins of the tumor is the first step in esophageal stent placement.
- Controlled radial expansion balloon dilators are preferable to bougies as the former allow direct visualization of the stricture and a more "controlled" dilation.
- The use of uncovered SEMS has fallen out of favor due to the high rate of obstructing tumor ingrowth, the recurrent dysphagia, and the need for repeated endoscopic interventions.
- A partially or fully covered SEMS is preferable as the covered portion will prevent the tumor ingrowth and tissue hyperplasia.

Post-procedural Care

A liquid diet can be resumed immediately for patients with malignant indications for esophageal stent placement. Diet can then be advanced as tolerated to a goal of reaching puree status; advancement beyond this level places the patient at risk for stent occlusion by large food particles. For patients in whom stents are placed for malignant tracheoesophageal fistula, esophageal perforation, or anastomotic leak, our practice is to withhold an oral diet until an esophagram (using water-soluble contrast) is obtained 24 h following stent deployment to ensure both proper positioning of the stent and closure of the leak.

Patients in whom stents are deployed across the EG junction require special attention. Because the natural barrier to reflux of gastric contents is rendered incompetent by the placement of the esophageal stent across the EG junction (unless using a prosthesis with an anti-reflux valve), aspiration remains a significant risk in these patients. For these individuals, twice daily proton pump inhibitors are prescribed indefinitely. We also suggest that these patients do not eat in close proximity to bedtime (2–3 h) and that the head of the bed is elevated to at least 30° at all times. This can be accomplished most easily by a specially designed wedge pillow available at most medical supply stores.

Outcomes

Although the concept of endoprosthesis placement for the palliation of malignant dysphagia had been around since the late nineteenth century, clinical success was hampered by high rates of complications and prolonged hospitalizations when using the available rigid plastic prosthetics. Stenting for palliation of malignant esophageal obstruction did not increase in popularity until over a century later, with the introduction into clinical practice of the self-expanding metal stent and a seminal randomized control trial demonstrating reduced complications and improved cost-effectiveness with SEMS versus rigid plastic prosthetics [18, 34]. By the following decade, high-quality data was available to compare uncovered SEMS versus covered SEMS. There were significantly higher rates of recurrent dysphagia, tumor ingrowth, and repeated endoscopic interventions in those receiving uncovered SEMS [72], since uncovered SEMS have fallen out of favor for their covered alternatives.

The ideal modality for the treatment of any patient with metastatic cancer and limited survival should meet the following criteria: wide availability, ease of use, minimal side effects, minimal complications, rapid symptom improvement, and minimal need for re-intervention [11]. With respect to esophageal malignancies, SEMS meet the majority of these criteria.

SEMS in Malignant Disease

There are numerous covered self-expandable stents available to treat esophageal malignancy (see Available Devices), but no study to date has compared their relative efficacy or adverse event rates in a head-to-head manner; therefore, no single manufacturer's covered stent has been proven superior [46]. SEPS, FCSEMS, and PCSEMS can be utilized in esophageal cancer with the latter two options preferred. The technical success of SEMS placement for esophageal malignancy is nearly 100% [41, 56, 69, 79]. Similarly, SEMS are highly efficacious in their ability to palliate dysphagia and close malignant fistulae [41, 51, 56, 57, 65, 69, 79]. A single center study comparing FCSEMS versus PCSEMS for benign and malignant esophageal disease included 252 patients receiving a total of 321 SEMS (112 FC and 209 PC) with 78% (n = 197) suffering from malignancy. Technical success with placement was high, 97.6%, with no significant difference between FCSEMS and PCSEMS. Relief of malignant dysphagia was achieved in 83.8% (n = 140/167) and control of fistulae, leaks, and perforations achieved in 84% (n = 21/25). The adverse event rate was 22.2% with most events related to stent migration (19%, n = 61/321). Use of a FCSEMS ($p < 0.001$), benign indication ($p = 0.022$), and distal location of deployment ($p = 0.008$) were significant independent risk factors for stent migration. There was a statistically significant difference in the rate of tissue ingrowth and overgrowth in PCSEMS (53.4%) versus FCSEMS (29.1%) ($p = 0.004$) [56]. The data herein aligns with other studies and suggests no significant difference exists in the ability of FCSEMS and PCSEMS to palliate malignant esophageal complications.

One of the largest obstacles that remain is preventing recurrent dysphagia. The use of a FCSEMS and stent deployment in the distal esophagus increase the likelihood of stent migration, while the use of a PCSEMS increases the probability of tissue ingrowth/overgrowth [56, 57]. It is estimated that recurrent dysphagia requiring repeat intervention occurs in up to 30% of patients, following covered SEMS placement. Depending on the clinical scenario, migrated stents can be retrieved and/or replaced, while patients in whom stents are occluded by tumor ingrowth can be treated with repeat stent placement or argon plasma coagulation [46]. Ultimately, the choice of FCSEMS versus PCSEMS is dictated by clinical scenario, lesion location, and endoscopist preference. Due to the elevated risk of migration, PCSEMS are to be considered when stenting the distal esophagus/gastroesophageal junction.

SEPS Versus SEMS in Malignant Disease

The introduction of a SEPS carried the promise of a cost-effective, easily removable option to alleviate malignancy-associated esophageal obstruction and complications. A randomized controlled trial evaluating 101 individuals with malignant dysphagia assigned 47 patients to receive a SEPS and 54 to receive a PCSEMS. The technical and initial clinical success was not significantly different. Multivariate analysis revealed a significantly higher rate of complications with SEPS versus PCSEMS (OR 2.3, 95% CI 1.2 to 4.4) including the incidence of late stent migration (13% versus 4%) [7]. Verschuur et al. randomly assigned 125 patients to receive PCSEMS (n = 42), SEPS (n = 41), or a FCSEMS (n = 42) to palliate esophageal and gastric cardia malignancy. The technical success rate was significantly lower in those assigned to SEPS placement (83% versus 100% in PCSEMS and 95% in FCSEMS) with equivalent clinical improvement in malignant dysphagia across stent types. Stent migration was more common with SEPS (29% versus 17% in PCSEMS and 12% in FCSEMS), while tumor ingrowth/overgrowth was higher in the PCSEMS (31%) and FCSEMS (24%) compared to SEPS (10%) [82].

The technical difficulties with SEPS placement are, in part, related to the large caliber stent introducer (see Available Devices) which ranges from 12 to 14 mm and limits its use in tight malignant obstructions. While the clinical success rates of SEPS are equivalent to PCSEMS and FCSEMS, the difficulties with placement and higher rates of stent migration make SEMS a preferred choice in the treatment of esophageal malignancy-related complications.

SEMS in Malignant Extrinsic Compression

Late stage extraesophageal and metastatic malignant processes can manifest with dysphagia via extrinsic esophageal compression. Multiple studies have evaluated the technical success, clinical success, and safety of SEMS placement for malignant extrinsic compression. A single center retrospective review identified 28 individuals with advanced lung cancer and malignant dysphagia including 8 individuals with concomitant tracheoesophageal fistulas. SEMS placement was technically successful in all 28 patients, and all patients achieved clinical improvement, including a 100% fistula occlusion rate. Transient pain was experienced by 42% of the individuals, and one individual (3.5%) experienced recurrent dysphagia and required a gastrostomy [3]. A prospective single center study evaluated 50 individuals with lung cancer and mediastinal metastasis complicated by malignant dysphagia and extrinsic esophageal compression. SEMS were successfully placed in 100% of the patients, and median stent patency exceeded median patient survival. Five patients (10%) experienced severe complications, including two perforations and three hemorrhages of which two individuals died from blood loss. Eight patients (16%) experienced recurrent dysphagia, all managed successfully with a repeat endoscopic intervention [80]. Lastly, a retrospective review comparing the efficacy of SEMS for intrinsic versus extrinsic malignant esophageal obstruction identified 105 individuals, 85 with an intrinsic and 20 with extrinsic (predominately lung cancer) malignant dysphagia. Overall the technical and clinical success was high (100% and 91%, respectively) with no significant difference in the clinical success between the intrinsic and extrinsic groups. Stent patency was greater in the intrinsic versus extrinsic group (131 +/− 85 days versus 54 +/− 45 days, respectively), due in part to the shorter survival of the extrinsic patient population. A subgroup analysis did not identify any difference in stent patency when comparing uncovered SEMS versus FCSEMS [53].

Given data to date, we conclude SEMS placement is highly effective at alleviating symptoms of malignant extrinsic esophageal compression. Nevertheless, a discussion regarding the potential complications of SEMS placement, including perforation, hemorrhage, pain, and recurrent dysphagia, must be performed for all eligible candidates being considered for stenting.

Benign Disease

The use of SEMS and SEPS for benign indications continues to evolve. FCSEMS and PCSEMS represent a minimally invasive alternative to address benign strictures and otherwise catastrophic nonmalignant esophageal complications including esophageal perforations and postsurgical leaks. A common concern is safe SEMS extraction as tissue ingrowth and overgrowth can predispose to difficult removal. As opposed to their metallic counterparts, SEPS can be easily removed or repositioned, making them an ideal candidate for treating benign esophageal conditions.

A number of studies have now demonstrated the clinical safety and efficacy of using SEMS and SEPS for benign indi-

cations [15, 16, 48, 56, 68, 77]. Swinnen et al. retrospectively reviewed 88 individuals who underwent placement of 153 SEMS for esophageal perforations or postoperative leaks. Technical success was 100% and successful resolution of the perforation or leak was achieved in 84.2% of cases. Stent removal for eligible patients was seen in 96.1% and aided by the placement of a SEPS within the SEMS [66]. A review of 52 patients receiving 83 stents (61 PCSEMS, 15 FCSEMS, 7 SEPS) for anastomotic leaks (n = 32), iatrogenic perforations (n = 13), Boerhaave syndrome (n = 4), and other indications (n = 3) achieved clinical success in 76% with no significant difference noted across stent type. Stent removal was successful in all but eight individuals who received a PCSEMS due to tissue ingrowth. Thirty-three complications were noted in 24 individuals including 10 (30.3%) stent migrations [74]. Evaluating SEPS only, Holm et al. evaluated 30 individuals who received 83 SEPS for benign indications. Stent migration occurred in almost 82% of patients who underwent SEPS for benign esophageal strictures, 75% of patients with anastomotic strictures, 59% of patients with anastomotic leaks, and in 29% of patients with radiation-induced strictures. Long-term symptomatic improvement following stent removal occurred in only 6% of all procedures [23].

Data on stenting benign strictures suggest limited clinical efficacy compared to the clinical success seen when stenting other benign conditions. Seven et al. reviewed 252 patients receiving 321 SEMS, 22% for benign indications, and reported 95.6% successful stent removal rate with 84% successful treatment of fistula, leaks, and perforations. In contrast, the rate of refractory benign stricture resolution was 53% [56]. In one of the largest studies to evaluate the use of partially and fully covered SEMS for benign diseases (n = 70), the treatment success rate for refractory benign strictures was 33.3%, while treatment success for perforations, fistulae, and anastomotic leaks was 100%, 71%, and 80%, respectively [68]. The stent migration rate was 40% and highest in those being treated for benign strictures.

Until large, randomized control trials are available, SEMS and SEPS appear to be safe and clinically efficacious at treating benign esophageal conditions with higher rates of success reported with fistulas, postoperative leaks, and perforations. The type of stent to use in these circumstances is dependent on endoscopist preference, clinical situation, and discussion with the patient regarding stent-specific risks.

Biodegradable Stents

Interest in biodegradable (BD) stents has arisen, mainly to address issues with SEPS and covered SEMS-related stent migration and to avoid the need for repeated interventions. Two such stents exist, neither of which are available within the United States. The Ella BD stent (ELLA-CS, Hradec Kralove, Czech Republic) is composed of polydioxanone, a suture material, and the poly-L-lactic acid (PLLA) BD stent (Marui Textile Machinery, Osaka, Japan) comprised of knitted PLLA monofilaments [22]. The stents will typically dissolve within 2–3 months and therefore do not require removal. A recent systemic review and meta-analysis evaluating SEPS, SEMS, and BD stent placement in refractory benign esophageal strictures revealed a pooled clinical success rate of approximately 40% with no significant difference in success, migration, or adverse event rate when treating with SEPS and SEMS versus biodegradable stents [19]. Further studies will be required to determine the clinical relevance and role of BD stents.

Given these findings, appropriate candidate selection, proper device placement, and close follow-up are indicated in patients considered for SEPS or completely covered SEMS placement for benign disease.

Available Devices

There are a large variety of esophageal stents currently available in the marketplace. Table 20.1 lists the characteristics of various covered SEMS which are currently available in the United States. As mentioned previously, there are no data to suggest clinical superiority of any one manufacturer's device over another for any indication.

Two additional stents are worth mentioning. The PolyFlex (Boston Scientific, Natick, MA) stent is the only currently available SEPS in the United States and the only self-expandable stent currently FDA approved for benign indications. This device is composed of polyester mesh embedded in silicone; it is completely covered. The stent is available in a number of diameters and lengths, the largest diameter being a 25 mm flare at the proximal end. The device must be assembled prior to deployment, and the delivery system is rather large, with a diameter of 12–14 mm. The Niti-S stent (Taewoong Medical, Seoul, South Korea) is a single- or double-layered nitinol stent with an inner layer fashioned from polyurethane. This combination prevents stent migration by allowing tumor ingrowth and intercalation into the outer mesh while at the same time reducing recurrent dysphagia by having a completely covered inner core [81]. This is the only self-expandable metal stent available with a through-the-scope deployment system that allows direct endoscopic visualization at the time of placement.

Enteral Stent Placement

Obstruction of the gastric outlet or duodenum is commonly seen with malignant neoplasms of the pancreatic head, bile duct, proximal small intestine and major papilla, and gastric antrum as well as by malignant mesenteric lymphadenopathy and, rarely, metastatic disease or local extension of

Table 20.1 Self-expandable esophageal stents available in the United States

	Ultraflex	Alimaxx-ES	Evolution	WallFlex	Niti-S	PolyFlex
Stent material	Nitinol	Nitinol	Nitinol	Nitinol	Nitinol	Polyester
Covering	UC and PC	FC	PC and FC	PC and FC	FC and available in double layer of nitinol	FC
Delivery system (Fr)	16	16	24	18.5	10.5 (TTS)	36 39 42
Length (cm)	10 12 15	7 10 12	8 10 12 12.5 15	12 15	6 8 10 12 14 15	9 12 15
Shaft/max. flare diameter (mm)	18/23 23/28	18/22	18/23 20/25	18/25 23/28	18/26 20/26	16/20 18/23 21/28
Degree of shortening (%)	30–40	0	35	30–40	35	0
Manufacturer	Boston Scientific	Merit Medical Endotek	Cook Medical	Boston Scientific	Taewoong Medical	Boston Scientific

UC uncovered, *PC* partially covered, *FC* fully covered, *TTS* through the scope

colonic neoplasms [2]. Gastric outlet obstruction complicating pancreatic cancer occurs in up to 15% of all cases [6]. Recurrent tumor or stricture in the afferent limb following a Whipple resection and radiation therapy for pancreatic cancer can lead to the development of an "afferent limb syndrome" resulting in biliary obstruction and cholangitis. This represents an additional indication for enteral stent placement.

Besides malignant disease, enteral stents have occasionally been utilized in patients with benign etiologies of gastric outlet obstruction, namely, peptic strictures, inflammatory strictures from gastroduodenal Crohn's disease, and annular pancreas, among others. However, advancements in endoscopic balloon dilation technologies and minimally invasive surgery have nearly eliminated the use of enteral stents for benign indications [6].

Contraindications

There are few contraindications to enteral stent placement for malignant gastric or duodenal outlet obstruction. Patients who are medically unfit for endoscopic procedures should not undergo enteral stent placement. Enteral stent placement is also contraindicated in patients with uncontrolled coagulopathy and in individuals with life expectancy of less than 4–6 weeks. Localized intestinal perforation in the setting of malignancy represents a contraindication to enteral stent placement. Finally, enteral stents should not be placed in patients with multiple sites of distal intestinal obstruction (i.e., carcinomatosis) as relief of the proximal point of obstruction is unlikely to provide palliation in these individuals [21].

Technique

Self-expanding metal stents for malignant gastric or duodenal outlet obstruction are usually placed endoscopically with fluoroscopic control. However, they can be placed by radiologists using fluoroscopy alone. Endoscopic delivery has the advantage of real-time investigation of the obstructing lesion and direct visualization of stent positioning and deployment. Most patients presenting with malignant gastroenteric obstruction will have had imaging with either a CT or contrast-enhanced radiograph (Fig. 20.6). Although such studies are useful for preprocedural planning, identification of the location and extent of the obstructing lesion, as well as determination of the presence of distal points of intestinal obstruction, it is not imperative that they be obtained prior to performing the procedure [21].

Nasogastric decompression is imperative prior to the initiation of conscious sedation or the induction of general anesthesia. Patients with severe gastric outlet obstruction are also prone to gastroparesis (see below). As a result of both the intestinal obstruction and poor gastric contractility, several liters of fluid or semisolid gastric contents may be retained, making the risk of aspiration in a nondecompressed patient

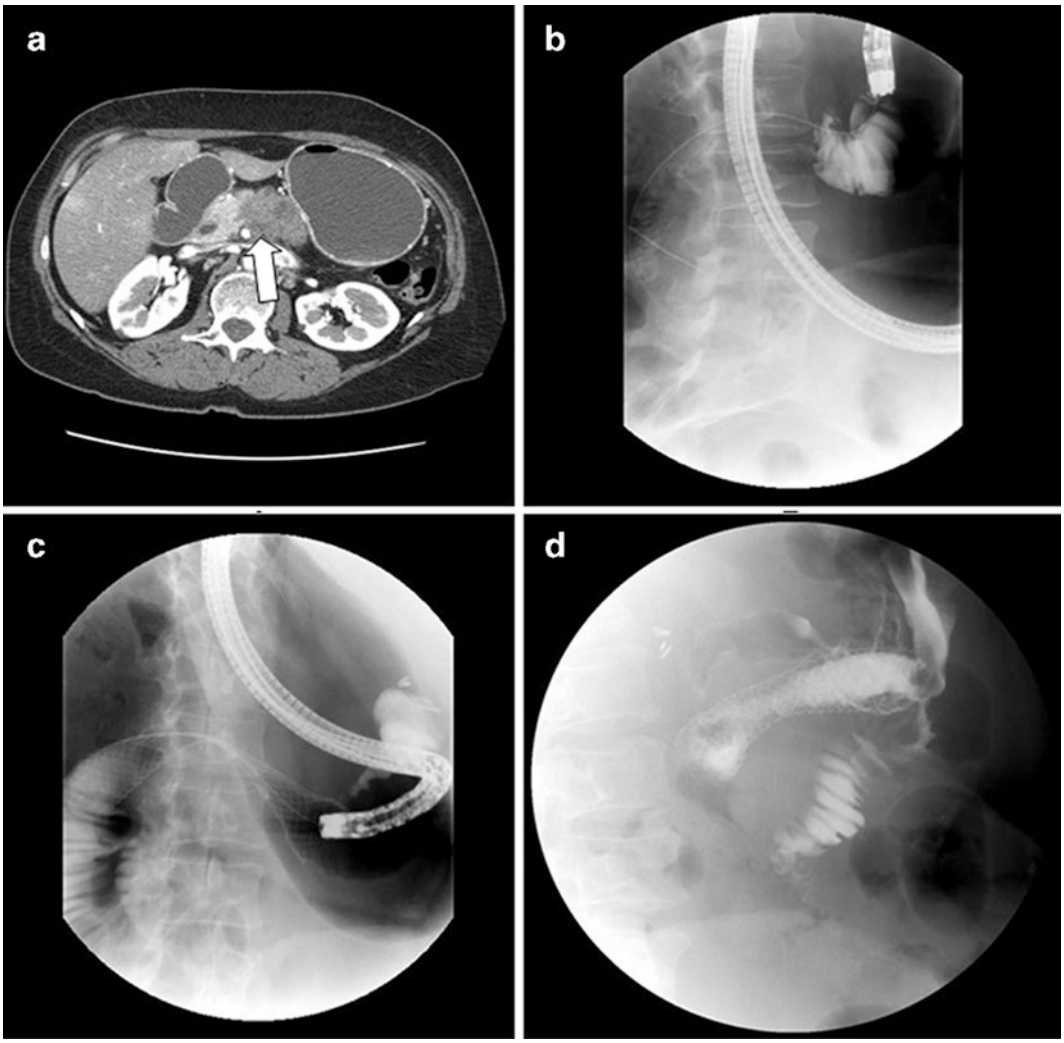

Fig. 20.6 Abdominal CT scan demonstrating a markedly dilated stomach and large pancreatic mass (*arrow*) (**a**). Contrast was injected following which a guide wire was placed across the stenosis (**b**). An uncovered SEMS deployment was successful (**c**); an upper GI series performed following stent deployment demonstrates passage of contrast through the stent (**d**) indicating luminal patency

significant. We usually prefer at least 24 h of nasogastric decompression or endotracheal intubation prior to endoscopic stent placement.

Once conscious sedation is achieved or general anesthesia induced, insertion of the endoscope typically begins with the patient in the left lateral decubitus position. The choice of endoscope depends on the location of the lesion: proximal lesions can be handled utilizing a therapeutic (3.7 mm working channel) upper endoscope or duodenoscope (4.2 mm working channel), while those distal to the second portion of the duodenum typically require the use of an adult colonoscope. If the obstruction can be passed using the endoscope, this should be done with extreme caution as the majority of enteral stents can be placed without crossing the stenosis. Balloon dilation is rarely indicated, except when required to pass a duodenoscope for performance of ERCP during the same procedure (see below) [21].

In the event that the stenosis is not crossed, a balloon catheter can be used to inject contrast beyond the obstruction so that the length of the stricture can be defined and an appropriate length stent selected (Fig. 20.6). A wire guide can then be placed through the stenosis into the distal bowel. The selected stent should be approximately 3–4 cm longer than the length of the stenosis to ensure adequate coverage on either side of the stricture [21]. Once the proper length stent is selected and advanced into position over the wire guide, deployment can proceed under endoscopic and fluoroscopic control. Most devices tend to deliver distally when released; therefore, gentle counter tension is used to ensure proper deployment and, ultimately, positioning. In some cases, direct visualization of the proximal margin of the stricture is not possible during deployment. This is especially true for lesions at the apex of the duodenum where the acute angulation and "straightening" of the endoscope as the stent is passed

through the working channel forces the endoscope tip into the stomach. In such cases, placement of an endoscopic clip or injection of contrast into the submucosa at the proximal margin of the stricture may be performed. This allows for visualization of the proximal margin during deployment in the event that stent deployment occurs with the endoscope tip in the stomach (see below).

In cases where the obstructing lesion extends into the duodenal bulb, the proximal end of the stent should be brought through the pylorus and positioned in the stomach. Most early generation self-expanding metal enteral stents contained sharp edges on the proximal and distal ends. Due to the thin-walled duodenum and increased risk of stent-related perforation, transpyloric deployment was preferable to leaving the proximal edge of the stent within the duodenal bulb. The design of the latest generation enteral stent (see below) has eliminated the sharp proximal and distal ends making (theoretically) deployment within the duodenal bulb safer, thus potentially obviating transpyloric positioning, unless clinically indicated [21].

Complications

The major risk of enteral stent placement is intestinal perforation, which has been reported to occur in 0.7% of individuals [6, 10]. The risk is increased in cases where balloon dilation is performed or when stents are deployed around intestinal angulations, which are relatively "fixed" in position due to obstructing malignant neoplasms. Because most patients in whom enteral stents are placed have an underlying advanced malignancy, surgical repair of stent-related intestinal perforation may be technically difficult or impossible, resulting in peritonitis and death. As such, proper informed consent of patients considered for enteral stent placement is imperative.

The performance of endoscopy in patients with gastric outlet obstruction can lead to aspiration of gastric contents and resultant pneumonia. This risk is increased in cases performed without adequate measures taken to protect the airway or insufficient gastric decompression. Another risk of enteral stent placement within the duodenum is biliary obstruction and precipitation of cholangitis. This complication is not limited to patients with a native papilla. Subclinically occluded biliary stents can become completely occluded by the radial expansive force of the duodenal stent. Accordingly, measurement of liver chemistries and a CT scan of the abdomen are essential parts of preprocedural planning for patients in whom duodenal stents may cross the major papilla. ERCP should be performed prior to duodenal stent placement in patients with evidence of biliary obstruction. However, "prophylactic" biliary stenting is not supported by any clinical evidence to date [21].

Other complications of enteral stent placement include stent migration (5%) and bleeding (0.5%) (especially with older stent designs) in addition to stent occlusion (18%) [6, 10, 21]. Stent migration in malignant disease is rare. Migrated stents may pass spontaneously or, in rare cases, lead to small bowel obstruction or delayed intestinal perforation requiring surgery. Occlusion of enteral stents can be secondary to food bolus impaction, tissue hyperplasia, or tumor ingrowth (Fig. 20.7). Food bolus impaction can typically be handled endoscopically, whereas ingrowth of tumor and tissue hyperplasia require placement of a second endoprosthesis [6, 21]. Finally, newer-generation enteral stents are fashioned from nitinol (see below). Although superior in terms of radial expansive force, these devices foreshorten. In cases where an adequate "safety" margin of 2–3 cm of stent on either end of the obstruction does not exist, recurrent intestinal obstruction following stent foreshortening can be observed. Stent revision (insertion of a longer stent) is required in such cases.

Post-Procedural Care

Patients are typically allowed nothing by mouth for the first 24 h following enteral stent placement as most prostheses require this period of time to reach maximum expansion. A liquid diet can be initiated after 24 h, and if tolerated, the diet advanced to a maximum of mechanical soft or puree. An upper GI series (Fig. 20.6) with small bowel follow-through should be obtained in patients with continued obstructive symptoms following enteral stent placement, in order to rule out early complications such as stent migration, malposition, or more distal intestinal obstruction. Patients with severe pain, fever, or leukocytosis should undergo a CT scan of the abdomen in order to evaluate for intestinal perforation. Many patients with long-standing gastric or duodenal outlet obstruction will have coexisting gastroparesis. In these cases, enteral stent placement may not provide adequate symptomatic relief, and treatment with promotility agents may be required. In patients for whom promotility agents do not provide adequate relief of symptoms, alternative methods of nutrition should be discussed and a decompressive gastrostomy considered.

Clinical Efficacy

Over the past several years, enteral SEMS placement has emerged as an alternative to surgery for the palliation of malignant gastric outlet obstruction. Several early uncontrolled case series have demonstrated technical success rates of greater than 90% [1, 12, 42]. Dormann and colleagues performed a systematic review of the published series on the use of SEMS for palliation of gastroduodenal malignancies.

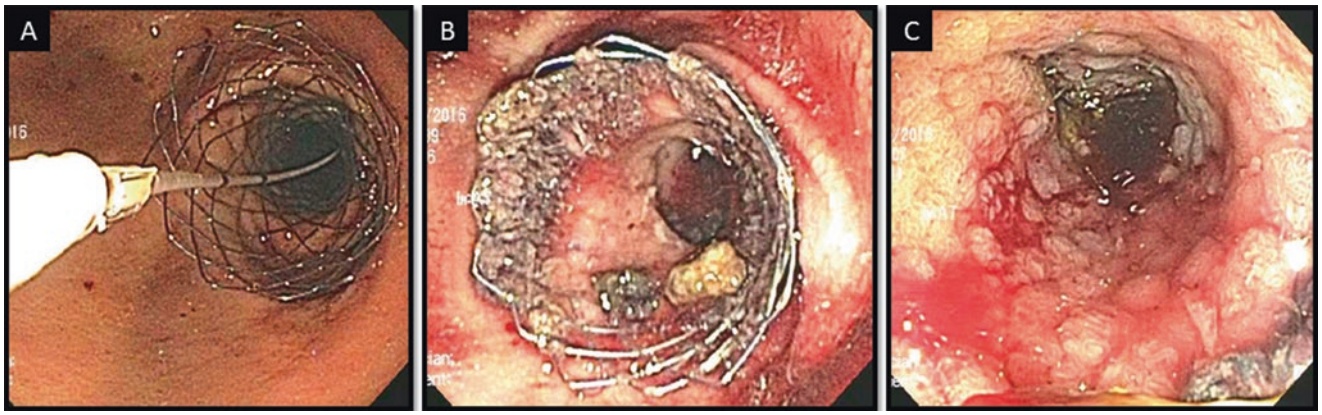

Fig. 20.7 Endoscopic placement (**a**) of a duodenal stent for malignant gastric outlet obstruction due to pancreatic adenocarcinoma. An endoscopy is performed 16 days later to investigate a source of GI blood loss (**b**) and (**c**) reveals nonobstructive tissue hyperplasia and granulation

Findings included successful stent deployment in 589 of 606 patients (97%) in whom it was attempted. Clinical success, as defined by resumption of oral intake following stent placement, was achieved in 89% of patients in whom stents could be successfully placed with full resolution of symptoms occurring at a mean of 4 days. Procedure-related mortality was zero. Major complications such as bleeding and perforation occurred in 1.2% of patients; stent migration was reported in 5% [10].

A more recent prospective multicenter cohort evaluating the efficacy of the Evolution duodenal stent revealed 89% technical success (95% CI 77–95%) with 72% clinical success (95%CI 58–83%). Multiple objective measures of gastric outlet obstruction revealed significant improvement. Stent dysfunction occurred in 14 individuals (30%) and included stent ingrowth (n = 9) and migration (n = 2). No perforation or hemorrhage was noted [75]. A similar single institution review of the WallFlex enteral stent identified 21 patients with malignant gastric outlet obstruction. The technical success in placement was 100% with 81% of individuals achieving improved clinical symptoms. There was no hemorrhage or perforation noted, but one patient (4.7%) developed pancreatitis [27]. In a large pooled analysis of 19 prospective studies including 1281 patients with malignant gastric outlet obstruction, the technical success of SEMS placement was 97.3%, and the clinical success was 85.7%. The complication rate was 19.6% with re-obstruction (12.6%) the commonest issue. Intestinal perforation was noted in 1.2% and major hemorrhage in 0.8% [76].

There remains limited data on the natural history and survival rates of post-stenting malignant gastric outlet obstruction. In the largest North American study to date, Oh et al. retrospectively reviewed 292 patients, 196 with pancreatic adenocarcinoma and 96 with non-pancreatic malignancy who underwent gastroduodenal stenting for malignant gastric outlet obstruction. The technical success rate was similar between both groups at 99% in the pancreatic and 100% in the non-pancreatic populations (p = 0.300). There was no difference on median post-stenting survival, 2.7 months versus 2.4 months (p = 0.600), in those with pancreatic versus non-pancreatic malignancy, respectively. Both post-stenting chemotherapy and the absence of distant metastasis were independently associated with increased survival. Clinical success defined by maintaining adequate oral intake without repeat endoscopic intervention was significantly higher in the non-pancreatic group versus pancreatic group (91% versus 71%, p = 0.004) at 2 months post-stenting but comparable at 12 months (70% versus 56%, p = 0.450). The frequency of re-intervention was similar at 30% versus 23% (p = 0.200) in the pancreatic and non-pancreatic groups with repeat stent placement the most common re-intervention. The overall adverse event rate was 29% with no significant difference between groups. A total of 84 stent occlusions occurred in 61 individuals (21%). Hemorrhage, stent migration, and perforation occurred in 5.1%, 4.4%, and 3.4% of individuals, respectively, and rates did not differ between groups [44].

There are now several series in the literature, which compare SEMS placement to surgical bypass for the treatment of malignant gastroduodenal outlet obstruction [26, 37, 39]. In a single center retrospective cohort, Khashab et al. compared 120 individuals who received enteral stenting for malignant gastric outlet obstruction to 277 individuals who underwent palliative gastrojejunostomy. The technical success was significantly different, but similarly high (99% gastrojejunostomy versus 96% enteral stenting, p = 0.004). Gastrojejunostomy was associated with a higher complication rate (22.1 versus 11.6, p = 0.02), while enteral stenting was associated with an increased risk of re-intervention (OR 9.18, $p < 0.0001$) but a shorter length of hospital stay (p = 0.005) [29].

As seen above, most have found high technical success rates for both procedures. However, patients who underwent

surgical bypass tended to have an increased duration of hospitalization, a higher rate of postoperative complications, and a longer time interval to restoration of oral intake. A survival benefit has not been demonstrated for either modality. Regardless, in patients with incurable malignancies and anticipated short-term survival, the advantages of SEMS placement may provide for an improved quality of life over surgery [21, 36].

Available Devices

At present, the devices approved in the United States for palliation of malignant gastroduodenal obstruction include the WallFlex duodenal stent (Boston Scientific) and the Evolution duodenal stent (Cook Medical). All devices are uncovered self-expandable metal stents that can be deployed either through the endoscope (10 Fr delivery system) or over a guide wire using fluoroscopic control. The length of the delivery systems (230 cm) facilitates passage through a colonoscope for deeper enteral deployment if required.

The WallFlex and Evolution enteral stents are fashioned from nitinol, and the diameter of the stent body is 22 mm, and available lengths are 6, 9, and 12 cm. The WallFlex has a single 27 mm proximal flare, and the Evolution stent has a double-flanged design with a 27 mm proximal and 27 mm distal flare.

Like its esophageal counterpart, the Niti-S Pyloric Stent (Taewoong Medical, Korea) is fashioned from a double-layered nitinol outer core with an inner polyurethane covering. Although this stent is not currently available in the United States, the double-layered design represents important technology, potentially reducing tumor ingrowth and resultant stent occlusion, which can require endoscopic re-intervention.

Alternative Treatments

The traditional alternatives to enteral stent placement for the treatment of malignant gastric or duodenal outlet obstruction include surgical gastroenteric anastomosis and placement of an enteric feeding tube combined with a decompressive gastrostomy, in addition to placement of a decompressive gastrostomy with or without parenteral nutrition.

Recent reports of safety and success using a novel endoscopic ultrasound-based technique to create a gastroenterostomy with a lumen-apposing fully covered self-expandable metal stent in cases of benign and malignant gastric outlet obstruction are promising and highlight the future potential of endoluminal stenting to address malignant obstruction (Fig. 20.8) [30].

Colonic Stenting

Obstructing colorectal neoplasms, namely, adenocarcinoma, can lead to significant morbidity and mortality. Not surprisingly, relief of obstruction from intrinsic neoplastic disorders of the large bowel is the leading indication for colonic stent placement [21]. Colonic stents can be placed to relieve obstruction for extracolonic malignancies, which cause extrinsic compression, leading to colonic obstruction [21]. Cancers of the prostate, ovary, and cervix can often lead to colonic obstruction due to this mechanism. Colonic stents have also occasionally been placed for benign disease including ischemic colonic strictures, strictures related to diverticular disease, and Crohn's and anastomotic strictures [14, 63, 67]. Endoscopic ultrasound and lumen-apposing self-expandable metals stents have broadened the indication for stenting benign conditions; however, at the present time this use has been limited to case reports (Fig. 20.9). The focus of the discussion that follows is colonic stenting for malignant obstruction.

In patients with malignant colonic obstruction, stents have been used in two scenarios. The first is in patients who either have metastatic disease at the time of presentation or in those who are poor surgical candidates. In this situation, colonic stenting is palliative. The second is in patients who are good surgical candidates with complete colonic obstruction in whom a bowel preparation is preferred to a diverting colostomy with Hartmann's pouch followed by a second surgery several weeks to months later. If successful in relief of obstruction, colonic stenting in this group of patients allows for a single-step operation [21].

Contraindications

As for other endoscopic procedures performed under conscious sedation, patients medically unfit for endoscopy should not undergo colonic stent placement. This procedure is also contraindicated in patients with signs or symptoms consistent with intestinal perforation and peritonitis. In some patients, obstructing colonic malignancies can perforate the colon yet not be associated with gross peritonitis. Identification of mesenteric fat at endoscopy should alert the endoscopist to the presence of a perforation, and the stent should not be placed. Patients with obstructing colonic lesions approximating the anal verge should not undergo colonic scenting as there may be insufficient clearance for expansion of the distal portion of the stent. In addition, stents placed in this region may cross the dentate line leading to severe discomfort.

Colonic stents should not be placed in patients with uncontrolled coagulopathy or those with life expectancy less

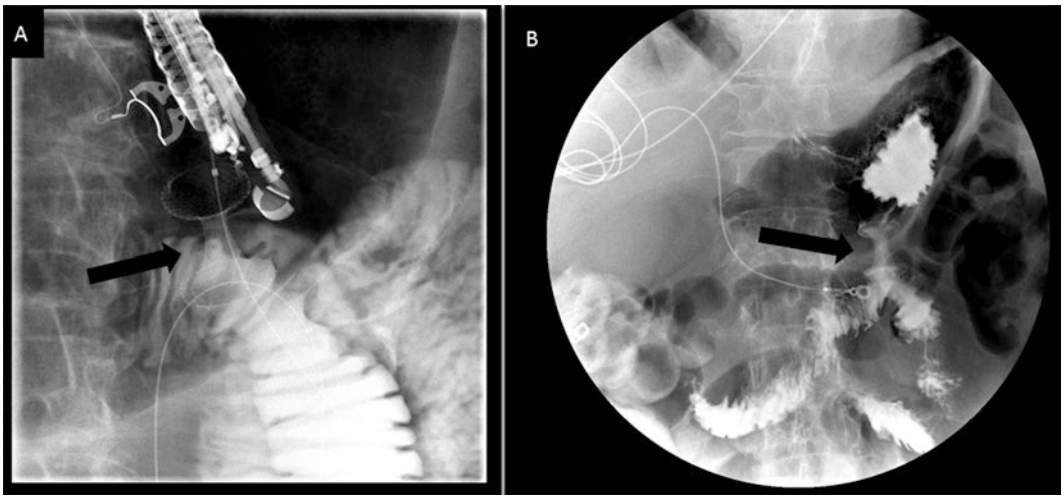

Fig. 20.8 Endosonographic placement of a gastrojejunostomy using a lumen-apposing fully covered self-expandable metal stent (**a**) in a patient with metastatic duodenal adenocarcinoma and a high-grade duodenal obstruction. An upper GI series and small bowel follow-through performed the following day (**b**) demonstrate stent patency and bypass of water-soluble contrast beyond the duodenum (Case details and images courtesy of Shayan Irani, MD)

Practical Considerations

- Colonic stents should not be placed in patients with uncontrolled coagulopathy or those with life expectancy less than 30 days.
- Patients with multiple obstructing colonic lesions are unlikely to benefit from the placement of a single colonic stent.

than 30 days. Finally, individuals with multiple obstructing colonic lesions are unlikely to benefit from the placement of a single colonic stent.

Procedure

Because patients with acute colonic obstruction cannot undergo full oral bowel preparation, colonic stents are typically placed into the unprepped colon. In patients with obstruction of the rectosigmoid or descending colon, enemas may be used to clear the distal colon. The choice of endoscope depends on the location of the obstruction. Lesions within the left colon up to the splenic flexure can typically be reached using a sigmoidoscope or therapeutic upper endoscope, while those in the more proximal colon will require the use of a colonoscope. Patients with acute colonic obstruction should undergo nasogastric suction to decompress the bowel proximal to the stenosis and reduce the risk of aspiration of gastric contents. A gastrografin enema should be performed for planning purposes in all patients with suspected proximal obstruction and in those patients with distal obstruction in whom additional stricture characterization is desired [21].

After sedating the patient, the endoscope is advanced through the unprepped colon to the level of the stenosis. Insufflation should be used judiciously as overdistension can lead to proximal bowel perforation. Once the level of the stenosis is reached, a stiff guide wire can be placed through the stricture using an ERCP catheter or balloon catheter. Injection of contrast through the stenosis should be performed to help to define the length of the obstruction (Fig. 20.10). Passage of the endoscope proximal to the stricture is not mandatory and can lead to colonic perforation. Because visualization may be difficult in the colon and some devices cannot be placed through the endoscope, an endoscopic clip should be placed 1–2 cm below the distal margin of obstruction to allow for fluoroscopic visibility. Alternatively, water- or lipid-soluble contrast material can be injected with a sclerotherapy needle to delineate stricture margins.

The choice of stent should be 3–4 cm longer than the estimated length of the obstruction in order to allow for adequate coverage, especially with stents fashioned from nitinol, which tend to foreshorten as they expand. Stents can be delivered through the working channel (Fig. 20.10) of the endoscope or over the guide wire alone. In either case, deployment should be performed under fluoroscopic control. Because obstructing colonic neoplasms can often cause acute angulations in the bowel, maintaining proper endoscope position during stem deployment can often require the assistance of a nurse, technician, or additional physician.

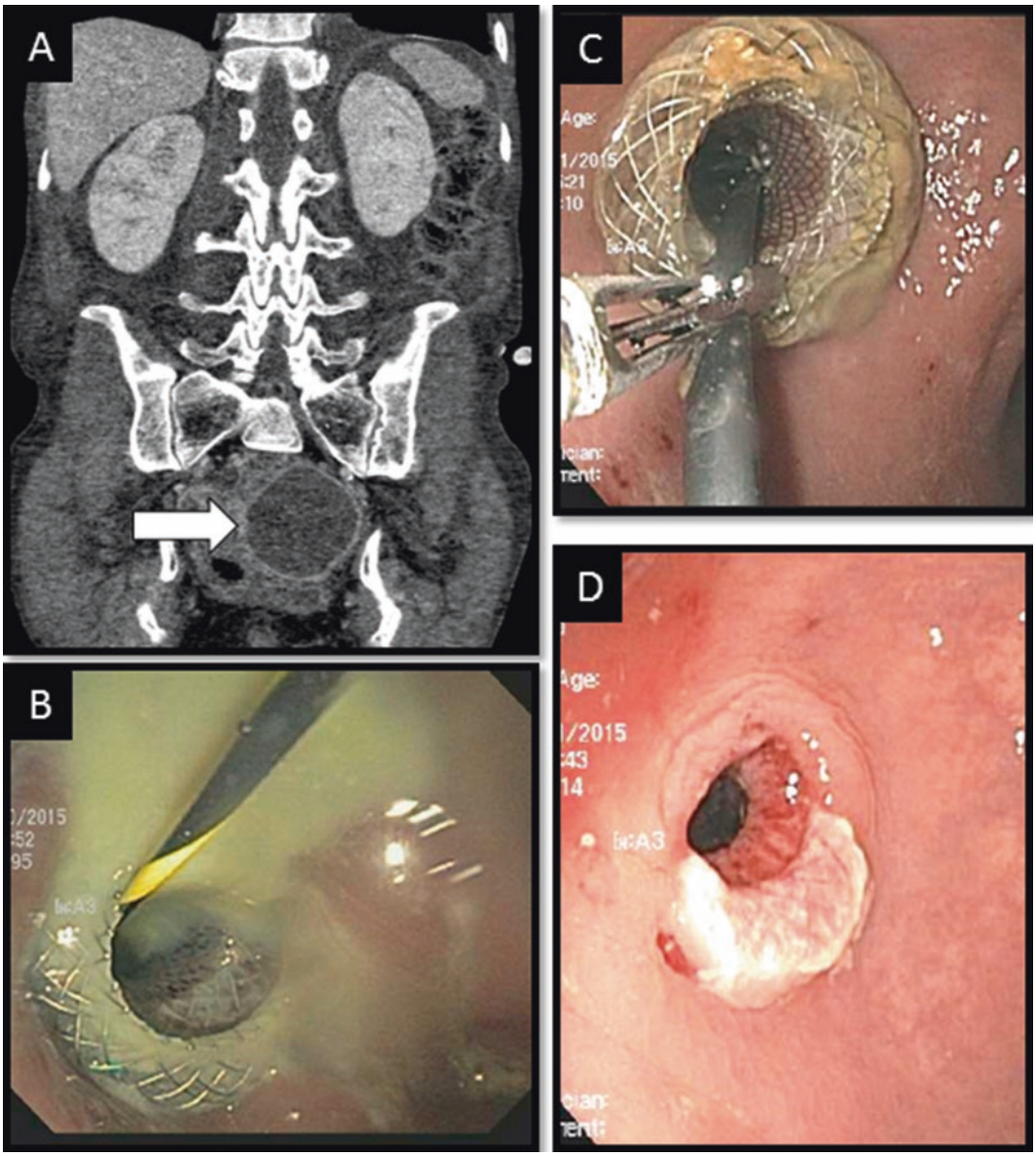

Fig. 20.9 Radiographic view of a difficult to drain perirectal abscess (**a**) in a poor surgical candidate. An endoscopic ultrasound-guided lumen-apposing self-expandable metal stent was used to drain the abscess (**b**). Two weeks later the stent was removed (**c**) and (**d**) with resolution of the abscess (Case details and images courtesy of Shayan Irani, MD)

Complications

The major complication associated with colonic stent placement is intestinal perforation. This occurs in approximately 5–7% of cases [78, 83]. Many cases of colonic perforation are encountered when stents are placed around acute angulations in the colon. This is due to straightening of the bowel, which occurs with expansion of the stent. In addition, prior case reports and a retrospective review implicated the anti-angiogenic chemotherapeutic agent, bevacizumab, as a potential contributor to stent-related colonic perforation [5, 64]. A more recent multicenter review identified bevacizumab as an independent risk factor for stent-related colonic perforation with a rate of 12.5% [78]. As in all cases of colonic perforation, prompt recognition, administration of broad-spectrum antibiotics, and surgical consultation are essential.

Other complications related to colonic stent placement include bleeding, stent migration (11.8%), and occlusion (7.3%) [83]. Like other enteral stents, occlusion is typically due to ingrowth of tumor or bolus impaction. In the case of tumor-related occlusion, revision with *a* second stent typically leads to clinical improvement. Migrated stents may pass spontaneously or require endoscopic removal if they become lodged at the anal verge.

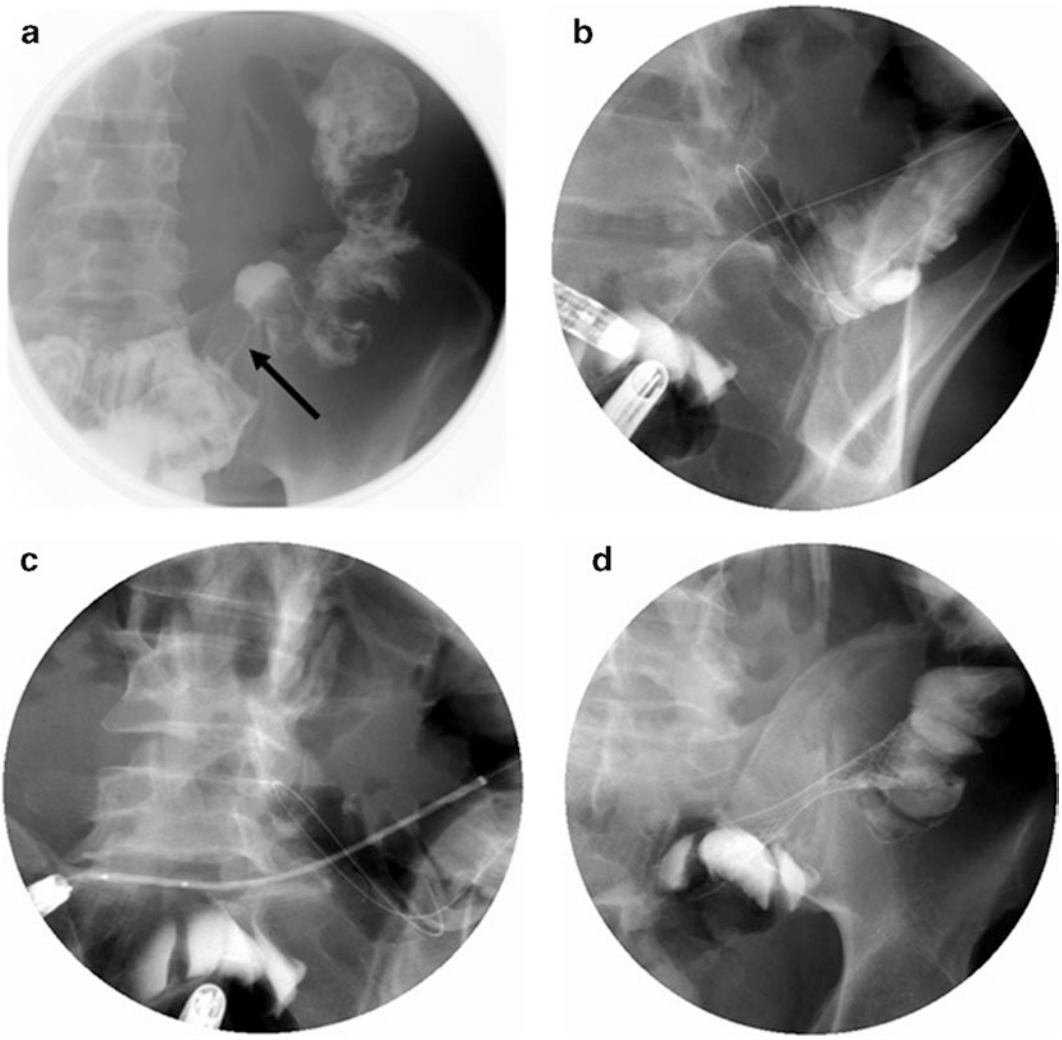

Fig. 20.10 Barium enema demonstrating a severe stenosis (*arrow*) in the sigmoid colon (**a**). A guide wire was placed beyond the stenosis following injection of contrast (**b**). A through-the-scope colonic SEMS was positioned across the stenosis over the guide wire, through the scope (**c**), and deployed in satisfactory position (**d**)

Postoperative Care

Most patients who undergo successful colonic stent placement experience immediate relief of symptoms. A clear liquid diet can be initiated after 24 h and if surgery is planned, a full bowel prep can be administered.

In patients undergoing palliative stenting, diet can be advanced as tolerated. Patients who do not experience colonic decompression following stent placement should undergo an abdominal radiograph to determine whether the stent has migrated or is malpositioned [21]. If the stent appears in good position with full expansion, repeat endoscopy can be considered to determine the reason for stent dysfunction or whether a second, upstream obstruction exists (more common in extrinsic malignancy). Alternatively, a water-soluble contrast study can be obtained initially. Patients with signs and symptoms of peritonitis following stent placement should undergo an urgent abdominal CT scan to evaluate for colonic perforation.

Clinical Data

Malignant Disease

Several case series and pooled analyses have now demonstrated the efficacy of colonic stent placement [50, 61, 83]. In a comprehensive review of available data, Sebastian and colleagues [55] reported a technical success rate of more than 93% for stent placement on the first attempt. Clinical success rates, as defined by colonic decompression (either clinically or radiographically), were found to be greater than 88%. Compared to surgery, SEMS placement in the colon was associated with a shorter duration of hospitalization, lower

rates of complications, and a decrease in the need for colostomy [43, 71]. The limited available evidence also suggests that initial SEMS placement for malignant colonic obstruction is a cost-effective strategy when compared to surgery [62, 70]. In many centers, an attempt at SEMS placement is now the preferred strategy for the initial management of acute colonic obstruction secondary to malignancy [32].

Benign Disease

Little is known about the feasibility, safety, and efficacy of colonic stenting in the management of nonmalignant colorectal strictures. In a multicenter retrospective study evaluating 43 patients with obstructive colonic symptoms due to anastomotic (n = 40), postischemic (n = 2), and postradiation (n = 1) strictures who underwent stenting with a FCSEMS, the technical success was 100% and the clinical success 81% (n = 35). However, migration was observed in 63% (n = 27), and recurrent obstructive symptoms occurred in 53% (n = 23) irrespective of stent migration [73]. A retrospective analysis of 11 individuals with refractory anastomotic strictures who underwent placement of an esophageal BD (polydioxanone based) revealed a 100% technical success rate with stent migration occurring within 2 weeks in four individuals (36%) who subsequently developed recurrent obstructive symptoms. Of the seven remaining patients, five developed complete symptomatic resolution and the other two required surgery [52].

From a conceptual standpoint, stenting appears to be a promising intervention for benign colorectal strictures; however, until optimized colorectal specific devices and further studies are available, the high rate of stent-related complications raises concerns over patient safety and suggests alternative endoscopic options must be sought initially to address these stricture-related ailments.

Available Devices

There are currently five SEMS approved by the US Food and Drug Administration for the palliation of malignant colonic obstruction. The colonic Wallstent, WallFlex, and Ultraflex Precision are all manufactured by Boston Scientific (Natick, MA). The colonic Wallstent is fashioned from Elgiloy and is available in a 20 or 22 mm diameter and lengths of 6 and 9 cm. The delivery system is 10 Fr, with a working length of 230 cm. The colonic WallFlex is fashioned from nitinol. However, as opposed to the Wallstent, the ends of the stent are interwoven, which may potentially decrease the risk of perforation. The WallFlex colonic stent is available in diameters ranging from 22 to 25 mm and has a 27 or 30 mm proximal flare. Lengths are 6, 9, and 12 cm, and they are inserted using a 10 Fr delivery system with a working length of either 135 or 230 cm. Finally, the Ultraflex Precision colonic stem is fashioned from nitinol and has a central diameter of 25 mm and a 30 mm proximal flare. This device can only be inserted over an endoscopically or fluoroscopically positioned guide wire using a 105-cm-long delivery catheter.

The colonic Z stent and Evolution colonic stents are manufactured by Cook Medical. The colonic Z stent is a stainless steel stent, which is available in lengths of 4, 6, 8, 10, and 12 cm. The stent can only be placed over a guide wire under fluoroscopic control as the delivery catheter is 10 mm. The stent is 25 mm in shaft diameter with a 35 mm proximal flare. The introducer is 40 cm in length and its use is, therefore, limited to the left colon. The Evolution colonic stent is a nitinol-based stent with a through-the-scope deployment system. It is available in lengths 6, 8, and 10 cm and has a 25 mm mid-body shaft diameter and 30 mm proximal and distal flange.

Alternative Procedures

Alternatives to colonic stenting for acute colonic obstruction include a diverting colostomy or, in patients who are not surgical candidates, placement of a transrectal colonic decompression tube.

Conclusions

- Self-expandable stents are utilized for the treatment of benign esophageal diseases including perforation, anastomotic leaks, and refractory benign esophageal strictures.
- Tumors located in the mid- to upper esophagus raise the theoretical risk of causing airway obstruction.
- The risk of stent migration is typically lowest in patients with intrinsic strictures of the esophagus.
- For most malignant lesions, a partially or fully covered SEMS is preferable to an uncovered stent in order to prevent the tumor ingrowth.
- The major drawback to partially or fully covered stents is the increased risk of stent migration.
- Stents placed across the gastroesophageal junction obliterate the natural reflux barrier, and patients almost invariably develop reflux of gastric contents into the proximal esophagus or oropharynx; specifically designed “anti-reflux” stents may help to decrease symptoms.
- Because endoscopic measurements may be slightly inaccurate, it is best to err on the side of a longer (rather than shorter) stent in order to decrease the risk of failing to palliate the obstructing lesion.

References

1. Adler DG, Baron TH. Endoscopic palliation of malignant gastric outlet obstruction using self-expanding metal stems: experience in 36 patients. Am J Gastroenterol. 2002;97:72–8.
2. Alam TA, Baines M, Parker MC. The management of gastric outlet obstruction secondary to inoperable cancer. Surg Endosc. 2003;17:320–3.
3. Altemur Karamustafaoglu Y, Yoruk Y. Self-expandable esophageal stents placement for the palliation of dysphagia as a result of lung cancer. Dis Esophagus. 2010;23:561–4.
4. Baron TH. Minimizing endoscopic complications: endoluminal stents. Gastrointest Endosc Clin N Am. 2007;17:83–104.
5. Cennamo V, Fuccio L, Mutri V, Minardi ME, Eusebi LH, Ceroni L, Laterza L, Ansaloni L, Pinna AD, Salfi N, Martoni AA, Bazzoli F. Does stent placement for advanced colon cancer increase the risk of perforation during bevacizumab-based therapy? Clin Gastroenterol Hepatol. 2009;7:1174–6.
6. Chopita N, Landoni N, Ross A, Villaverde A. Malignant gastroenteric obstruction: therapeutic options. Gastrointest Endosc Clin N Am. 2007;17:533–44.
7. Conio M, et al. A randomized prospective comparison of self-expandable plastic stents and partially covered self-expandable metal stents in the palliation of malignant esophageal dysphagia. Am J Gastroenterol. 2007;102:2667–77.
8. DaVee T, Irani S, Leggett CL, Berzosa Corella M, Grooteman KV, Wong Kee Song LM, Wallace MB, Kozarek RA, Baron TH. Stent-in-stent technique for removal of embedded partially covered self-expanding metal stents. Surg Endosc. 2015;30(6):2332–41.
9. De Olabozal J, Roberts J, Hoeltgen T, Berkelhammer C. Double stenting to prevent airway compression in proximal malignant esophageal strictures. Am J Gastroenterol. 2001;96:2800–1.
10. Dormann A, Meisner S, Verin N, Wenk LA. Self-expanding metal stents for gastroduodenal malignancies: systematic review of their clinical effectiveness. Endoscopy. 2004;36:543–50.
11. Dua KS. Scents for palliating malignant dysphagia and fistula: is the paradigm shifting? Gastrointest Endosc. 2007;65:77–81.
12. Dumas R, et al. Palliative endoscopic treatment of malignant duodenal stenosis by metal prosthesis_. Gastroenterol Clin Biol. 2000;24:714–8.
13. Farivar AS, Vallieres E, Kowdley KV, Wood DE, Mulligan MS. Airway obstruction complicating esophageal stent placement in two post-pneumonectomy patients. Ann Thorac Surg. 2004;78:e22–3.
14. Forshaw MJ, Sankararajah D, Stewart M, Parker MC. Self-expanding metallic stents in the treatment of benign colorectal disease: indications and outcomes. Color Dis. 2006;8:102–11.
15. Freeman RK, Van Woerkom JM, Ascioti AJ. Esophageal stent placement for the treatment of iatrogenic intrathoracic esophageal perforation. Ann Thorac Surg. 2007a;83:2003–7. discussion 2007-8
16. Freeman RK, Ascioti AJ, Wozniak TC. Postoperative esophageal leak management with the Polyflex esophageal stent. J Thorac Cardiovasc Surg. 2007b;133:333–8.
17. Freeman RK, Van Woerkom JM, Vyverberg A, Ascioti AJ. Esophageal stent placement for the treatment of spontaneous esophageal perforations. Ann Thorac Surg. 2009;88:194–8.
18. Frimberger E. Expanding spiral-a new type of prosthesis for the palliative treatment of malignant esophageal stenoses. Endoscopy. 1983;15(Suppl 1):213–4.
19. Fuccio L, Hassan C, Frazzoni L, Miglio R, Repici A. Clinical outcomes following stent placement in refractory benign esophageal stricture: a systemic review and meta-analysis. Endoscopy. 2016;48:141–8.
20. Ginsberg GG. Palliation of malignant esophageal dysphagia: would you like plastic or metal? Am J Gastroenterol. 2007;102:2678–9.
21. Gupta K, Freeman M. Enteral and colonic self-expanding metallic stents. Rev Gastroenterol Disord. 2008;8:83–97.
22. Hamm YH, Kim GH. Plastic and biodegradable stents for complex and refractory benign esophageal stents. Clin Endosc. 2014;477:295–300.
23. Holm AN, de la Mora Levy JG, Gostout CJ, Topazian MD, Baron TH. Self-expanding plastic stents in treatment of benign esophageal conditions. Gastrointest Enclose. 2008;67:20–5.
24. Homann N, Noftz MR, Klingenberg-Noftz RD, Ludwig D. Delayed complications after placement of self-expanding stents in malignant esophageal obstruction: treatment strategies and survival rate. Dig Dis Sci. 2008;53:334–40.
25. Irani S, Baron TH, Gluck M, Gan I, Ross AS, Kozarek RA. Preventing migration of fully covered esophageal stents with an over-the-scope clip device (with videos). Gastrointest Endosc. 2014;79:844–51.
26. Jeurnink SM, et al. Gastrojejunostomy versus stent placement in patients with malignant gastric outlet obstruction: a comparison in 95 patients. J Surg Oncol. 2007;96:389–96.
27. Kanno Y, Ito K, Fujita N, Noda Y, Kobayashi G, Horaguchi J, Koshita S, Ogawa T, Masu K, Hirasawa D, Sugawara T, Koike Y, Hashimoto S, Ishii S. Efficacy and safety of a WallFlex enteral stent for malignant gastric obstruction. Dig Endosc. 2013;25:386–91.
28. Kantsevoy SV, Bitner M. Esophageal stent fixation with endoscopic suturing device (with video). Gastrointest Endosc. 2012;76:1251–5.
29. Khashab M, Alawad AS, Shin EJ, Kim K, Bourdel N, Singh VK, Lennon AM, Hutfless S, Sharaiha RZ, Amateau S, Okolo PI, Makary MA, Wolfgang C, Canto MI, Kalloo AN. Enteral stenting versus gastrojejunostomy for palliation of malignant gastric outlet obstruction. Surg Endosc. 2013;27:2068–75.
30. Khashab MA, Kumbhari V, Grimm IS, Ngamruengphong S, Aguila G, El Zein M, Kalloo AN, Baron TH. EUS-guided gastroenterostomy: the first U.S. clinical experience (with video). Gastrointest Endosc. 2015;82:932–8.
31. Kawasaki R, Sano A, Matsumoto S. Long-term outcomes and complications of metallic stents for malignant esophageal stenoses. Kobe J Med Sci. 2003;49:133–42.
32. Kozarek RA. Making sense out of colonic stents. Gastrointest Endosc. 2008;67:85–7.
33. Kozarek RA, Raltz S, Brugge WR, et al. Prospective multicenter trial of esophageal Z-stent placement for malignant dysphagia and tracheoesophageal fistula. Gastrointest Endosc. 1996;44:562–7.
34. Knyrim K, Wagner HJ, Bethge N, Keymling M, Vakil N. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. N Engl J Med. 1993;329:1302–7.
35. Hu L, Marriott A, Wilbraham L, Tunnah S, England RE, Martin DF. Effectiveness of open versus antireflux stents for palliation of distal esophageal carcinoma and prevention of symptomatic gastroesophageal reflux. Radiology. 2002;225:359–65.
36. Lowe AS, et al. Self-expandable metal stent placement for the palliation of malignant gastroduodenal obstruction: experience in a large, single, UK Centre. Clin Radiol. 2007;62:738–44.
37. Maetani I, et al. Self-expandable metallic stent placement for palliation in gastric outlet obstructions caused by gastric cancer: a comparison with surgical gastrojejunostomy. J Gastroenterol. 2007;40:932–7.
38. Mariette C, Gronnier C, Duhamel A, Mabrut JY, Bail JP, Carrere N, Lefevre JH, Meunier B, Collet D, Piessen G, FREGAT Working Group–FRENCH–AFC; FREGAT Working Group-FRENCH-AFC. Self-expanding covered metallic stent as a bridge to surgery in esophageal cancer: impact on oncologic outcomes. J Am Coll Surg. 2015;220:287–96.
39. Mehta S, et al. Prospective randomized trial of laparoscopic gastrojejunostomy versus duodenal stenting for malignant gastric outflow obstruction. Surg Endosc. 2006;20:239–42.

40. Mudumbi S, Velazquez-Aviña J, Neumann H, Kyanam Kabir Baig KR, Mönkemüller K. Anchoring of self-expanding metal stents using the over-the-scope clip, and a technique for subsequent removal. Endoscopy. 2014;46:1106–9.
41. Nagaraja V, Cox MR, Eslick GD. Safety and efficacy of esophageal stents preceding or during neoadjuvant chemotherapy for esophageal cancer: a systematic review and meta-analysis. J Gastrointest Oncol. 2014;5:119–26.
42. Nassif T, et al. Endoscopic palliation of malignant gastric outlet obstruction using self-expandable metallic stents: results of a multicenter study. Endoscopy. 2003;35:483–9.
43. Ng KC, et al. Self-expanding metallic stent as a bridge to surgery versus emergency resection for obstructing left-sided colorectal cancer: a case-matched study. J Gastrointest Surg. 2006;10:798–803.
44. Oh SY, Edwards A, Mandelson M, Ross A, Irani S, Larsen M, Gan SI, Gluck M, Picozzi V, Helton S, Kozarek RA. Survival and clinical outcome after endoscopic duodenal stent placement for malignant gastric outlet obstruction: comparison of pancreatic cancer and nonpancreatic cancer. Gastrointest Endosc. 2015;82:460–8.
45. Oida T, Mimatsu K, Kano H, Kawasaki A, Kuboi Y, Fukino N, Kida K, Amano S. Double stents: airway stenting after esophageal-stent implantation for esophageal cancer. Hepato-Gastroenterol. 2011;58:1985–8.
46. Papachristou GI, Baron TH. Use of stents in benign and malignant esophageal disease. Rev Gastroenterol Disord. 2007;7:74–88.
47. Pellen MG, Sabri S, Razack A, Gilani SQ, Jain PK. Safety and efficacy of self-expanding removable metal esophageal stents during neoadjuvant chemotherapy for resectable esophageal cancer. Dis Esophagus. 2012;25:48–53.
48. Radecke K, Gerken G, Treichel U. Impact of a self-expanding, plastic esophageal stent on various esophageal stenoses, fistulas, and leakages: a single-center experience in 39 patients. Gastrointest Endosc. 2005;61:812–8.
49. Raijman I, Siddique I, Ajani J, Lynch P. Palliation of malignant dysphagia and fistulae with coated expandable metal stents: experience with 101 patients. Gastrointest Endosc. 1998;48:172–9.
50. Repici A, et al. Stenting of the proximal colon in patients with malignant large bowel obstruction: techniques and outcomes. Gastrointest Endosc. 2007;66:940–4.
51. Repici A, Jovani M, Hassan C, Solito B, Di Mitri R, Buffoli F, Macrì G, Fregonese D, Cennamo V, De Bellis M, Anderloni A, Siersema PD. Management of inoperable malignant oesophageal strictures with fully covered WallFlex(®) stent: a multicentre prospective study. Dig Liver Dis. 2014;46:1093–8.
52. Repici A, Pagano N, Rando G, Carlino A, Vitetta E, Ferrara E, Strangio G, Zullo A, Hassan C. A retrospective analysis of early and late outcome of biodegradable stent placement in the management of refractory anastomotic colorectal strictures. Surg Endosc. 2013;27:2487–91.
53. Rhee K, Kim JH, Jung DH, Han JW, Lee YC, Lee SK, Shin SK, Park JC, Chung HS, Park JJ, Youn YH, Park H. Self-expandable metal stents for malignant esophageal obstruction: a comparative study between extrinsic and intrinsic compression. Dis Esophagus. 2015;24:224–8.
54. Rustgi AK, El-Serag HB. Esophageal carcinoma. N Engl J Med. 2014;371:2499–509.
55. Sebastian S, Johnston S, Geoghegan T, Torreggiani W, Buckley M. Pooled analysis of the efficacy and safety of self-expanding metal stenting in malignant colorectal obstruction. Am J Gastroenterol. 2004;99:2051–7.
56. Seven G, Irani S, Ross AS, Gan SI, Gluck M, Low D, Kozarek RA. Partially versus fully covered self-expanding metal stents for benign and malignant esophageal conditions: a single center experience. Surg Endosc. 2013;27:2185–92.
57. Sharma P, Kozarek R. Practice parameters Committee of American College of gastroenterology. Role of esophageal stents in benign and malignant diseases. Am J Gastroenterol. 2010;105:258–73.
58. Shin JH, Song HY, Ko GY, et al. Esophagorespiratory fistula: long-term results of palliative treatment with covered expandable metallic stents in 61 patients. Radiology. 2004;232:252–9.
59. Siddiqui AA, Loren D, Dudnick R, Kowalski T. Expandable polyester silicon-covered stein for malignant esophageal strictures before neoadjuvant chemoradiation: a pilot study. Dig Dis Sci. 2007;52:823–9.
60. Siddiqui AA, Sarkar A, Beltz S, Lewis J, Loren D, Kowalski T, Fang J, Hilden K, Adler DG. Placement of fully covered self-expandable metal stents in patients with locally advanced esophageal cancer before neoadjuvant therapy. Gastrointest Endosc. 2012;76:44–51.
61. Siddiqui A, Khandelwal N, Anthony T, Huerta S. Colonic stent versus surgery for the management of acute malignant colonic obstruction: a decision analysis. Aliment Pharmacol Ther. 2007;26:1379–86.
62. Singh H, Latosinsky S, Spiegel BM, Targownik LE. The cost-effectiveness of colonic stenting as a bridge to curative surgery in patients with acute left-sided malignant colonic obstruction: a Canadian perspective. Can J Gastroenterol. 2006;20:779–85.
63. Small AJ, Young-Fadok TM, Baron TH. Expandable metal stent placement for benign colorectal obstruction: outcomes for 23 cases. Surg Endosc. 2008;22:454–62.
64. Small AJ, Coelho-Prabhu N, Baron TH. Endoscopic placement of self-expandable metal stents for malignant colonic obstruction: long-term outcomes and complication factors. Gastrointest Endosc. 2010;71:560–72.
65. Stewart DJ, Balamurugan R, Everitt NJ, Ravi K. Ten-year experience of esophageal self-expanding metal stent insertion at a single institution. Dis Esophagus. 2013;26:276–81.
66. Swinnen J, Eisendrath P, Rigaux J, Kahegeshe L, Lemmers A, Le Moine O, Devière J. Self-expandable metal stents for the treatment of benign upper GI leaks and perforations. Gastrointest Endosc. 2011;73:890–9.
67. Suzuki N, et al. Colorectal stenting for malignant and benign disease: outcomes in colorectal stenting. Dis Colon Rectum. 2004;47:1201–7.
68. Suzuki T, Siddiqui A, Taylor LJ, Cox K, Hasan RA, Laique SN, Mathew A, Wrobel P, Adler DG. Clinical outcomes, efficacy, and adverse events in patients undergoing esophageal stent placement for benign indications: a large multicenter study. J Clin Gastroenterol. 2016;50(5):373–8. (in press)
69. Talreja JP, Eloubeidi MA, Sauer BG, Al-Awabdy BS, Lopes T, Kahaleh M, Shami VM. Fully covered removable nitinol self-expandable metal stents (SEMS) in malignant strictures of the esophagus: a multicenter analysis. Surg Endosc. 2012;26:1664–9.
70. Targownik LE, et al. Colonic stent vs. emergency surgery for management of acute left-sided malignant colonic obstruction: a decision analysis. Gastrointest Endosc. 2004;60:865–74.
71. Tilney HS, et al. Comparison of colonic stenting and open surgery for malignant large bowel obstruction. Surg Endosc. 2007;21:225–33.
72. Vakil N, et al. A prospective, randomized, controlled trial of covered expandable metal stents in the palliation of malignant esophageal obstruction at the gastroesophageal junction. Am J Gastroenterol. 2001;96:1791–6.
73. Vanbiervliet G, Bichard P, Demarquay JF, Ben-Soussan E, Lecleire S, Barange K, Canard JM, Lamouliatte H, Fontas E, Barthet M, Ponchon T, Saurin JC, Research Committee of the French Society of digestive endoscopy (SFED). Fully covered self-expanding metal stents for benign colonic strictures. Endoscopy. 2013;45:35–41.
74. van Boeckel PG, Dua KS, Weusten BL, Schmits RJ, Surapaneni N, Timmer R, Vleggaar FP, Siersema PD. Fully covered self-expandable metal stents (SEMS), partially covered SEMS and self-expandable plastic stents for the treatment of benign esophageal ruptures and anastomotic leaks. BMC Gastroenterol. 2012;12:19.

75. van den Berg MW, Haijtink S, Fockens P, Vleggaar FP, Dijkgraaf MG, Siersema PD, van Hooft JE. First data on the evolution duodenal stent for palliation of malignant gastric outlet obstruction (DUOLUTION study): a prospective multicenter study. Endoscopy. 2013;45:174–81.
76. van Halsema EE, Rauws EA, Fockens P, van Hooft JE. Self-expandable metal stents for malignant gastric outlet obstruction: a pooled analysis of prospective literature. World J Gastroenterol. 2015;21:12468–81.
77. van Halsema EE, van Hooft JE. Clinical outcomes of self-expandable stent placement for benign esophageal diseases: a pooled analysis of the literature. World J Gastrointest Endosc. 2015;7:135–53.
78. van Halsema EE, van Hooft JE, Small AJ, Baron TH, García-Cano J, Cheon JH, Lee MS, Kwon SH, Mucci-Hennekinne S, Fockens P, Dijkgraaf MG, Repici A. Perforation in colorectal stenting: a meta-analysis and a search for risk factors. Gastrointest Endosc. 2014;79:970–82.
79. van Heel NC, Haringsma J, Boot H, Cats A, Vanhoutvin SA, Kuipers EJ. Comparison of 2 expandable stents for malignant esophageal disease: a randomized controlled trial. Gastrointest Endosc. 2012;76:52–8.
80. van Heel NC, Haringsma J, Spaander MC, Bruno MJ, Kuipers EJ. Esophageal stents for the relief of malignant dysphagia due to extrinsic compression. Endoscopy. 2010;42:536–40.
81. Verschuur EM, Kuipers EJ, Siersema PD. Esophageal stents for malignant strictures close to the upper esophageal sphincter. Gastrointest Endosc. 2007;66:1082–90.
82. Verschuur EM, Repici A, Kuipers EJ, Steyerberg EW, Siersema PD. New design esophageal stents for the palliation of dysphagia from esophageal or gastric cardia cancer: a randomized trial. Am J Gastroenterol. 2008;103:304–12.
83. Watt AM, Faragher G, Griffin TT, Rieger NA, Maddern GJ. Self-expanding metallic stents for relieving malignant colorectal obstruction: a systematic review. Ann Surg. 2007;246:24–30.
84. Zwischenberger JB, Savage C, Bidani A. Surgical aspects of esophageal disease: perforation and caustic injury. Am J Respir Crit Care Med. 2002;165:1037–40.

Colonoscopic Polypectomy

21

Peter H. Rubin and Jerome D. Waye

Introduction

As gastrointestinal endoscopy has continued to evolve so has its application from primarily a diagnostic modality capable only of photographs and biopsies to an ever more powerful therapeutic tool. In the realm of colonoscopy, this has meant increased capability for definitive removal of polypoid lesions. Colonoscopists have been enabled to become more aggressive in removing polyps, less deterred by size or location. Since as many as 50% of colons harbor some form of polyp, the colonoscope remains a most effective minimally invasive way to remove premalignant polyps and some self-contained colonic mucosal malignancies [1–5].

Polyp Pathologic Classification

It is still useful to consider the pathology of colon polyps as either "hyperplastic" or "dysplastic." The hyperplastic polyp has virtually no malignant potential, whereas an estimated 10–20% of dysplastic polyps may advance to malignancy.

Dysplastic polyps are subclassified microscopically as "tubular adenomas," "tubulo-villous adenomas," or "villous adenomas." A more recently described polyp type is the sessile "serrated polyp" or sessile "serrated adenoma" with subtypes that may be either predominately hyperplastic or adenomatous [6]. Since these are potentially premalignant, they need to be discovered and removed. Generally, the more "villous" components present in a polyp and the larger the size, the more likely a concurrent or eventual malignancy.

Despite the increased optical definition and potential for some magnification available with current colonoscopic instruments, it remains difficult for the endoscopist to be certain of the microscopic type of a polyp encountered at colonoscopy. Since the recommended guideline interval between colonoscopies has lengthened and the next examination may be a decade away, most endoscopists have adopted the strategy that almost any polyp that is encountered should be removed. An exception to this is the finding of often multiple, diminutive, pale, smooth, glistening polyps in the rectum or distal sigmoid (Fig. 21.1). These are most likely hyperplastic and as such can be left alone without resection or concern.

Polyp Endoscopy Describers

Surface Appearance

It is useful for the endoscopist to observe closely the surface pattern of a polyp. Employing "narrow band imaging' (NBI) can enhance this visual inspection (Fig. 21.2). Adenomatous polyps typically have a visible pit pattern that renders the surface irregular, lobular, or "cerebriform" (Fig. 21.3). When arising in the left colon, these adenomatous polyps may be attached to fibrous stalks and are referred to as "pedunculated" (Fig. 21.4). Hyperplastic polyps, on the other hand, tend to appear smooth, pale, featureless, and glistening (Fig. 21.5).

Macroscopic Appearance

Many endoscopists have adopted the "Paris criteria" descriptions, and this may be useful in providing a more standardized descriptive nomenclature [7].

"Flat, Elevated, Pedunculated"

The Paris classification defines polyps based on their gross appearance as "flat" (0-II, elevated less than 2.5 mm from the mucosal surface), "sessile"(0-IS, elevated >2.5 mm and

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without a stalk), or "pedunculated" (0-IP, elevated, with attached stalk between the mucosal wall and polyp head). Pedunculated polyps tend to occur in the left colon, where colonic muscular contractions have pulled the polyp away from the adjacent wall, resulting in a fibrous stalk. Flat polyps are more challenging to detect, requiring meticulous colonic cleansing and scrutiny by the colonoscopist [8].

Size

Polyp size can be estimated by comparison to a reference metric such as a closed biopsy forceps or snare catheter (about 2.5 mm). Small polyps measure less than 1 cm in diameter. These generally have the least malignant potential, and most can be removed by avulsion with forceps or snare. Polyps can range in size from a barely detectable few millimeters ("diminutive") to a lumen filling 5 or more centimeters [9, 10] (Fig. 21.6).

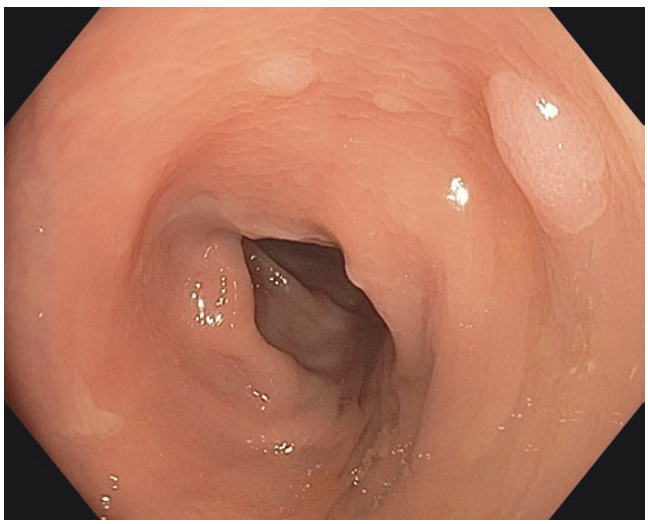

Fig. 21.1 Pale, featureless rectal hyperplastic polyps

Location

Polyps may be located anywhere in the colon. Whereas endoscopists can be quite certain in describing a location in the rectum or cecum, they are far less accurate for polyps arising between these extremes. This is because of the long and often serpentine colon segments between the cecum and rectum. Accuracy of localization may be increased when an adjacent flexure (hepatic or splenic) is included in the description. The distances marked on endoscope shafts are not reliable at all and, in fact, often misleading because of stretching, looping, and pleating of the colon during passage of the colonoscope. When it is necessary to delineate an accurate location of a polyp or polypectomy site to guide

Practical Considerations

Polyp describers

- It is important for the endoscopist to observe closely the surface pattern of a polyp. Narrow band imaging (NBI) can enhance this visual inspection
- Polyp size can be estimated by comparison to a reference metric such as a closed biopsy forceps (about 2.5 mm)or snare catheter
- The distances marked on endoscope shafts are not reliable and, in fact, often misleading because of stretching, looping, and pleating of the colon during passage of the colonoscope

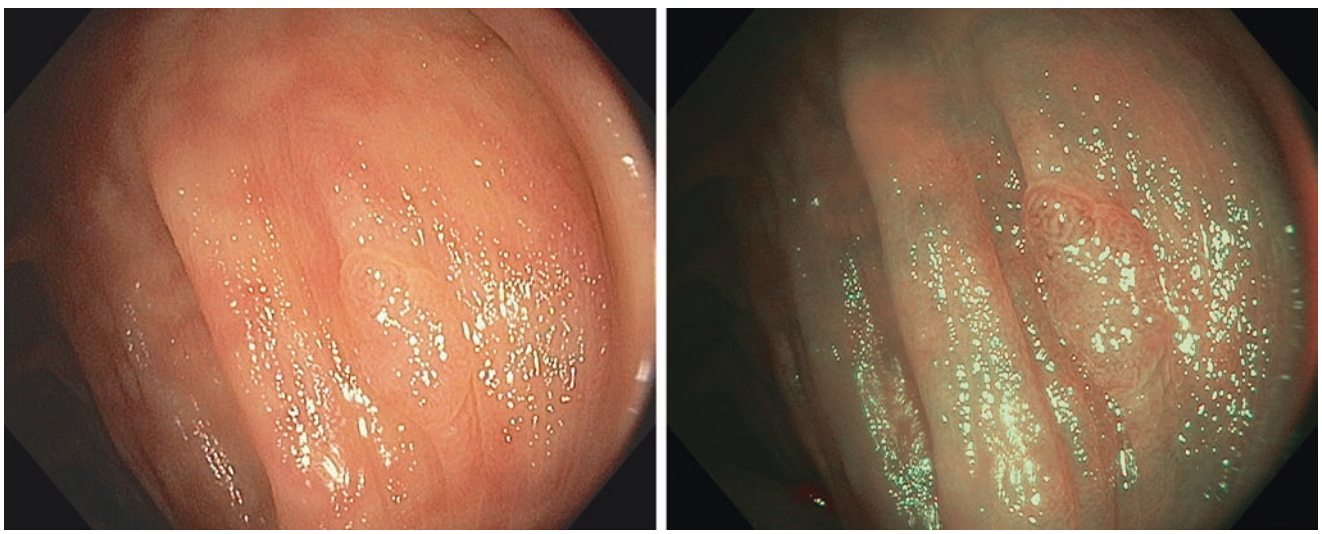

Fig. 21.2 (**a**) Sessile tubular adenoma polyp with white light (left) and (**b**) with narrow band imaging (right)

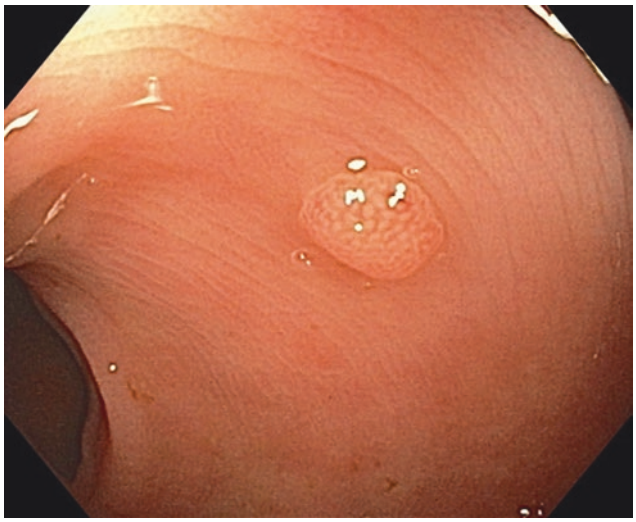

Fig. 21.3 Small tubular adenoma with pitted, "cerebriform" appearance

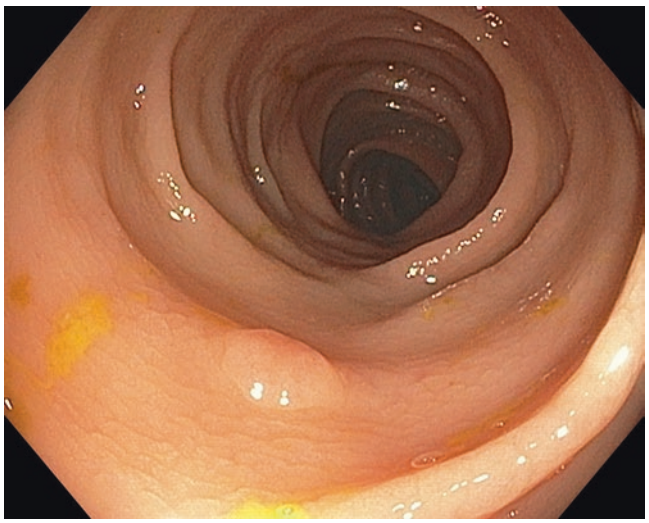

Fig. 21.5 Small, smooth, glistening, featureless hyperplastic polyp

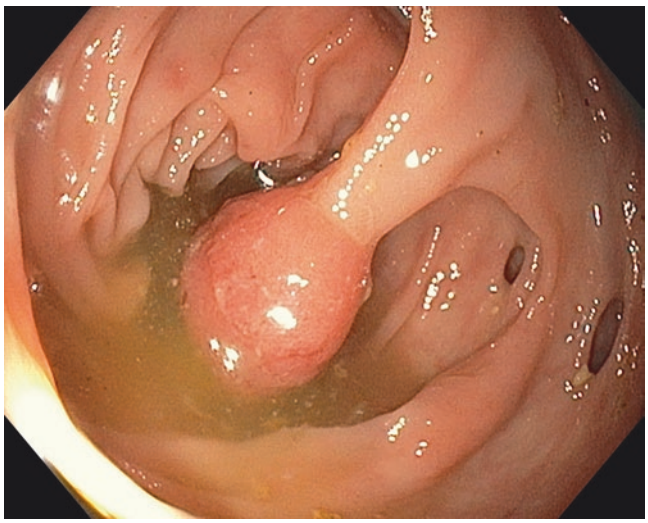

Fig. 21.4 Pedunculated tubular adenoma

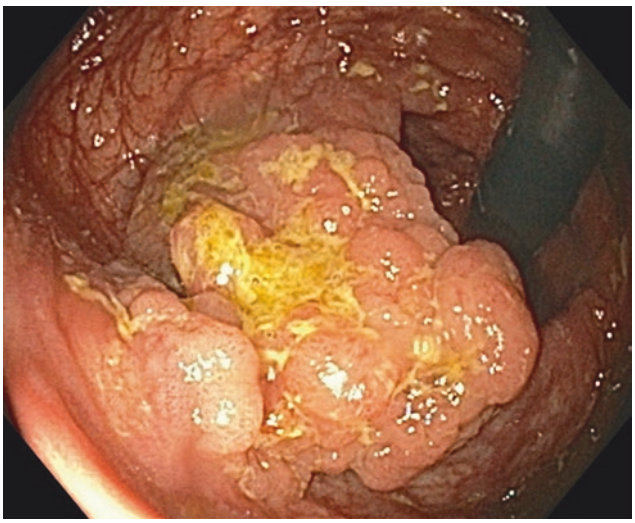

Fig. 21.6 A 4 cm sessile polyp in the ascending colon (seen during U-turn maneuver)

future examinations or surgery, it is best to inject a carbon marker suspension adjacent to the polypectomy site as a permanent tattoo, visible by endoluminal endoscopy as well as by the surgeon's external inspection (Fig. 21.7).

Polyp Detection

Polyps may be elusive. The colon is segmented by its haustra, and this coiled spring-like anatomy makes it a tedious and daunting task to peer into every depressed area between haustra and on the far side of haustral folds or flexures. Studies of the location of polyps that colonoscopy has missed have emphasized the right colon, far side of haustral folds, and low rectum as the most challenging areas of the colon for missing a polyp. Further barriers to polyp detection include colonic spasm, pleating of the colon over the endoscope shaft on insertion, sigmoid haustral hypertrophy, diverticulosis, suboptimal colon cleansing, failure to make a U-turn in the right colon and rectum, as well as too rapid an examination.

Colonoscope withdrawal time has been correlated with successful polyp detection, leading to the recommendation that scope withdrawal from the cecum should take an average of 6 min [11]. If the patient will not be examined again for a decade, it is mandatory that the colonoscopic inspection be as thorough as possible.

Studies in which a colonoscopic examination was followed immediately by another (tandem colonoscopy) have reported as much as a 20% miss rate on the first exam [12]. It must be admitted that most of the "missed" lesions tend to

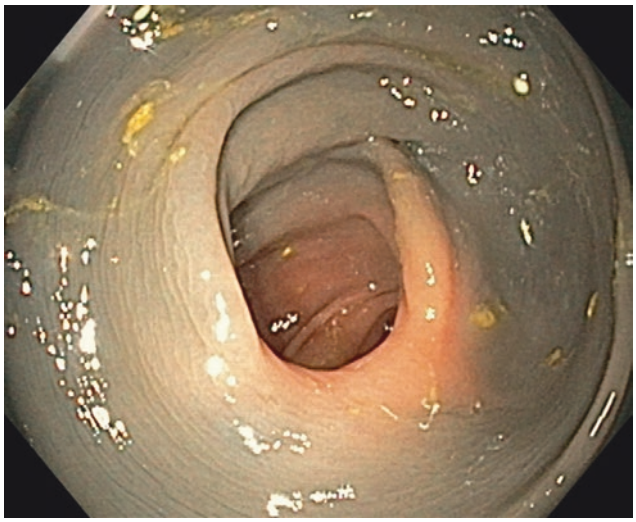

Fig. 21.7 Prior polypectomy site marked in four quadrants with stain from tattoo

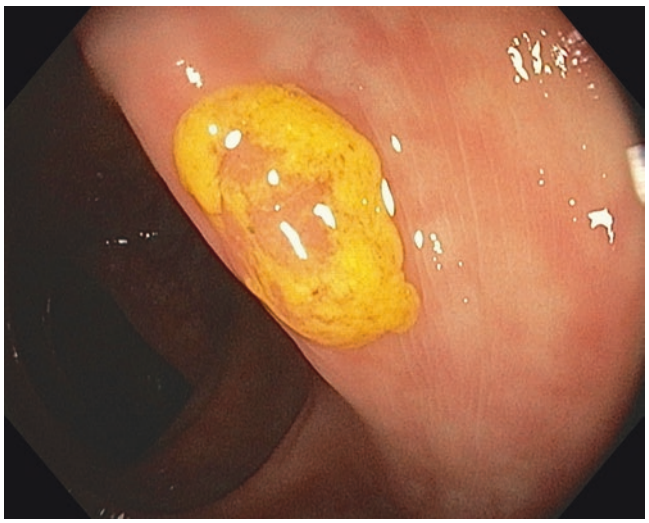

Fig. 21.8 Sessile serrated polyp with adherent mucus

be small and unlikely to become malignant before the next examination. Nevertheless these findings are humbling and emphasize the need for a careful, unrushed examination of a well-prepared colon.

Most endoscopists make a concerted effort to detect polyps during the withdrawal phase of the colonoscopy. Sometimes, however, a small polyp is found during insertion. Since these may be difficult and time-consuming to find on withdrawal, it is prudent to remove those polyps on detection.

Measures to Maximize Polyp Detection

Once the cecum or terminal ileum has been reached, the scope is withdrawn slowly, making every effort to observe the entire circumference of the lumen, turning the scope tip like the sweep "second" hand of a clock. To accomplish this it may be necessary to examine a colonic segment several times, perhaps shifting the patient's position from left lateral decubitus to supine or even prone. With the recent series of more maneuverable colonoscopes, it is often possible and desirable to make a U-turn in the right colon (enabling observation of the proximal side of the haustra). It is also relatively easy and advisable to U-turn in the rectum in order to detect low rectal or anal lesions.

"Serrated" polyps may be especially challenging to detect because they tend to be relatively flat and hug the haustral folds. They may be detected by a subtle stain of brownish mucus on the colon wall caused by the pigmentation of bile adhering to mucus secreted by the abundance of goblet cell in these polyps (Fig. 21.8). Careful observation is needed since only a slight crenellation of the mucosal surface may mark the site after lavage of the telltale mucus coat [6, 13].

Detection of small, subtle polyps may be facilitated by utilizing image enhancement such as "narrow band imaging" (NBI) available on some colonoscopes (Fig. 21.2).

Practical Considerations

Polyp detection

- Multiple, small, identical, pale, glistening polyps in the rectum can be ignored without polypectomy
- Adenomatous polyps tend to have a visible pit pattern and "cerebriform" appearance
- Sites where polyps may be most difficult to detect are the right colon, far side of and between haustral folds and flexures, and low rectum
- Polyp detection can be improved by: withdrawal time of >6 min, making U-turn in the right colon and rectum
- Small polyps detected during insertion should be removed at that time
- Serrated polyps often are covered with yellowish mucus

Patient Preparation for Polypectomy

Catharsis

Meticulous colon cleansing is essential not only for polyp detection but also for safety during use of electrocautery. A poorly prepared colon may contain high levels of methane and other flammable gaseous materials, raising the risk of combustion during electrocautery.

Antiplatelets and Anticoagulants

While these agents may be continued for purely diagnostic colonoscopy, they are not conducive to safe polypectomy.

The details of their discontinuation and resumption may involve dialog with cardiologist or vascular colleagues.

Patients with implanted cardiac defibrillators pose a relative contraindication if electrocoagulation is to be employed because of concern for inducing a cardiac arrhythmia or an unintended electrical shock. Many implanted defibrillators must be inactivated during polypectomy and then reactivated when no further electrosurgical equipment is being used. Pacemakers pose no problem for electrosurgery because the pathway for return of electrical current flow is directed from the snare wire to the large return electrode, usually affixed to the thigh, excluding the pacemaker from the pathway of current flow [14].

Practical Considerations

Patient preparation

- All potential complications should be discussed with the patient prior to planning of colonoscopy
- Meticulous colon cleansing is essential not only for polyp detection but also for safety during use of electrocautery
- A dialog with patient's cardiologist or vascular surgeon is important prior to discontinuation and resumption of anticoagulants and antiplatelet agents
- Patients with implanted cardiac defibrillators pose a relative contraindication if electrocoagulation is to be employed because of concern for inducing a cardiac arrhythmia or an unintended electrical shock

Techniques of Polypectomy: Small (<1 cm) Polyps

"Cold" Forceps or Snare Polypectomy

The size and configuration of the polyp will determine the polypectomy technique employed. For diminutive polyps (up to 3 mm in diameter), electrocautery may not be necessary [15]. An advantage of "cold" forceps removal is that the resected specimen is encased in the closed forceps and need not be searched for, as may be the case after snare polypectomy. This technique avoids thermal injury to the resected specimen and to the colon adjacent to the polyp. Even for small polyps, several passes of the forceps may be necessary to accomplish complete removal.

A conventional snare without application of electrical current also can be employed when removing a polyp of 7–8 mm or less. A small-sized snare is best for removing these small polyps and can remove both the polyp and a small rim of adjacent mucosa. Sometimes recovery of the snare-resected small polyp can be a time-consuming challenge. Such "cold" polypectomy may cause bleeding since hemostasis depends on the patient's intrinsic clotting, but with small polyps this is seldom a meaningful issue.

A variation of forceps polypectomy is the specialized "hot" forceps, connected to an electrocautery source. This may be useful in removing polyps up to 10 mm in size. The polyp is grasped by the forceps and tented from the surrounding colon wall into the colon lumen, and cautery is applied. A band of white tissue will be seen at the edge of the forceps, indicating thermal injury, and the polyp can then be removed by withdrawing the forceps. If bleeding or residual polyp remains, the site can be coagulated by application of electrocautery by way of the closed hot forceps.

Technique of Polypectomy: Larger (>1 cm) Polyps

The goal is complete removal with minimal damage to the surrounding colon wall [16]. It is worth recalling that the thickness of the colon wall is very thin, varying from 1.4 to 2.3 mms. Since application of electrocautery by snare or forceps causes some adjacent thermal injury, the challenge is to balance completeness of polyp removal with minimal damage to nearby "innocent bystander" colon. A persistent problem with electrocautery is that the thermal injury always involves the base and edges of the resected specimen and may interfere with the pathologist's attempts to study the basal and lateral margins [9].

To achieve complete and safe polypectomy of the larger polyps, the colonoscopist can utilize several useful techniques.

Endoscopic Mucosal Resection (EMR)

This entails elevating the polyp by injecting fluid into the submucosa before performing polypectomy. This elevating cushion of injected fluid minimizes the risk of transmural thermal injury to the colon by increasing the distance from cautery margin to the deeper muscularis propria and serosa [17–20].

Sterile saline is the most commonly utilized fluid for submucosal injection, but many other solutions have been used in an attempt to achieve a longer lasting effect. Better visual definition of the polyp's margins may be achieved by adding a few drops of methylene blue to the fluid before injection. Multiple injections may be required to elevate the polyp. It is best to begin the injections on the proximal or upstream side of the polyp to achieve an elevation of 5–10 mm.

Failure to achieve elevation (non-lifting) may be due to intraperitoneal injection (too deep), to intraluminal injection (too superficial), or to the polyp being adherent to the submucosa. This adherence may be a consequence of scarring from previous polypectomy, underlying colitis, or it may imply malignant infiltration of the submucosa [21].

Applying the Snare

It is crucial to have the endoscopy assistant check that the electrocautery generator and connections are functioning and to mark the snare handle shaft at the point where the closing wire snare tip is flush with the tip of the plastic catheter encasing the wire loop. Before deploying the snare, it is necessary to orient the polyp so that it lies near the "5 o'clock" position. This will optimize placement of the snare. Maneuvers useful in repositioning the polyp may include:

- Advancing past the polyp to a more proximal segment of the colon then returning to the polyp site. This may straighten the scope, which makes the tip more responsive.
- Evacuating some insufflated air to partially collapse the lumen. This may bring the polyp closer to the tip of the scope and help with desired snare placement.
- Torquing the instrument shaft. This will rotate the view and often brings the polyp to the desired location.
- Rotating the patient to a supine or even prone position. This will shift the entire view to enable the desired orientation.

The scope tip is manipulated so that the tip of the opened plastic catheter encasing the opened snare is positioned to be at the near border of the polyp. Pushing the tip of the opened wire loop into the proximal colon wall can splay the deployed loop and make it wider if needed to capture a large polyp. Since the majority of polyps are less than 1 cm in diameter, a small snare (3 × 1 cm) is the most effective tool for most polypectomies.

For pedunculated polyps, the ideal site for polypectomy is midway on the stalk between the base of the polyp head and the surrounding wall. The snare should be closed tightly in order to stop blood flow and coapt the blood vessel walls. The polyp may assume a dusky appearance just prior to transection.

For sessile lesions in the range of 1.5–2.0 cm, the snare should be positioned to remove all visible polypoid tissue as well as a small cuff of normal tissue immediately adjacent to the polyp. Once the snare has encircled the polyp, it is closed snugly around the polyp base. Larger lesions will require "piecemeal" resection, with each snare capture taking less than 2 cm of adenomatous tissue.

Delivering Electrocautery

Before applying electrocautery, it is important to assure that the snare has not caught an adjacent fold of mucosa on either the near or far side of the polyp. This can be accomplished by (a) jiggling the closed snare and assuring there is no movement of the adjacent wall and (b) checking the mark on the shaft of the snare handle to be certain that the gap between the tightened slide bar and the mark is small, which indicates no inadvertently ensnared extra tissue.

Once the snare has been closed and adjacent wall has been cleared, the polyp is tented into the lumen, thereby stretching the base of the polyp upward. Care should be taken to prevent the tip of the polyp from contact with the opposite colon wall, which could result in a "*contrecoup*" burn. With the snared polyp elevated into the lumen, electrocautery can be applied. Most colonoscopists utilize pure coagulation current for polyp resection because it provides maximal hemostasis. When a white line of desiccation and cauterization is observed at the site of the closing snare, full closure is accomplished while continuing to apply cautery current. Immediately after polypectomy, the site is inspected for hemostasis and completion of polypectomy. Only then is attention turned to retrieving the resected polyp.

Piecemeal Polypectomy

When dealing with a larger polyp, it is best to deploy the snare around one <2 cm portion of the polyp at a time ("piecemeal polypectomy"). This is accomplished by positioning the wire snare to close on only one part of the polyp base and adjacent polyp tissue. By repeating this process to the adjacent portions of the polyp base, the entire polyp can be resected Fig. 21.9 [22].

If there are small amounts of residual polyp at the periphery of the polypectomy site, this perimeter can be "touched up" by application of argon plasma coagulation without increasing the risk of perforation [23].

Polyp Retrieval

If the polyp is small, it can be aspirated through the biopsy channel and collected in a plastic polyp retrieval trap or a gauze pad placed within the tip of the suction catheter that

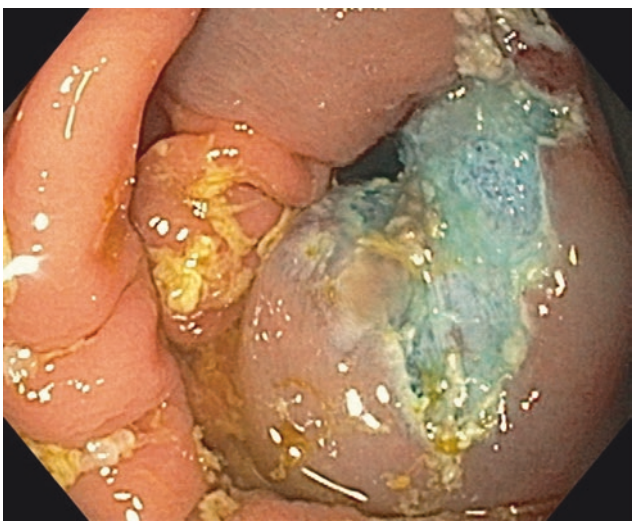

Fig. 21.9 Complete polypectomy after endoscopic mucosal resection. The blue base is the submucosa infiltrated by fluid tinted with methylene blue. The margins have been treated with argon plasma coagulation

connects the endoscope to the suction machine. A small amount of water can be introduced and then suctioned to aid with this retrieval. If the polyp is too large for aspiration through the scope, then the endoscopist has a number of options: (a) use the snare to "cold cut" the resected polyp into smaller pieces which can then be aspirated, (b) re-snare the resected polyp and drag it out with the colonoscope shaft, (c) apply suction to affix the polyp to the tip of the scope and withdraw the scope, or (d) retrieve the polyp in a basket or net. Except for the first of these options, any of these maneuvers will preclude a careful examination of the rest of the colon and will require the endoscopist to repeat the intubation in order to scrutinize the luminal surface distal to the resected polyp for additional polyps or other lesions.

"Difficult" Polyps

While most colonoscopic polypectomies can be accomplished handily, there are certain features that portend a challenging or even impossible removal. Among these are polyp size, configuration, extent of base attachment, orientation, location, and surrounding anatomy. A polyp that is very large and very flat, occupies more than one-third of the lumen's circumference, arises from the proximal or upstream side of a fold, lies in the depression between haustra or is protruding from a diverticular or appendiceal orifice, poses a challenge even to the most seasoned and aggressive colonoscopist. Preliminary considerations should include the following:

- Is it likely that the polyp can be removed in toto during this procedure*?* Repeat examinations at a later time entail added risks such as further electrocautery injury to previously compromised adjacent colon wall and encountering fibrosis and scarification from prior polypectomy.
- In the event of brisk bleeding or perforation, can the patient be hospitalized expeditiously?
- Has sufficient time been allotted to perform this procedure? An endoscopy unit schedule that is geared to performing multiple straightforward examinations may not be appropriate for a lengthy polypectomy procedure. A harried, rushed endoscopist is not suitable for undertaking a difficult polypectomy.

Polyp Size

Large polyps can be removed with appropriate precautions (Fig. 21.6). Since the polyp may virtually fill the lumen, it is important first to probe and inspect the base of the polyp to ascertain how wide the attachment is and to seek a stalk. If the base is broad, the polyp is likely to require piecemeal removal, whereas if a stalk can be found, a single snaring may suffice [22]. The stalk may be elusive because the head of the polyp may have prolapsed distally and may be all that the colonoscopist sees initially.

Polyp Base

When confronted with a broad-based polyp, especially when it is arising in the right colon, it may be prudent to inject the base of the polyp with fluid, perhaps tinged with a few drops of methylene blue. The fluid protects against deeper thermal damage, especially useful if multiple pieces are to be resected (piecemeal polypectomy). Any remaining fragments of polyp can be cauterized with the tip of the snare or, by employing an argon plasma coagulator [23] (Fig. 21.9).

Flat Polyps

These polyps (Paris 0-II) may be more difficult to both detect and remove. Their lack of elevation may preclude successful lassoing with a wire snare especially if absolutely flat (Paris 0-IIb). Even submucosal injection may not make a flat polyp elevated enough for snaring. One simple technique is to aspirate air, which, by decreasing the lumen circumference, will relatively elevate the flat polyp. Another technique is to suck the polyp into the suction channel, thereby tenting it up and making it more amenable to snaring. A third strategy is to utilize a thinner or smaller snare.

Polyp Location

Polyps located at the orifices of the appendix, a diverticulum, or the ileocecal valve can pose therapeutic challenges. For periappendiceal polyps, the endoscopist must be certain that the polypoid structure is not an inverted appendix. Since periappendiceal and peri-diverticular polyps seldom arise from deep within the orifice, they often can be prolapsed with forceps or snare into the colon lumen before applying cautery current.

Endoscopic Submucosal Dissection (ESD)

This more advanced endoscopic technique involves needle knives instead of snares to perform electrocautery cutting into the fluid-filled submucosa. As is done for EMR, a submucosal cushion is created. A special electrocautery cutting tool is used to incise through the mucosa adjacent to the polyp and burrow into the edematous submucosa beneath the lesion. By careful application of cautery, staying away from the *muscularis propria*, and repeated submucosal injections, the polyp is removed in its entirety. This provides the pathologist with an intact, complete specimen. Since this is a more invasive procedure than EMR, there is a higher risk of perforation, although these often can be closed with endoscopically placed clips [19].

The "Impossible" Polyp

Parallel advances in laparoscopic surgery provide the endoscopist with a viable surgical option to a difficult colonoscopic polypectomy. This may be the best option for:

- A large rectal polyp for which a trans-anal, full-thickness surgical resection might be most appropriate
- Some very broad-based (>4 cm) polyps, extending over several haustral folds
- Sessile polyps previously resected colonoscopically but found on reexamination to have recurred repeatedly. Rather than subject the patient and endoscopist to repeated arduous colonoscopy and cauterization (especially if the polyp is located in the relatively thin right colon), it may be most reasonable to refer for laparoscopic segmental resection.

In those instances when the colonoscopist deems the polyp to be endoscopically unresectable, the site should be marked by injecting a carbon suspension fluid submucosally as a tattoo to mark the site (Fig. 21.7). These markers should be placed in all four quadrants nearby so that the area is readily visible to the surgeon approaching from the serosal perspective. A polypectomy site may be similarly marked so the area can be located precisely during subsequent follow-up procedures [24].

Practical Considerations

Polypectomy technique

- Polyps <7–8 mm can be removed by "cold" without electrocautery forceps or snare
- During EMR adding methylene blue to the saline being injected may enhance the visualization of polyp margins
- Polyp not lifting may be due to prior polypectomy, colitis, tumor infiltration of submucosa, or inadequate submucosal injection
- Optimal orientation of the polyp may be accomplished by straightening scope, evacuating air, torquing colonoscope shaft, or rotating patient
- For pedunculated polypectomy, place snare between the base of polyp head and bottom of stalk
- Polyps >2 cm may require "piecemeal" polypectomy

Post-Polypectomy Care

After routine, uncomplicated colonoscopic polypectomy, the patient may resume a full diet, although low roughage is frequently recommended, especially if the polyp had been located in the right colon. Aspirin and nonsteroidal anti-inflammatory medications are held for at least 5 days, although the patient remains at risk for late post-polypectomy bleeding (vide infra). Anticoagulants can be resumed within 24 h. All other medications may be resumed later in the day of the polypectomy.

Practical Considerations

Post-polypectomy

- Identification of polypectomy site, except for the cecum or rectum, may be erroneous and require injection of tattoo marker
- Bleeding at polypectomy site may occur immediately or as late as several weeks after procedure
- Repeat colonoscopy is indicated relatively early for multiple adenomas, villous adenomas, malignant polyps, large polyps resected piecemeal, and recurrent polyps
- Polypectomy may be therapeutic for malignant polyps with well-differentiated cancer, completely resected with no lymphatic or vascular involvement, and clear margins

Potential Complications of Colonoscopic Polypectomy

Bleeding

Hemorrhage after polypectomy may be immediate or delayed [25]. It is more likely after removal of large polyps in the right colon. Immediate bleeding can be addressed by injection of dilute (1:10,000) epinephrine solution, by superficial application of argon plasma coagulator with limited pressure and cautery using a bipolar probe, or by endoscopic hemostatic clip application. A small amount of oozing may be controlled by application of electrocautery current with the tip of the snare. If the polyp were pedunculated, the residual stalk can be snared again and the bleeding thereby tamponaded, followed by further cautery or clipping.

Late bleeding may occur within 2 weeks of polypectomy, due to sloughing of the clot or eschar before complete reepithelialization. This delayed bleeding is seen most often in patients who had resumed anticoagulants, aspirin, or nonsteroidal anti-inflammatory preparations. Post-polypectomy bleeding usually subsides on its own but may require repeat colonoscopy and injection, cautery, or clipping.

Perforation

The reported incidence of post-polypectomy perforation is in the range probably of less than 1 per 1000 cases. Perforation more likely happens with large, sessile polyps, in the elderly, and when submucosal lifting is not done prior to resection.

Less common than overt perforation is "post-polypectomy coagulation syndrome." This manifests within several days of the polypectomy with abdominal pain, low-grade fever, and mildly elevated WBC. It is believed to be due to full-thickness thermal injury to the colon wall. It almost always subsides within a few days and is treated with a low-roughage diet, antibiotics, and reassurance.

Post-Polypectomy Surveillance

Guidelines for surveillance after polypectomy depend upon the nature of the polyp resected [26]. Although colonoscopy remains the gold standard for polyp detection and removal, it is not perfect. Discovering and removing hyperplastic polyps is considered an essentially negative colonoscopy, and, as such, a surveillance colonoscopy can be delayed for 10 years. After removal of a single or a few adenomas, the interval before follow-up colonoscopy has been set at 5 years. A shorter interval may be appropriate for multiple dysplastic polyps, large polyps removed piecemeal, villous pathology, positive family history of colorectal cancer, and suboptimal colon preparation [27].

Polyps found at subsequent colonoscopies may represent new polyps, a recurrence at the site of previous polypectomy, or could be a lesion missed on the prior examination. Despite careful technique, close observation of the polypectomy site and "touching up" the polypectomy margins and base with cautery or argon plasma coagulator residual polypoid tissue may lead to polyp recurrence [23]. If there is significant concern about having performed a complete polypectomy, it is sensible to mark the polypectomy site with a carbon suspension tattoo and recall the patient for repeat colonoscopy to assure complete resection.

The Malignant Polyp

A small minority of benign-appearing polyps harbor malignant cells. If these cells have breached the muscularis mucosa and entered the submucosa, they have potential access to lymphatics and blood vessels, can metastasize, and therefore are labeled "invasive" [10, 28]. These are to be distinguished from malignant-appearing cells that have *not* crossed from lamina propria through the muscularis mucosa into the submucosa. The term used to describe this entity is "high-grade dysplasia." These lesions were termed "carcinoma in situ," but since they have no metastatic potential, this term has been disavowed.

Macroscopic Appearance

Polyps harboring malignant cells tend to be larger, more irregularly shaped or notched, and more firm to probing and biopsy and frequently are friable. They may be ulcerated, and, if invading deeper submucosa (more than 1000 microns deep), they may not elevate well with submucosal injection [9].

Approach to the Suspected Malignant Polyp

Polyps suspicious for malignancy should be extensively biopsied and their site tattooed with submucosal carbon-based marker. A complete colonoscopy should be performed to look for synchronous lesions and remove other polyps.

For colonoscopic polypectomy to be effective in resecting these polyps, complete excision is mandatory. This is best done in one, thorough colonoscopic intervention. Scarification at the polypectomy base may limit the effectiveness of subsequent colonoscopy to achieve complete polypectomy [29].

It is important to provide the pathologist with as much of the specimen as can be retrieved. It is not unusual for the surface of a polyp to be only dysplastic, while malignant cells can be found deeper in the polyp or in the base. For pedunculated polyps, the snare should be placed relatively low on the stalk to provide as large a "clean" margin as possible from the polyp head. For sessile polyps, the goal is to remove a perimeter of normal adjacent mucosa to permit the pathologist to comment on margin of resection. Electrocautery inadvertently destroys tissue near the resection margin, which could be confounding and/or therapeutic.

Approach to the Unsuspected Malignant Polyp

On the fortunately rare occasion when a resected benign-appearing polyp is found to be malignant, it is necessary to apply accepted standards to determine what the next course of action should be for that patient. The polypectomy site should be identified by repeat colonoscopy as soon as possible unless there is assurance that the location is known (close to identifiable landmarks such as the cecum or rectum). Hopefully the polypectomy site can be identified by scar or clot and the site tattooed and its margins extensively biopsied.

Overall Approach to Malignant Polyps

The following factors need to be weighed:

- Are the margins of the resected specimen free of malignant cells? If so, how wide is that margin?
- Is the malignancy well differentiated?
- Is there any invasion of lymphatics or blood vessels?
- Was the polyp pedunculated?
- Does the endoscopist believe the polyp was removed in toto?
- Was the polyp removed in one piece?
- What are the patient's comorbidities for surgery?

Colonoscopic polypectomy is usually an adequate treatment for polyps considered by the endoscopist to be resected completely and having well-differentiated adenocarcinoma, showing no invasion of lymphatics or blood vessels, and having clear resection margins. CT scan and follow-up colonoscopies are indicated [27].

Summary

Colonoscopic polypectomy has advanced as a major means of screening, surveying, and ridding the colon of polyps. With improved optics and instrumentation, colonoscopy can detect and then safely and permanently remove polyps of almost any size or attachment, including those with early, endoscopically resectable malignancies. Post-polypectomy colon perforation, bleeding, and polyp recurrence remain real but acceptable risks.

References

1. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J Clin. 2008;58:130–60.
2. Rabeneck L, Paszat LF, Saskin R, Stukel TA. Association between colonoscopy rates and colorectal cancer mortality. Am J Gastroenterol. 2010;105:1627–32.
3. Brenner H, Chang-Claude J, Seller CM, Rickert A, Hoffmeister M. Protection from colorectal cancer after colonoscopy: a population-based case-control study. Ann Intern Med. 2011;154:22–30.
4. Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal cancer deaths. N Engl J Med. 2012;366:687–96.
5. Waye JD, Aisenberg J, Rubin PH. Practical colonoscopy. London: Wiley; 2013.
6. Rex DK, Ahnen DJ, Baron JA, et al. Serrated lesions of the colorectum: review and recommendations from an expert panel. Am J Gastroenterol. 2012;107:1315–29.
7. Lambert R, Kudo SE, et al. Pragmatic classification of superficial neoplastic colorectal lesions. Gastrointest Endosc. 2009;70:1182–99.
8. Soetikno RM, Kaltenbach T, Rouse RV, et al. Prevalence of nonpolypoid (flat and depressed) colorectal neoplasms in asymptomatic and symptomatic adults. JAMA. 2008;299:1027–35.
9. Ahlawat SK, Gupta N, Benjamin SB, Al-Kawas FH. Large colorectal polyps: endoscopic management and rate of malignancy: does size matter? J Clin Gastroenterol. 2011;45:347–54.
10. Chaput U, Alberto SF, Terris B, et al. Risk factors for advanced adenomas amongst small and diminutive colorectal polyps: a prospective mono-center study. Dig Liver Dis. 2011;43:609–12.
11. Barclay RL, Vicari JJ, Daughty AS, et al. Colonoscopy withdrawal times and adenoma detection during screening colonoscopy. N Engl J Med. 2006;355:2533–41.
12. Rex DK, Cutler CS, Lemmel GT, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. Gastroenterology. 1997;112:24–8.
13. Tadepalli US, Feihel D, Miller KM, et al. A morphologic analysis of sessile serrated polyps observed during routine colonoscopy. Gastrointest Endosc. 2011;74:360–8.
14. Tanigawa K, Yamashita S, Maeda Y, et al. Endoscopic polypectomy for pacemaker patients. Chin Med J. 1995;108:579–81.
15. Repici A, HaHassan C, Vitetta E, et al. Safety of cold polypectomy for <10 mm polyps at colonoscopy: a prospective multicenter study. Endoscopy. 2012;44:27–31.
16. Sanaka MR, Thota PN. Efficacy of colonoscopic polypectomy in removing large polyps. Gastrointest Endosc. 2010;72:906–10.
17. Ferrara F, Luigiano C, Ghersi S, et al. Efficacy, safety and outcomes of 'inject and cut' endoscopic mucosal resection for large sessile and flat colorectal polyps. Digestion. 2010;82:213–20.
18. Moss A, Bourke MJ, Williams SL, et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterology. 2011;140:1908–18.
19. Tanaka S, Kashida H, Saito Y, et al. JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc. 2015;27:417–34.
20. Moss A, Williams SJ, Hourigan LF, et al. Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. Gut. 2015;64:57–65.
21. Uno Y, Munakata A. The nonlifting sign of invasive colon cancer. Gastrointest Endosc. 1994;40:485–9.
22. Iishi H, Tatsuta M, Iseki K, et al. Endoscopic piecemeal resection with submucosal saline injection of large sessile colorectal polyps. Gastrointest Endosc. 2000;51:697–700.
23. Nesbakken A, Kristinsson J, Svinland A, Lunde OC. Endoscopic snare resection followed by laser ablation in the treatment of large sessile rectal adenomas. Scand J Surg. 2011;100:99–104.
24. Ponsky JL, King JF. Endoscopic marking of colon lesions. Gastrointest Endosc. 1975;22:42–3.
25. Sawhey MS, Salfiti N, Nelson DB, et al. Risk factors for severe delayed postpolypectomy bleeding. Endoscopy. 2008;40:115–9.
26. Lieberman DA, Rex DK, Winawer SJ, et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force. Gastroenterology. 2012;143:894–57.
27. Butte JM, Tang P, Gonen M, et al. Rate of residual disease after complete endoscopic resection of malignant colonic polyp. Dis Colon Rectum. 2012;55:122–7.
28. Ueno H, Mochizuki H, Hahiguchi Y, et al. Risk factors for an adverse outcome in early invasive colorectal carcinoma. Gastroenterology. 2004;127:385–94.
29. Cooper GS, Xu F, Barnholtz Sloan JS, Koroukian SM, Schluchter MD. Management of malignant colonic polyps: a population-based analysis of colonoscopic polypectomy versus surgery. Cancer. 2011;118:651–9.

Colonic Decompression

22

Tiing Leong Ang, Daphne Ang, and James Chi Yong Ngu

Background

Acute colonic obstruction is a gastrointestinal emergency that is associated with the impairment of gas and fecal transit, resulting in colonic luminal distension. If not recognized and treated appropriately, complete obstruction resulting in massive bowel distension, electrolyte derangement, bacterial translocation, bowel ischemia, and perforation may occur.

Clinically these patients present with nausea, vomiting, pain and abdominal distension, and the absence of flatus or stool passage if complete obstruction is present. Abdominal examination will reveal a distended tympanic abdomen, with sluggish or absent bowel sounds. In the presence of complications such as ischemia or perforation, systemic signs such as fever and tachycardia may be evident, accompanied by features of peritonism. Plain abdominal radiography will demonstrate colonic dilatation, with a cutoff being observed in cases of mechanical obstruction.

Various causes of colonic obstruction have been described. These can be classified into mechanical and nonmechanical etiologies, usually distinguished with the aid of abdominal computer tomography. Fluoroscopic studies with a contrast enema may be used as an alternative imaging modality. The most common cause of a mechanical colonic obstruction is due to a primary colonic malignancy (Figs. 22.1 and 22.2) [1].

Colonic obstruction may also result from benign causes such as colonic volvulus (Fig. 22.3), stricturing Crohn's disease and acute colonic pseudo-obstruction (Ogilvie's syndrome), which is a syndrome of massive distension of the colon without a mechanical cause, which can lead to bowel ischemia and perforation (Fig. 22.4). The pathophysiology of acute colonic pseudo-obstruction is not well understood but is thought to be due to an imbalance between the parasympathetic and sympathetic nervous systems, with a decreased parasympathetic tone and/or an increased sympathetic tone resulting in a dilated colon [2, 3]. It is usually associated with a predisposing condition such as trauma, surgery, severe infections, neurological diseases, cardiac diseases, electrolyte imbalance, and metabolic alterations [4]. It is crucial to differentiate acute colonic pseudo-obstruction from toxic megacolon due to severe *Clostridium difficile* infection or severe ulcerative colitis given the difference in management.

Regardless of the etiology, colonic obstruction is potentially life-threatening, and a delay in diagnosis can result in poor outcomes. Apart from supportive measures like fluid and electrolyte replacement, endoscopy may play a role in the management of these patients [1]. This chapter focuses on the treatment for patients presenting with acute colonic obstruction, with particular emphasis on the indications, contraindications, technique, and outcome of endoscopic decompression. To contextualize the role of endoscopic therapy, it will summarize the importance of medical treatment and the role of surgery. Three conditions will be highlighted in this review, namely, acute colonic pseudo-obstruction, sigmoid volvulus, and obstructing colorectal carcinoma.

Initial Supportive and Medical Treatment of Colonic Obstruction

Regardless of the etiology, the initial supportive treatment for colonic obstruction is similar. Patients are kept fasted and given intravenous fluids, taking care to correct any electrolyte abnormalities. A nasogastric tube is inserted to provide proximal gastrointestinal decompression. Laxatives are avoided, and medications that can impair colonic motility, such as opiates, are discontinued.

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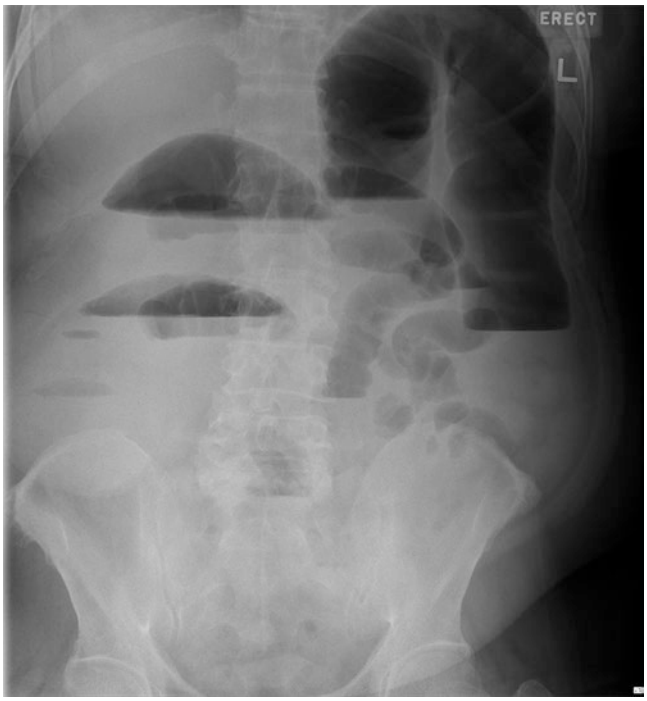

Fig. 22.1 X-ray image of colonic dilatation due to obstructing colorectal cancer

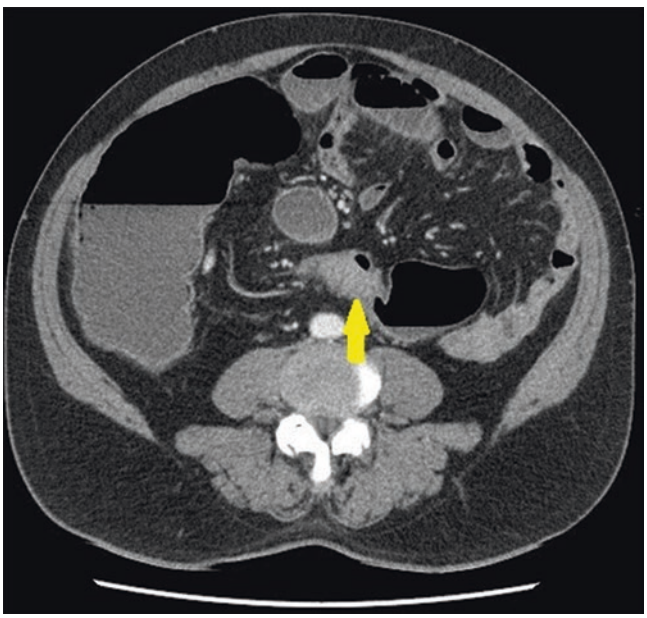

Fig. 22.2 Computer tomography view of malignant colonic stricture (*arrow*)

In cases of acute colonic pseudo-obstruction, specific pharmacological treatment with intravenous neostigmine is available for colonic decompression and is actually the mainstay of treatment should there be no response to initial supportive therapy after a period of about 48 h. Neostigmine, a reversible acetylcholinesterase inhibitor, increases the

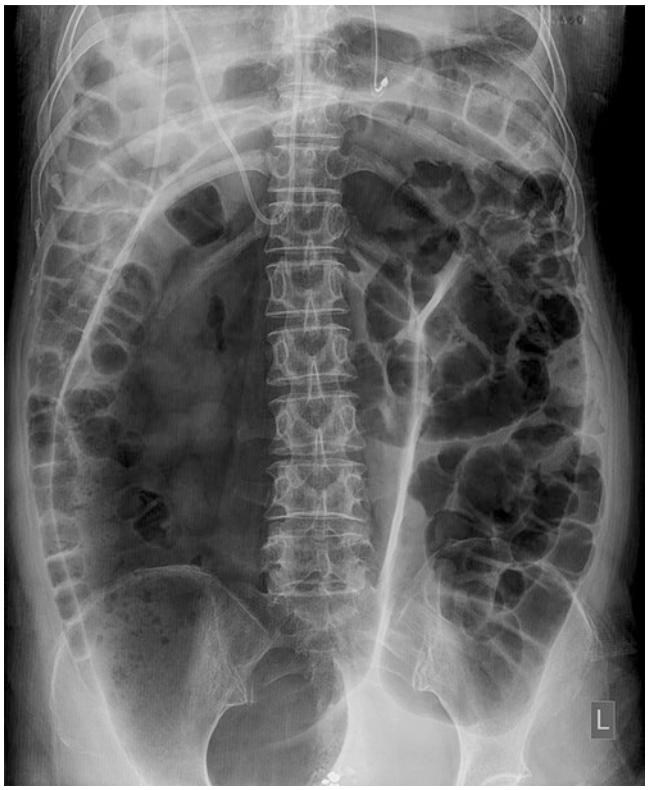

Fig. 22.3 X-ray image of sigmoid volvulus

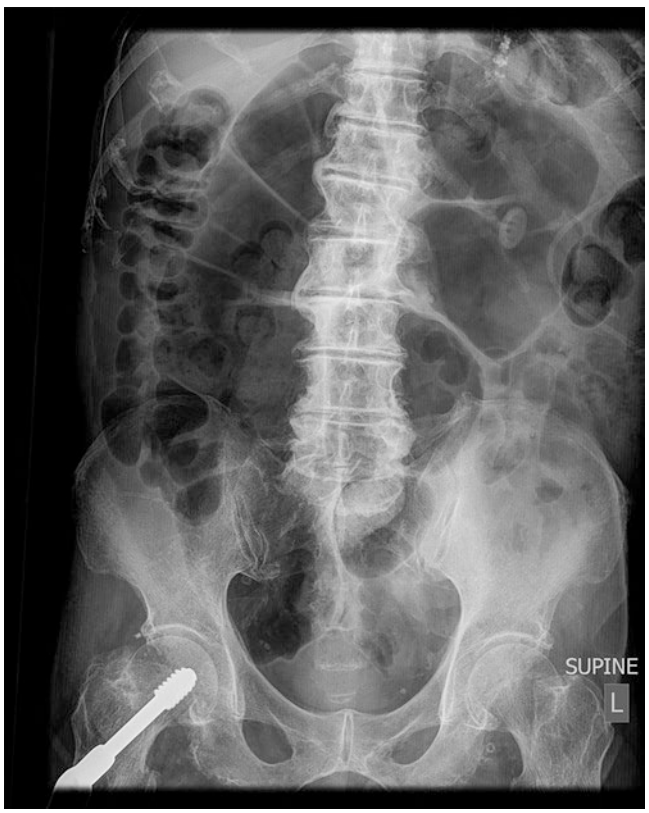

Fig. 22.4 X-ray image of acute colonic pseudo-obstruction

activation of muscarinic receptors by preventing the breakdown of acetylcholine, thus promoting colonic motor activity. Three small randomized controlled trials have been performed, and success rates ranging from 85% to 94% were reported [5–7]. Recurrence rates ranging from 0% to 27% were reported. It is a safe drug, but potentially serious adverse events such as bronchospasm, bradycardia, and hypotension have been reported. Vital signs and electrocardiogram should therefore be monitored closely during infusion of the drug. Endoscopic decompression is used as second-line treatment if the condition remains refractory.

In cases of mechanical colonic obstruction such as sigmoid volvulus and colorectal malignancies, endoscopic decompression can be attempted after initial resuscitation, in lieu of an emergency surgery [1, 8, 9].

Indication for Endoscopic Decompression

Endoscopic decompression is indicated for acute colonic pseudo-obstruction not responding to medical therapy. No randomized controlled trials are available. The evidence comes from retrospective series. Among those series with more than 20 cases, success at the initial procedure, with or without tube placement, ranged from 61% to 100%, and ultimate clinical success after 1 or more procedures was 73–88% [10–15]. Results of nonrandomized retrospective comparative studies suggest that recurrence rates were significantly lower after placement of decompression tubes following colonoscopy [14–16].

Endoscopic detorsion and decompression are a primary therapeutic modality for sigmoid volvulus. Colonoscopy also serves to exclude the presence of colorectal malignancy. Retrospective case series have reported successful decompression in 70–80% of cases [9, 17], although recurrences are common [18, 19]. Repeat endoscopic decompression can be performed for recurrent sigmoid volvulus in patients who are not surgically fit [9]. Volvulus can also occur in the cecum or transverse colon, where endoscopic decompression may not be feasible, and the mainstay of treatment would be surgery.

Endoscopic insertion of a self-expanding metallic stent (SEMS) is indicated for relief of malignant colonic obstruction. In patients with potentially curable colorectal cancer presenting with obstruction, placement of a SEMS can serve as a bridge to surgery. A recent meta-analysis concluded that SEMS serve as a safe and effective bridge to subsequent surgery in patients with obstructing left-sided colon cancer [20]. Seven randomized controlled trials comparing SEMS ($n = 195$) and emergency surgery ($n = 185$) were included in this meta-analysis. The mean technical success rate of colonic stent placement was 76.9% (ranges 46.7–100%). There was no statistically significant difference in the postoperative mortality (SEMS 10.7% vs. emergency surgery 12.4%). The SEMS group had lower overall morbidity (33.1% vs. 53.9%, $p = 0.03$), higher successful primary anastomosis rate (67.2% vs. 55.1%, $p < 0.01$), and lower permanent stoma rate (9% vs. 27.4%, $p < 0.01$). Concerns have been raised regarding a higher local recurrence rate affecting oncological outcome after SEMS placement, especially in cases of stent perforation [21]. However, other authors have reported conflicting results [22, 23]. Guidelines published by the European Society of Gastrointestinal Endoscopy did not endorse the use of SEMS for potentially curable left-sided malignant colonic obstructions due to this controversy. SEMS may, however, be considered as an alternative to emergency surgery in patients with an increased risk of perioperative mortality (ASA score III or higher and/ or age > 70 years) [8]. The guidelines also recommended SEMS as the preferred intervention for the palliation of non-curable malignant colonic obstruction. Two meta-analyses, including randomized and nonrandomized studies, compared SEMS with surgery for palliation of malignant colonic obstruction. The technical success rates of SEMS ranged from 88% to 100%, while the rates of initial clinical improvement were significantly higher after palliative surgery (100%) compared with SEMS (93%, $P < 0.001$). The use of SEMS was associated with a significantly shorter length of stay and lower intensive care unit admission rate while permitting a shorter time to initiation of chemotherapy (16 vs. 33 days) [24, 25].

Practical Considerations

- Patients should be appropriately resuscitated and clinically stable prior to attempting endoscopic decompression.

Indications

- Acute colonic pseudo-obstruction not responding to intravenous neostigmine
- Sigmoid volvulus
- Obstructed colorectal cancer as bridge to surgery in patients at higher risk for immediate surgery
- Palliation of unresectable obstructed colorectal cancer

Contraindications to Endoscopic Decompression

Endoscopic decompression is contraindicated in the presence of bowel gangrene and perforation. This may be suspected based on clinical features such as signs of sepsis, fever, leukocytosis, and abdominal peritonism. In the context of colorectal cancer with malignant obstruction, palliative stent placement should not be performed if the patient is being treated or considered for treatment with anti-angiogenic therapy (e.g., bevacizumab), given the high risk of colonic perforation. A meta-analysis reported a significantly increased perforation rate in patients receiving bevacizumab (12.5%) compared with patients who received no concomitant therapy during colorectal stenting (9.0%). Chemotherapy without bevacizumab was not associated with an increased risk of stent perforation [26].

Practical Considerations

- Suspect presence of bowel gangrene or perforation when signs of sepsis and peritonitis are present.

Contraindications

- Bowel ischemia and gangrene
- Bowel perforation
- Colorectal cancer patients being treated or considered for treatment with anti-angiogenic therapy

Instruments and Accessories

A colonoscope with a large working channel (3.8 mm) to facilitate suctioning should be used. For insertion of colonic stent in the left colon, a therapeutic gastroscope with a large working channel (3.7 mm) can also be used to access the site of stricture and may actually be easier to handle than a colonoscope. Insufflation should be minimized, with CO2 preferred to air due to the steep diffusion gradient across colonic wall of the former. A water irrigation pump aids in the clearance of colonic fecal debris, although this should be minimal in the case of a complete obstruction. We routinely administer a fleet enema to our patients prior to attempting the procedure in order to optimize visualization.

In the decompression of pseudo-obstruction and obstructing colorectal cancer, additional accessories are required. These include a standard catheter used for cannulation, in order to direct the insertion of a guide-wire and a stiff 4.8 m 0.035" guide-wire. After successful decompression for pseudo-obstruction, a 175 cm 14Fr decompression tube (Cook Medical, Winston-Salem, USA) is inserted and left in place for a few days. In the case of malignant obstructions, SEMS are deployed. These stents are available from various companies such as Boston Scientific, Cook Medical, and Taewoong-Medical Co., with minor differences in the stent designs and deployment systems. In general, the diameter of the stents ranges from 22 to 25 mm, the distal flare from 27 to 30 mm, and the length from 6 to 12 cm. The appropriate length of stent should be based on the stricture length measured on pre-procedural imaging or intra-procedural fluoroscopy – the flares of the stent should cover 2 cm on either end of the stricture.

Practical Considerations

- The length of colonic stent to be used is to be based on the length of the stricture. It should traverse the stricture but not be excessively long. If the stricture is situated at a colonic bend, a slightly longer stent may be required so that the opening of the stent does not impinge against the adjacent colonic wall.
- Uncovered colonic stents are preferred over covered stents due to a lower risk of stent migration.

Instrument and accessories	Examples
Colonoscope with 3.8 mm working channel; therapeutic gastroscope with 3.7 mm working channel (for colonic stenting)	Olympus Medical, Tokyo, Japan; Pentax Medical, Tokyo, Japan; FUJIFILM Corporation, Tokyo, Japan
CO2 insufflator	UCR CO2 Regulation Unit (Olympus)
Water irrigation pump	Olympus OFP-2 pump with disposable MAJ-1651 auxiliary channel water tube set and the MAJ-1652 auxiliary channel adaptor (Olympus)
Standard ERCP catheter	Classic ERCP Catheter (Cook Medical, Winston-Salem, USA)
480 cm 0.035" guide-wire	Jagwire™ (Boston Scientific, Natick, MA, USA); Tracer Metro® Wire Guide (Cook Medical)
14 Fr colon decompression set (This set comprises of a guiding catheter [6 Fr, 181 cm], guide-wire [0.035", 480 cm], and decompression catheter with 10 elongated side ports [14 Fr, 175 cm])	Cook Medical
Colonic self-expandable metallic stent	Wallflex™ colonic stent (Boston Scientific); Evolution® Colonic Controlled-Release Stent (Cook Medical); Niti-S™ Enteral colonic Stents (Taewoong-Medical Co., Seoul, South Korea)

The Procedure

General Steps

The endoscopy procedure is performed using no sedation or with sedation using intravenous midazolam. The patient lies in a left lateral position. Minimal insufflation (with CO2 and not air) is used as the colonoscope is carefully inserted; solid debris is irrigated using the water pump; fluids and air are suctioned as the endoscope is advanced.

Acute Colonic Pseudo-obstruction

The colonoscope is carefully inserted to the cecum, and during this process all distension is suctioned. Prolonged attempts to achieve cecal intubation are not required, because decompression can be achieved by reaching the hepatic flexure. The colonic decompression set is then utilized. The 0.035" guide-wire is advanced through the working channel of the colonoscope into the cecum, under combined endoscopic and fluoroscopic guidance. The colonoscope is then slowly and carefully withdrawn, while the position of the guide-wire is maintained by forward insertion, with the position checked by fluoroscopy. The tip of the guide-wire should reside in the cecum or right colon. The 14 Fr decompression tube with the inner guiding catheter is then inserted over the guide-wire under fluoroscopic guidance and advanced till the right colon or cecum (Fig. 22.5). The guide-wire and inner catheter are removed, and the decompression tube is connected to gravity drainage. The tube is secured with tape to the inner thigh of the patient. The decompression tube should be flushed every 6 h to prevent occlusion. It usually passes out spontaneously over 3 days as peristalsis improves; otherwise it is removed after 3 days.

Sigmoid Volvulus

The colonoscope is carefully inserted with minimal air insufflation and should be stopped immediately if the mucosa appears gangrenous, in order to minimize the risk of bowel perforation. A spiral sphincter-like "twist" of mucosa may be encountered at the point of torsion. Shortening of the endoscope during intubation process will usually reduce the volvulus, and after passage of the endoscope past the point of torsion, the mucosa proximal to the volvulus is identified as a distended segment filled with fecal material, in contrast with the empty lumen distal to the volvulus. In fact, one should expect a rush of stool and gas once the point of torsion has been traversed. If the volvulus is not reduced by shortening, then careful twisting of the endoscope for detorsion can be performed. If detorsion is successful and no ischemic bowel is encountered, a rectal tube is left in place, and elective resection is scheduled.

Obstructing Colorectal Malignancy

The endoscope is inserted up to the the level of the malignant stricture (Fig. 22.6). The stricture site is carefully examined to localize the narrowed opening. A cannulating catheter is used to guide the insertion of a 0.035" guide-wire across the stricture, and the catheter is then inserted across the stricture, under combined endoscopic and fluoroscopic guidance. Undiluted contrast is injected through the catheter to confirm an intraluminal position, with no evidence of colonic perforation (Fig. 22.7). Contrast injection can also be used to delineate the length of the stricture, and the appropriate length of stent is then chosen. The catheter is then withdrawn while keeping the guide-wire in place under combined endoscopic and fluoroscopic guidance. The SEMS is usually

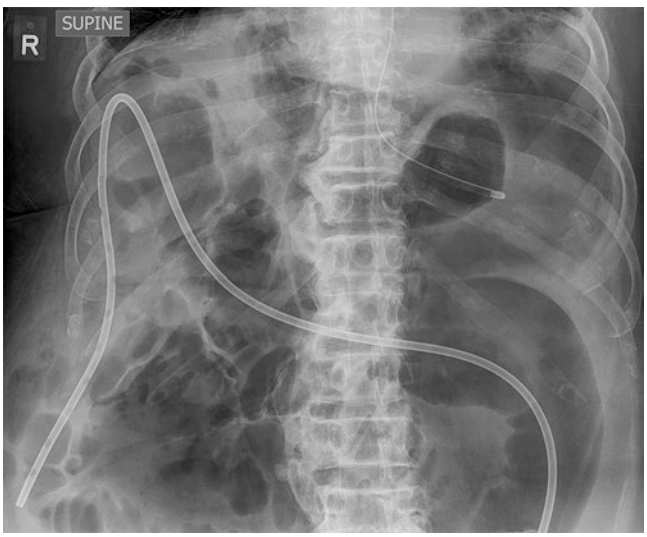

Fig. 22.5 X-ray image of decompression inserted endoscopically for management of acute colonic pseudo-obstruction

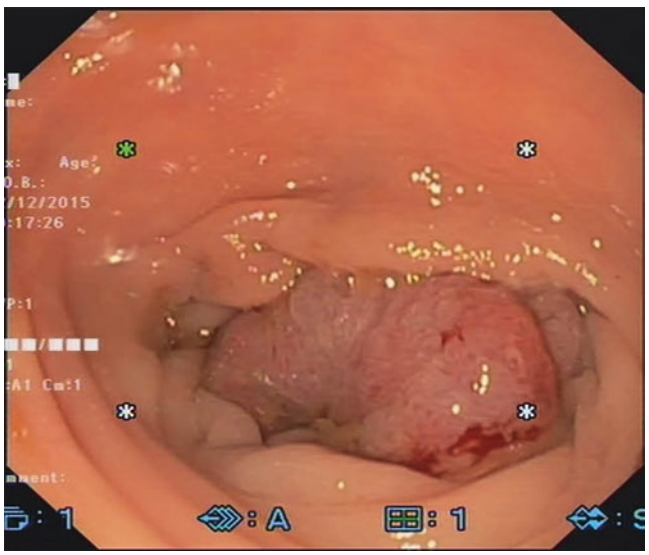

Fig. 22.6 Endoscopic view of obstructing colorectal cancer

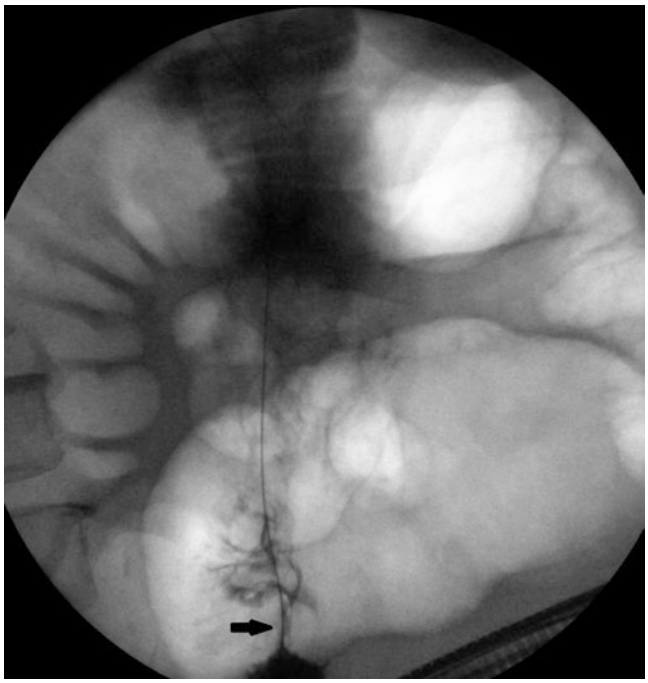

Fig. 22.7 Fluoroscopic view of malignant colonic stricture (*arrow)*

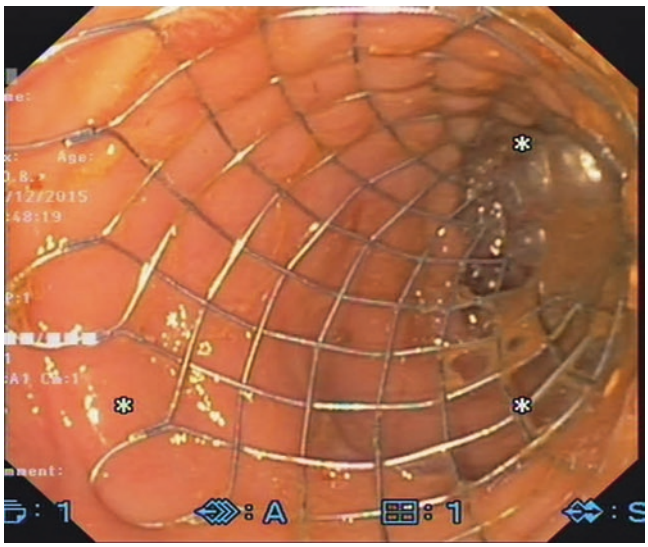

Fig. 22.8 Endoscopic view after insertion of colonic stent

compressed in a 10F through-the-scope delivery catheter. This device is exchanged over the guide-wire through the endoscope working channel and then into the colonic lumen across the stricture. As the stent is being deployed, there is a tendency for it to migrate proximally into the colon. It is crucial for the endoscopist to maintain outward traction on the delivery catheter to allow the distal end of the stent to deploy beyond the stricture. Failure to do so would result in the stent being positioned too proximally in the colon. Upon full deployment, the stent should straddle the stricture with its flares extending 2 cm on either end (Figs. 22.8 and 22.9).

Biopsies of the tumor should preferably be performed after SEMS insertion, as the endoscopic view of the stricture lumen can be obscured by the bleeding after biopsies.

Practical Considerations

- Bowel preparation: fleet enema should be given to clear the distal solid fecal material in order to improve the endoscopic view.
- It is important to maintain minimal insufflation during endoscopy.

Steps

1. Acute colonic pseudo-obstruction
   - The colonoscope is carefully inserted to the cecum, with active suctioning throughout the process.
   - A 0.035” guide-wire is advanced through the working channel of the colonoscope into the cecum.
   - The colonoscope is then withdrawn while maintaining the guide-wire by forward insertion, under fluoroscopic control.
   - The 14 Fr decompression tube with the inner guiding catheter is then inserted over the guide-wire under fluoroscopic guidance and advanced till the right colon or cecum.
   - The guide-wire and inner catheter are removed, and the decompression tube is connected to gravity drainage.
2. Sigmoid volvulus
   - The colonoscope is carefully inserted with minimal air insufflation to the point of torsion.
   - Shortening of the endoscope during intubation process will usually reduce the volvulus.
   - If the volvulus is not reduced by shortening, then careful twisting of the endoscope for detorsion can be performed.
   - A rectal tube is left, and elective resection is scheduled.
3. Obstructed colorectal malignancy
   - Stricture visualized by endoscope.
   - Insertion of catheter and 0.035” guide-wire across the stricture.
   - Contrast injection to confirm length of stricture and removal of catheter.
   - Insertion of the stent delivery system across the stricture over the guide-wire.
   - It is important to maintain outward traction on the delivery catheter to allow the distal end of the stent to deploy beyond the stricture.
   - Deployment of the stent.

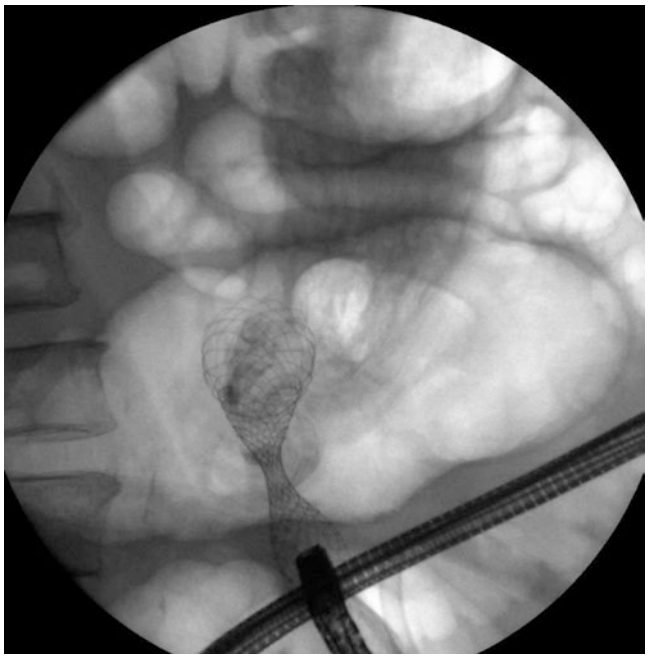

Fig. 22.9 Fluoroscopic view after insertion of colonic stent

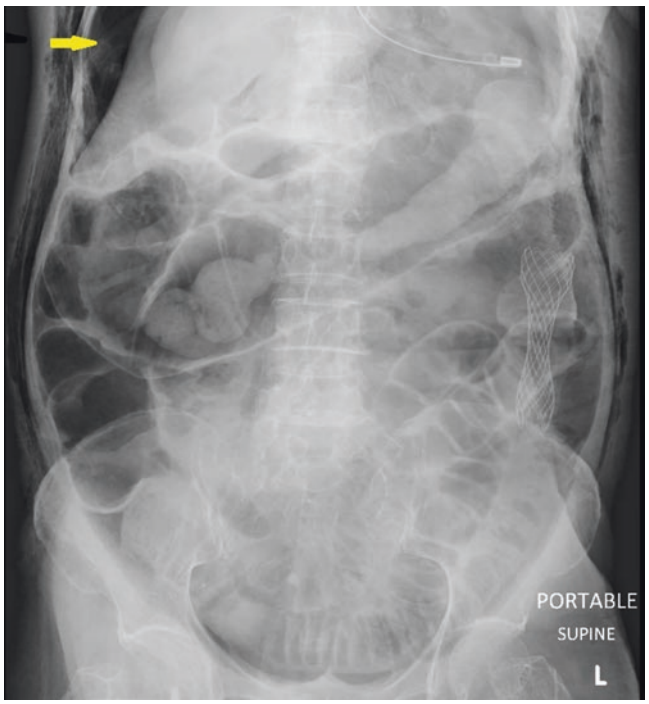

Fig. 22.10 X-ray image of pneumoperitoneum (*arrow*) after insertion of colonic stent

Complications

The main complication of concern with endoscopic colonic decompression is perforation which may not be associated with significant bleeding (Fig. 22.10). In the case of colonic stenting, additional adverse events include stent malfunction and migration. In the context of endoscopic decompression for acute colonic pseudo-obstruction, perforation rates ranged from 0% to 5% [10–14]. In the context of colonic stent placement, complications can be classified as early (within 30 days) or late (after 30 days). The main early complications are perforation (range 0–12.8%), stent failure after technically successful stent deployment (range 0–11.7%), stent migration (range 0–4.9%), re-obstruction (range 0–4.9%), pain (range 0–7.4%), and bleeding (range 0–3.7%). Late complications include re-obstruction (range 4.0–22.9%), stent migration (range 1.0–12.5%), and rarely perforation (range 0–4.0%) [8]. Among patients who underwent palliative stenting, median stent patency was 106 days (66–288), with 80% maintaining stent patency till death or end of follow-up. In contrast, among patients being bridged to surgery, stent patency is usually maintained until surgery [8].

Practical Considerations

- Avoid endoscopy if there are signs of peritonism.
- Do not dilate a malignant colonic stricture prior to stent placement.
- Use a 25-mm-diameter uncovered colonic stent to minimize the risk of stent migration.

Complications

- Sedation-related adverse events
- Perforation
- Bleeding
- Migration of colonic stent
- Occlusion of colonic stent

Follow-Up

After successful endoscopic decompression, the abdominal distension will promptly resolve. In the event of worsening distension, one needs to exclude the possibility of colonic perforation. This can be confirmed by fluoroscopy or an erect

chest X-ray. Needle aspiration may be required to decompress the resultant tension pneumoperitoneum while awaiting immediate surgical consult.

Sigmoid volvulus occurs more commonly in elderly patients who may be at high risk of operative morbidity and mortality. In patients who are fit for surgery, consideration should be given to elective sigmoidectomy after initial decompression in order to minimize recurrence. Less invasive techniques including colopexy procedures may be appropriate for selected patients, although the recurrence rates are generally reported to be higher than resection.

In the case of SEMS, a plain abdominal radiograph should be obtained 24 h after procedure to assess for positioning and full deployment of the stent. Patients should be placed on a low-residue diet and regular laxatives to minimize the risk of stent occlusion due to fecal impaction. For patients with potentially curable disease, interval surgery is scheduled in 2 weeks to allow for optimization of patient physiology and for the bowel distension and edema to resolve. For cases of palliative stenting, patients should be informed of and monitored for late stent-related complications.

Conclusions

A summary of the management of suspected and confirmed colonic obstruction is given in Fig. 22.11. Endoscopic decompression is a highly effective minimally invasive technique for treatment of colonic obstruction. In the case of acute colonic pseudo-obstruction, it should be attempted after failure of supportive medical therapy and intravenous neostigmine therapy. It is the first-line treatment option for sigmoid volvulus, but elective surgical is still needed to prevent recurrence. In the management of acutely obstructed colorectal malignancy, SEMS insertion is an accepted means of palliation and can potentially serve as a bridge to elective

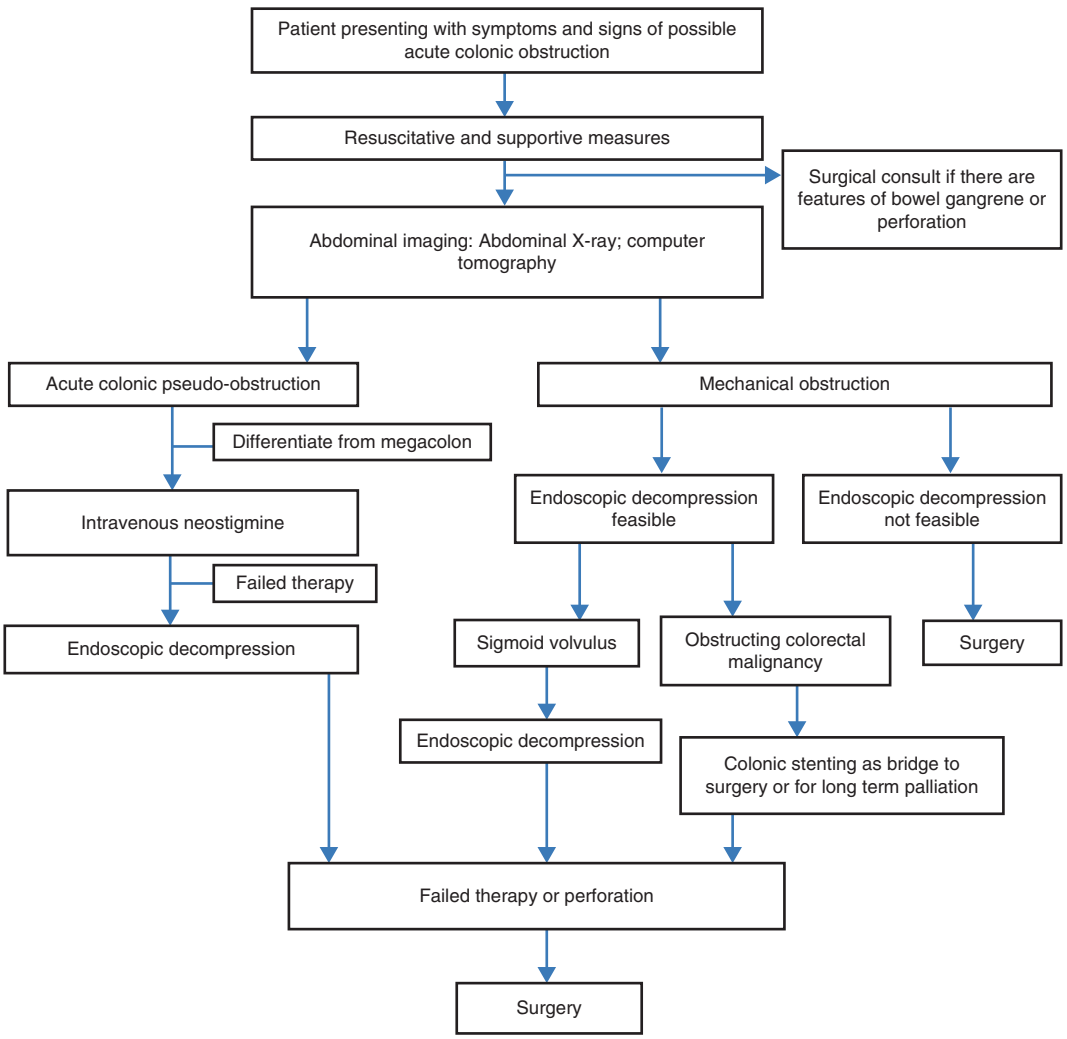

Fig. 22.11 Management algorithm of suspected and confirmed colonic obstruction

surgery in curable disease. To optimize procedural success and minimize complications, careful patient selection and meticulous care during the endoscopic procedure are crucial.

References

1. Harrison ME, Anderson MA, Appalaneni V, Banerjee S, Ben-Menachem T, Cash BD, Fanelli RD, Fisher L, Fukami N, Gan SI, Ikenberry SO, Jain R, Khan K, Krinsky ML, Maple JT, Shen B, Van Guilder T, Baron TH, Dominitz JA. The role of endoscopy in the management of patients with known and suspected colonic obstruction and pseudo-obstruction. Gastrointest Endosc. 2010;71:669–79.
2. Saunders MD. Acute colonic pseudo-obstruction. Best Pract Res Clin Gastroenterol. 2007;21:671–87.
3. Ogilvie H. Large intestine colic due to sympathetic deprivation; a new clinical syndrome. BMJ. 1948;2:671–3.
4. Vanek VW, Al-Salti M. Acute pseudo-obstruction of the colon (Ogilvie's syndrome). An analysis of 400 cases. Dis Colon Rectum. 1986;29:203–10.
5. Hutchinson R, Griffiths C. Acute colonic pseudo-obstruction: a pharmacological approach. Ann R Coll Surg Engl. 1992;74:364–7.
6. Ponec RJ, Saunders MD, Kimmey MB. Neostigmine for the treatment of the acute colonic pseudo-obstruction. N Engl J Med. 1999;341:137–41.
7. Amaro R, Rogers AI. Neostigmine infusion: new standard of care for acute colonic pseudo-obstruction? Am J Gastroenterol. 2000;95:304–5.
8. van Hooft JE, van Halsema EE, Vanbiervliet G, Beets-Tan RG, JM DW, Donnellan F, Dumonceau JM, Glynne-Jones RG, Hassan C, Jiménez-Perez J, Meisner S, Muthusamy VR, Parker MC, Regimbeau JM, Sabbagh C, Sagar J, Tanis PJ, Vandervoort J, Webster GJ, Manes G, Barthet MA, Repici A. European Society of Gastrointestinal Endoscopy. Self-expandable metal stents for obstructing colonic and extracolonic cancer : European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy. 2014;46:990–1053.
9. Gingold D, Murrell Z. Management of colonic volvulus. Clin Colon Rectal Surg. 2012;25:236–44.
10. Jetmore AB, Timmcke AE, Gathright JB Jr, Hicks TC, Ray JE, Baker JW. Ogilvie's syndrome: colonoscopic decompression and analysis of predisposing factors. Dis Colon Rectum. 1992;35:1135–42.
11. Nivatvongs S, Vermeulen FD, Fang DT. Colonoscopic decompression of acute pseudo-obstruction of the colon. Ann Surg. 1982;196:598–600.
12. Strodel WE, Nostrant TT, Eckhauser FE, Dent TL. Therapeutic and diagnostic colonoscopy in non-obstructive colonic dilatation. Ann Surg. 1983;197:416–21.
13. Bode WE, Beart RW Jr, Spencer RJ, Culp CE, Wolff BG, Taylor BM. Colonoscopic decompression for acute pseudoobstruction of the colon (Ogilvie's syndrome). Report of 22 cases and review of the literature. Am J Surg. 1984;147:243–5.
14. Geller A, Petersen BT, Gostout CJ. Endoscopic decompression for acute colonic pseudo-obstruction. Gastrointest Endosc. 1996;44:144–50.
15. Lavignolle A, Jutel P, Bonhomme J, Cloarec D, Cerbelaud P, Lehur PA, Galmiche JP, Le Bodic L. Ogilvie's syndrome: results of endoscopic exsufflation in a series of 29 cases. Gastroenterol Clin Biol. 1986;10:147–51.
16. Harig JM, Fumo DE, Loo FD, Parker HJ, Soergel KH, Helm JF, Hogan WJ. Treatment of acute non-toxic megacolon during colonoscopy: tube placement versus simple decompression. Gastrointest Endosc. 1988;34:23–7.
17. Oren D, Atamanalp SS, Aydinli B, Yildirgan MI, Başoğlu M, Polat KY, Onbaş O. An algorithm for the management of sigmoid colon volvulus and the safety of primary resection: experience with 827 cases. Dis Colon Rectum. 2007;50:489–97.
18. Ballantyne GH, Brandner MD, RWJr B, Ilstrup DM. Volvulus of the colon. Incidence and mortality. Ann Surg. 1985;202:83–92.
19. Hines JR, Geurkink RE, Bass RT. Recurrence and mortality rates in sigmoid volvulus. Surg Gynecol Obstet. 1967;124:567–70.
20. Huang X, Lv B, Zhang S, Meng L. Preoperative colonic stents versus emergency surgery for acute left-sided malignant colonic obstruction: a meta-analysis. J Gastrointest Surg. 2014;18:584–91.
21. Sloothaak DA, van den Berg MW, Dijkgraaf MG, Fockens P, Tanis PJ, van Hooft JE, Bemelman WA. Collaborative Dutch stent-in study group. Oncological outcome of malignant colonic obstruction in the Dutch stent-in 2 trial. Br J Surg. 2014;101:1751–7.
22. Tung KL, Cheung HY, Ng LW, et al. Endo-laparoscopic approach versus conventional open surgery in the treatment of obstructing left-sided colon cancer: long-term follow-up of a randomized trial. Asian J Endosc Surg. 2013;6:8–81.
23. Ghazal AH, El-Shazly WG, Bessa SS, El-Riwini MT, Hussein AM. Colonic endolumenal stenting devices and elective surgery versus emergency subtotal/total colectomy in the management of malignant obstructed left colon carcinoma. J Gastrointest Surg. 2013;17:1123–9.
24. Liang TW, Sun Y, Wei YC, Yang DX. Palliative treatment of malignant colorectal obstruction caused by advanced malignancy: a self-expanding metallic stent or surgery? A system review and meta-analysis. Surg Today. 2014;44:22–33.
25. Zhao XD, Cai BB, Cao RS, Shi RH. Palliative treatment for incurable malignant colorectal obstructions: a meta-analysis. World J Gastroenterol. 2013;19:5565–74.
26. van Halsema EE, van Hooft JE, Small AJ, Baron TH, García-Cano J, Cheon JH, Lee MS, Kwon SH, Mucci-Hennekinne S, Fockens P, Dijkgraaf MG, Repici A. Perforation in colorectal stenting: a meta-analysis and a search for risk factors. Gastrointest Endosc. 2014;79:970–82.

Acute Colonic Bleeding

23

Gustavo A. Machicado and Dennis M. Jensen

Introduction

The term "lower gastrointestinal bleeding" usually refers to a bleeding site distal to the ligament of Treitz [1]. "Hematochezia" is the clinical term applied to the passage of bright red blood or maroon-colored stool, with or without clots, per rectum. We prefer to use "severe hematochezia" rather than lower gastrointestinal (LGI) or colonic bleeding, because it is a more clinically accurate term. Also, the terms "lower or colonic GI bleeding" assume that all patients with severe hematochezia have colonic bleeding sites, which is incorrect. About 15–20% of patients with severe hematochezia have upper gastrointestinal (UGI) sources of bleeding, another 4–6% have documented bleeding from the small bowel between the ligament of Treitz and the terminal ileum, and another 3–5% have no source identified [1, 2].

The majority of ambulatory adult patients with hematochezia present with low-grade or self-limited bleeding and do not require hospitalization or urgent intervention. Such patients can be managed as outpatients. A smaller group of patients experience severe hematochezia and require hospitalization because of the volume of blood loss or symptoms due to severe anemia or comorbidity [1, 2]. Another group of patients develop severe hematochezia while already hospitalized for other medical or surgical conditions (i.e., "inpatient" hematochezia). These are often the patients with very severe hematochezia, and they usually require a systematic and expeditious approach to their resuscitation, preparation for colonoscopy, diagnosis, and treatment.

We recommend an aggressive and systematic approach to all patients hospitalized with severe hematochezia. This includes preparation of the patient with oral purge, while undergoing resuscitation, followed by urgent colonoscopy for diagnosis and treatment. This is in contrast to a traditional approach which may include angiography (urgently) or elective GI procedures when the bleeding appears to stop. Our endoscopic approach is similar to that used for patients with severe upper gastrointestinal hemorrhage. This approach changes outcomes of patients, particularly for those with severe or persistent hematochezia [1, 2].

The purposes of this chapter are to describe severe hematochezia, early resuscitative measures of the patient, our approach to the early diagnosis and treatment of the various lesions responsible for severe hematochezia (or "lower GI bleeding"), and results of this approach. We also review a traditional medical, angiographic, and surgical approaches to severe hematochezia and contrast outcomes and costs of traditional and urgent endoscopic management strategies.

Epidemiology

Acute LGI bleeding occurs with more frequency in the elderly who suffer from comorbid conditions. The incidence of colonic bleeding has been reported to increase from 1 to 100,000 for patients in the third decade of life to as much as 20–30 per 100,000 in patients in the eighth and ninth decades of life [3]. LGI bleeding is about one-fifth as common as upper gastrointestinal (UGI) bleeding [3–6]. However, this ratio may change in the future, because of the decreasing incidence of peptic ulcer disease and aging of the population.

Mortality rates of LGI hemorrhage are usually less than 5% but are higher in patients who have emergency surgery

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[3]. Similar to UGI hemorrhage, patients who start bleeding while in the hospital for an unrelated medical/surgical condition (defined as "inpatient" hematochezia) have a much higher mortality rate (23%) than those who are admitted to the hospital for LGI bleeding (2.4%) [3]. Although the reasons for this are not completely clear, most patients with inpatient hematochezia have severe comorbid conditions, and these are aggravated by severe bleeding.

Practical Considerations: Epidemiology and Mortality LGI Bleeding

- LGI bleeding is common in the elderly including patients with comorbidities.
- The mortality rate is low, except in those with inpatient start of bleeding.

Resuscitation and Initial Evaluation

When patients present in shock (severe volume depletion, hypotension, and tachycardia), they require good intravenous access (two large bore intravenous lines) and vigorous replacement of intravenous fluids and/or blood. For patients with coagulopathies (prolonged prothrombin time [PT] or international normalized ratio [PT-INR] either from liver disease or anticoagulant therapy [warfarin]) and ongoing hematochezia, fresh frozen plasma (FFP) transfusions to correct coagulopathies are recommended. Fresh frozen plasma replaces most liver-dependent coagulation factors, thereby improving clotting. Patients with severe thrombocytopenia (e.g., platelet count less than 50,000) or severe chronic renal failure may require platelet transfusions for definitive hemostasis of ongoing hematochezia. Treatment of comorbidities and close monitoring in an intensive care unit or a telemetry unit by skilled nurses are also highly recommended. Refer to Table 23.1.

The patient with severe hematochezia should have a complete medical history and careful physical examination performed. The medical history may give the physician clues as to the potential sources and location of the bleeding site.

Table 23.1 Resuscitation and management of patients with severe hematochezia [1, 2, 7–9]

Establish one or preferably two large-bore intravenous lines
Assess intravenous volume and replace vigorously
Evaluate degree of blood loss and replace with packed RBCs
Evaluate coagulation and correct with FFP, platelets, and/or desmopressin acetate (DDAVP)
Place a nasogastric or orogastric tube to check for a possible UGI source of blood or bile
Treat comorbid conditions

Abbreviations: *RBCs* red blood cells, *FFP* fresh frozen plasma

Elderly patients with cardiac or peripheral vascular disease who present with abdominal pain, diarrhea, and hematochezia may have ischemic colitis. A history of cirrhosis can suggest varices, most often esophageal or gastric, but rectal varices or anastomotic varices also can present as severe hematochezia. Severe heart disease (particularly valvular) or chronic renal insufficiency can be associated with bleeding from GI angiomas. Histories of inflammatory bowel disease (IBD), peptic ulcer disease, diverticulosis, or internal hemorrhoids might indicate potential bleeding sites and etiologies. A history of recent colonic polypectomy, particularly of a large sessile polyp, should suggest delayed bleeding from a post-polypectomy ulcer. Abdominal pain, weight loss, fever, diarrhea, or vomiting are important in the differential diagnosis of inflammatory, infectious, or malignant lesions.

As part of medical history, it is also important to elicit and list all medications, including over-the-counter (OTC) drugs and herbal medications, which the patient with GI bleeding has taken acutely or chronically. It is recommended that physicians or nurses speak with family members and ask them to bring in medication bottles of the patient with hematochezia, both OTC and prescription. Some of these drugs may either cause GI lesions or aggravate GI bleeding by interfering with intrinsic coagulation of the patient. Aspirin (in any dose, including 81 mg per day), nonsteroidal anti-inflammatory drugs (NSAIDs), antiplatelet drugs, anticoagulants, antibiotics, inflammatory bowel disease drugs, or antiarrhythmics may cause either GI lesions or cause or aggravate GI hemorrhage. Herbal medications such as gingko, echinacea, and ginseng may also cause or worsen GI hemorrhage from any preexisting gut lesion. SSRIs have also been associated with an increased risk of GI bleeding [10].

Practical Considerations: Medical and Drug History

- A careful medical history will give clues to the potential source and location of bleeding site in patients with rectal bleeding.
- Review medications including over-the-counter drugs and herbal preparations to assess risk factors.
- Manage patients with severe acute bleeding with resuscitation, similar to UGI bleeding.

Approach to the Patient with Severe Hematochezia: Clinical Algorithm

Depending on the clues obtained during the history and physical examination, one can approach the diagnostic evaluation of the patient in a more rational manner (refer to Fig. 23.1). Should the patient give a history of liver cirrhosis,

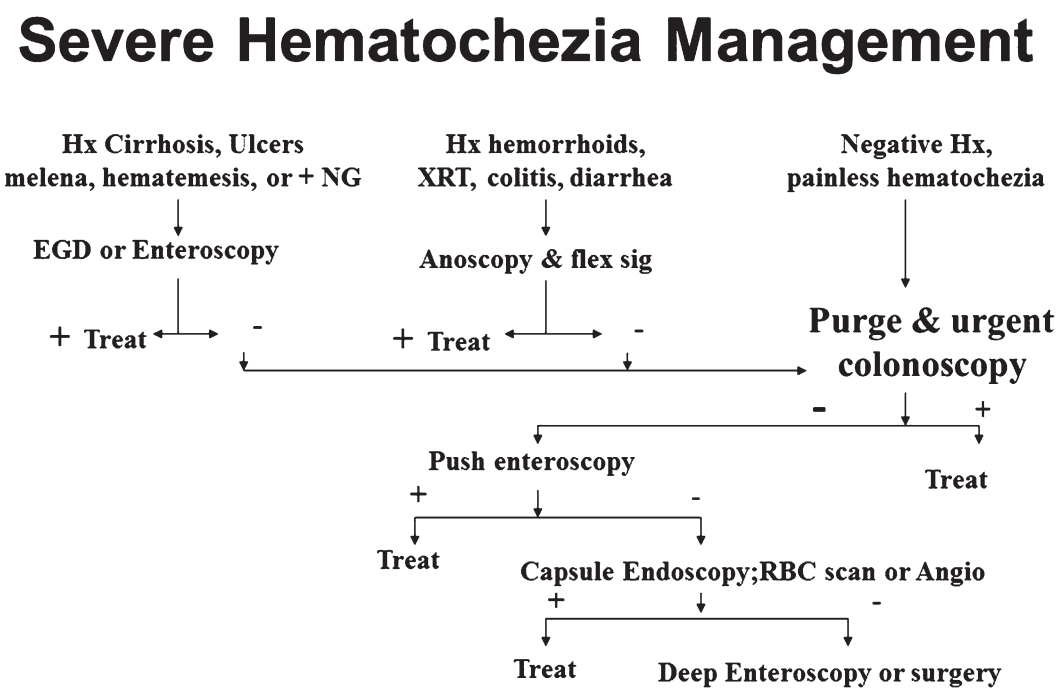

Fig. 23.1 CURE Hemostasis Research Group algorithm for management of patients with severe hematochezia [1, 8, 9, 11]

ulcers, recent (within 30 days) aspirin or NSAID use, passage of melena, or hematemesis, then an UGI source of bleeding should be excluded first before urgent colonoscopy either by upper endoscopy or push enteroscopy. Also, since the most common site of bleeding in severe inpatient hemorrhage is the foregut, a push enteroscopy is recommended urgently before purging and colonoscopy in such patients. If the patient gives a history of hemorrhoids, pelvic radiation, colitis/proctitis, or diarrhea, then we first perform anoscopy (with a clotted instrument) and flexible sigmoidoscopy after enemas are given to clear the distal colon of blood and stool. If both studies prove to be negative, we purge the patient to clean the colon and perform urgent colonoscopy, whenever they are free of stool, clots, and red blood. If there is no significant history or physical findings to suggest any location for the bleeding, we use bowel preparation and urgent colonoscopy for primary diagnosis and treatment. Should urgent colonoscopy and anoscopy not yield a diagnosis, we perform push enteroscopy. Then, if the patient does not have a localization or etiologic source, we recommend further workup. If the patient has continued bleeding or rebleeding, we recommend either capsule endoscopy or RBC scanning and/or abdominal angiography. If all studies are negative for identification of a bleed site, then we recommend capsule endoscopy. If either a bleeding lesion is found or localization of active bleeding but no lesion seen, we recommend either single- or double-balloon enteroscopy. Refer to Fig. 23.1 which outlines our current approach to patients with severe hematochezia.

Practical Considerations: Where to Look First

- For patients with severe hematochezia who have a history of cirrhosis, ulcers, and orthostatic hypotension, or a recent history of melena or hematemesis, perform a foregut examination first to diagnose and treat a UGI source.
- For patients with a recent history of bleeding hemorrhoids, diarrhea, colitis, or pelvic radiation, perform an anoscopy and flexible sigmoidoscopy first.
- For others with a negative history, purge the patient until clear and perform urgent colonoscopy.

Diagnostic Evaluations

The first step to diagnosis should be to determine whether the bleeding source is likely to be upper GI, small bowel, or colonic site. We recommend placement of a nasogastric (NG) or orogastric (OG) tube for gastric lavage since 27.3% of our patients with severe hematochezia in a recently updated cohort study are bleeding from an UGI tract site. Other risk factors for an UGI source include a history of cirrhosis, UGI bleeding from ulcers, portal hypertension, inpatient hematochezia, and hypotension or shock [1–3]. Although the value of a nasogastric tube aspirate has been questioned by others [12], we still find it useful and recommend its use to exclude an UGI bleeding source in a large

proportion of patients, particularly those with a peptic ulcer history or patients with inpatient hematochezia [7]. When bile is obtained in the presence of ongoing hematochezia, there is continuity with the duodenum, and an UGI lesion is unlikely as the source of the hematochezia. If no evidence can be found of UGI bleeding, then an urgent colonoscopy (within 12 h), after adequate colon preparation, is highly recommended for diagnosis and possible hemostasis. If the colonoscopy with terminal ileal intubation is negative, we recommend a careful examination of the anus and distal rectum with a slotted anoscope to evaluate for bleeding internal hemorrhoids and to exclude fissures and anal tumors. We have found this to be a safe approach, and the diagnostic yield with this urgent clinical and endoscopic algorithm was 93.1% [1]. In contrast, colonoscopy in an unprepared colon is often nondiagnostic (particularly in diverticular bleeding or angiomas) and can be dangerous. Urgent colonoscopy of a well-prepared patient is not only an effective diagnostic tool but also allows for therapeutic intervention. It is a cost-effective approach to the management of these patients [8].

Practical Considerations

- For patients with severe hematochezia without a history of hematemesis or melena, either a nasogastric or orogastric tube and gastric lavage are recommended to exclude signs of UGI bleeding (blood in stomach vs. bile).
- For those with signs of blood, do an EGD first.
- For those with bile, prep the patient for urgent colonoscopy, and leave NG tube if the patient can't drink the prep solution (such as Golytely®).

Colonoscopy

Colonoscopy is performed using a video colonoscope which is a flexible tube with a miniature camera at the tip. The distal end of the instrument is maneuverable which allows the endoscopist to direct the instrument through the entire colon during insertion. In addition, colonoscopes have an irrigation port to keep the lens clear and another port for target irrigation of focal areas. An open channel is included for suctioning material during the procedure and for the passage of a variety of therapeutic tools. Through this port, the endoscopist may also obtain biopsies for pathological assessment or to perform hemostasis.

Thousands of colonoscopies are performed throughout the world every day. The procedure is performed safely and comfortably under mild sedation (e.g., conscious sedation). Complications may occur, but serious ones are rare and include bowel perforation, severe bleeding, post-coagulation syndrome, and other extremely rare and unexpected events such as splenic rupture. The incidence of colonic perforation during routine diagnostic colonoscopy is reported to be 0.01–0.2% [13–16]. In those undergoing polypectomy, perforation rates have been reported from 0.01% to 0.32% [13–16]. Bleeding following a diagnostic colonoscopy has been reported in 0.09% and a rate of 1.7% for severe post-polypectomy ulcer bleeding (PPIU) in 25,000 colonoscopies [13]. As larger polyps are being removed in high-risk or elderly patients on anticoagulants or antiplatelet drugs, the risk of delayed PPIU bleeding appears to be increasing [17, 18]. Post-coagulation syndrome occurs when there is transmural coagulation of the colonic wall, including the serosa [13–16]. Patients with this syndrome usually have acute localized abdominal pain, focal peritoneal signs, leukocytosis, and fever. However, there is no radiological evidence of bowel perforation or free air in the peritoneum. A CT scan may show thickening or edema of the colon wall in the area of coagulation, but no free air. Most patients fully recover with medical treatment and do not require surgery. The incidence of this complication following colonic coagulation such as during polypectomy has been reported at 0.5–1.2% [16].

Bowel Preparation

Complete bowel cleansing is the most important aspect for successful emergency colonoscopy in patients with severe hematochezia. For a thorough examination, the colon needs to be cleared of particulate matter, including stool, clots, and blood. After excluding a UGI source of hemorrhage (refer to Fig. 23.1), we administer a polyethylene glycol-based balanced electrolyte purge (e.g., Golytely® or Colyte®) either orally or via an NG tube. Metoclopramide 10 mg IV can be administered 15–30 min prior to starting the purge for its prokinetic and antiemetic effects. Since many of these patients already have an NG tube in place to check for UGI bleeding, it is easier to leave it in place for the purge. A liter of solution is administered every 30–45 min until the rectal effluent clears of solid matter and clots. In our experience, 6–8 liters of this fluid are usually needed in hospitalized patients with severe hematochezia to achieve this goal, although more purge may be required in cases of severe or ongoing bleeding. Refer to Table 23.2.

Care should be taken with those patients who have congestive heart failure, massive ascites, or chronic renal failure on hemodialysis. Volume overload is common because in addition to net absorption during purge, patients also are receiving IV fluids and blood products for resuscitation. A careful assessment of volume status is recommended prior to starting the purge. An increase in third-space fluid and intravascular volume should be treated preemptively. Specifically, if there is clinical evidence of congestive heart failure, IV diuretics are indicated. In patients with chronic renal failure on dialysis, hemodialysis concurrent with the

colonic purge is highly recommended. In patients with tense ascites, a therapeutic paracentesis should be performed to diminish the risk of respiratory compromise during colonoscopy. In this subgroup of patients who are also receiving IV fluids and transfusions of blood products, as well as the colon purge, volume overload and worsening of comorbid conditions are common if diuresis, paracentesis, or dialysis are not performed before or simultaneously with the colon purge [1, 2].

Practical Considerations: Urgent Colonoscopy

- Urgent colonoscopy is safe and effective for diagnosis and treatment in well-prepared patients.
- We recommend giving 6–8 liters of a PEG-based solution (such as Golytely®) over 3–5 h either via NG tube or by drinking it to clear the colon of all blood, clots, and stool before urgent colonoscopy.
- Consumption of 1 liter every 30–45 min is recommended.
- Patients prone to fluid retention (heart failure) may require diuresis, paracentesis (cirrhotics), or dialysis (chronic renal failure) to prevent fluid overload during the colon prep.

CURE Hemostasis Group Results with an Urgent Endoscopic Approach to Severe Hematochezia

The CURE Hemostasis Research Group recently updated a large prospective cohort study of consecutive patients who were admitted to the hospital because of significant hematochezia and now includes 1152 patients [1, 2, 9]. The patients either had persistent bleeding or had stopped bleeding after hospitalization. The approach to the diagnosis in these patients was the same as with the group of persistently bleeding patients (i.e., resuscitation, placement of an NG tube to exclude an UGI bleeding site, colonic purge, and urgent colonoscopy), and this is shown in Fig. 23.1.

For the 1152 patients with severe hematochezia in recent CURE studies [1, 2, 9], colonic bleeding sites were found in 61.3% (706 patients). An UGI source of the hematochezia (e.g., ulcers, varices, or angiomas) was diagnosed in 27.3% (315 patients). A small bowel source was present in 4.4% (51 patients), and no source was found in 6.9% (80 patients). Refer to Fig. 23.2. The three most common colonic sources of bleeding were diverticulosis (32.6%), ischemic colitis (12.2%), and internal hemorrhoids (10.8%). Refer to Table 23.3. Less common lesions included rectal ulcer, colitis (such as infectious or inflammatory bowel disease), postpolypectomy ulcer, colon polyp or cancer, and colon angiomas or radiation telangiectasias. Identification of major stigmata of hemorrhage (i.e., active bleeding, non-bleeding visible vessel, adherent clot, or a flat spot) at urgent colonoscopy after good colon preparation and endoscopic treatment was often possible in patients with focal lesions. Low-risk patients with a presumptive diagnosis (e.g., a lesion without stigmata of hemorrhage) and/or no severe comorbidities could be triaged to a less intensive level of care as well as to earlier discharge.

Practical Considerations: Localization and Etiology of Severe Hematochezia

- For patients hospitalized with severe hematochezia, UGI sources were found in 27.3%, but these were most common in cirrhotic patients, those with a history of ulcers or those with signs of bleeding recently (melena, hematemesis, or a positive NG aspiration for blood).
- Small bowel sources were uncommon – 4.4%.
- Colonic location was the most common – 61.3%.
- The most common colon etiologies were diverticulosis, ischemia, internal hemorrhoids, rectal ulcers, and angioma syndromes.

Table 23.2 Colon preparation prior to urgent colonoscopy in patients with severe hematochezia [1, 2, 8, 9]

Metoclopramide (if no contraindications) 10 mg intravenously or intramuscularly 5–30 min prior to starting purge and repeat every 4–6 h for nausea and to improve gastric emptying
Polyethylene glycol-based balanced electrolyte solution (Golytely®, Nulytely®, or Colyte®) orally or via nasogastric tube at 1 liter every 30–45 min until effluent is clear of clots, stool, and blood
Usually 6–8 liters of purge solution are required over 3–5 h to clean the colon of the blood, clots, and stool
In patients with tense ascites, perform therapeutic paracentesis to prevent respiratory compromise during colonoscopy
If patient is in congestive heart failure, treat with intravenous diuretics, or if in renal failure, use concurrent hemodialysis

Alternate Procedures

Traditional Management of Severe Hematochezia in Adults

The traditional medical-surgical-angiographic management of severe hematochezia in adults is shown in Fig. 23.3. In this approach, patients with ongoing hematochezia have emergency angiography, and, if it is positive, angiographic embolization or surgery is performed [1, 2, 7, 8]. If the initial angiogram is negative but there is rebleeding, then an RBC scan is performed, or the angiogram is repeated. For patients without

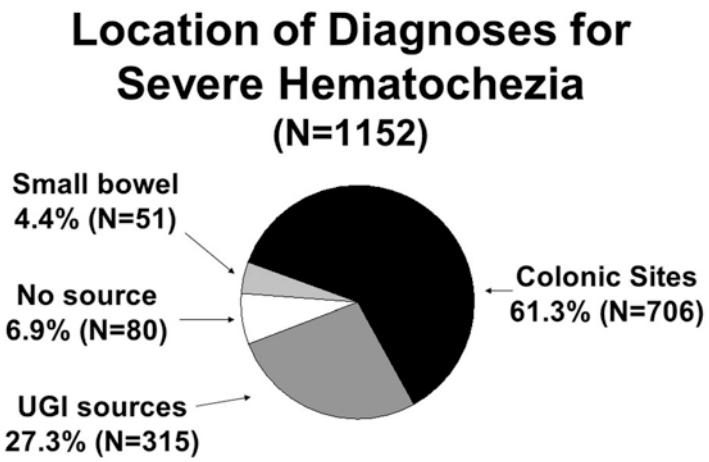

Fig. 23.2 For 1152 patients hospitalized for severe hematochezia, the final sites (location) of hemorrhage are shown, from a large prospective CURE study, utilizing the management algorithm shown in Fig. 23.1 [1, 7, 12, 13]

Table 23.3 The eight most common colonic sources of severe hematochezia[a]

Diverticulosis	32.6%
Ischemic colitis	12.2%
Internal hemorrhoids	10.8%
Rectal ulcers	8.5%
Colitis (UC, *C. diff*, Crohn's, or other types)	7.5%
Colon angiomas or radiation telangiectasias	7.2%
Post-polypectomy ulcer	7.1%
Colon cancer or polyps – ulcerated	6.1%

CURE Hemostasis Research Group Study [1, 2, 7–9]
(706 total severe hematochezia patients with colonic sources of bleeding)
[a]Expressed as the percent of all colonic sources of severe hematochezia. *UC* is ulcerative colitis; Crohn's is colitis; *C. diff* is *Clostridium difficile*

rebleeding or those with self-limited hematochezia, elective colonoscopy (or in the past barium enema) was performed. Therapy (medical, colonoscopic, angiographic, or surgical) depended upon the site of the bleeding or localization of anatomic non-bleeding lesions (such as diverticulosis or angiodysplasias) and comorbidities of the patients [9, 20–24].

Emergency Abdominal Angiography

Angiography has been reported to be useful for diagnosis and treatment of patients with severe hematochezia [7, 8, 12, 20–22]. The advantages of angiography are that skilled angiographers are able to diagnose and treat some patients with severe hematochezia. The study can be done without colonic purging or while purging is being performed. With selective injections, visualization of hindgut, midgut, and foregut lesions (bleeding or non-bleeding) is feasible. Angiography can complement the urgent endoscopic approach (colonoscopy and enteroscopy) for diagnosis and treatment (see Fig. 23.1). Angiographic embolization for actively bleeding colon diverticula is reported to be 80% effective but is not as effective for other colon lesions where rebleeding occurs in 40% of cases [21].

The main disadvantage of angiography is that a relatively high blood flow (~ 0.5 mL/min) is required to see extravasation (e.g., active bleeding) into the gut lumen, and this is rare for colon lesions. Refer to Fig. 23.4 for an example of active bleeding (e.g., contrast extravasation). Active bleeding is the stigma of hemorrhage seen in only 30% of patients with definitive diverticular bleeding diagnosed by urgent colonoscopy. Another major disadvantage of angiography is that it cannot detect non-bleeding stigmata of hemorrhage which are significantly more common than active bleeding [1, 2, 8, 9]. Other non-bleeding stigmata (such as clot, visible vessel, or spot) are not seen on angiograms but account for the other 70% diagnosed as definitive diverticular bleeding on urgent colonoscopy. Indirect evidence of gut wall lesions (such as early-filling veins or neovascularity of tumors) is suggestive of potential bleeding sites. However, the examination is not definitive without extravasation of contrast into the lumen.

Non-bleeding stigmata of hemorrhage (visible vessels, adherent clot, or flat spot) and mucosa lesions cannot be detected by angiography. In the most common colonic diagnosis (diverticulosis) based upon prevalence of stigmata on urgent colonoscopy, only about 30% of definitive diverticular patients could be diagnosed by emergency angiography because about 70% of patients have non-bleeding stigmata (as diagnosed by urgent colonoscopy). The latter non-bleeding stigmata of hemorrhage cannot be detected by either emergency angiography or RBC scanning. Therefore, the sensitivity of either angiography or RBC scanning for diagnosis and localization of colonic bleeding site for diverticular hemorrhage are quite low. While localization is sometimes possible, a specific etiologic diagnosis is usually not possible with angiography alone. For elderly patients, com-

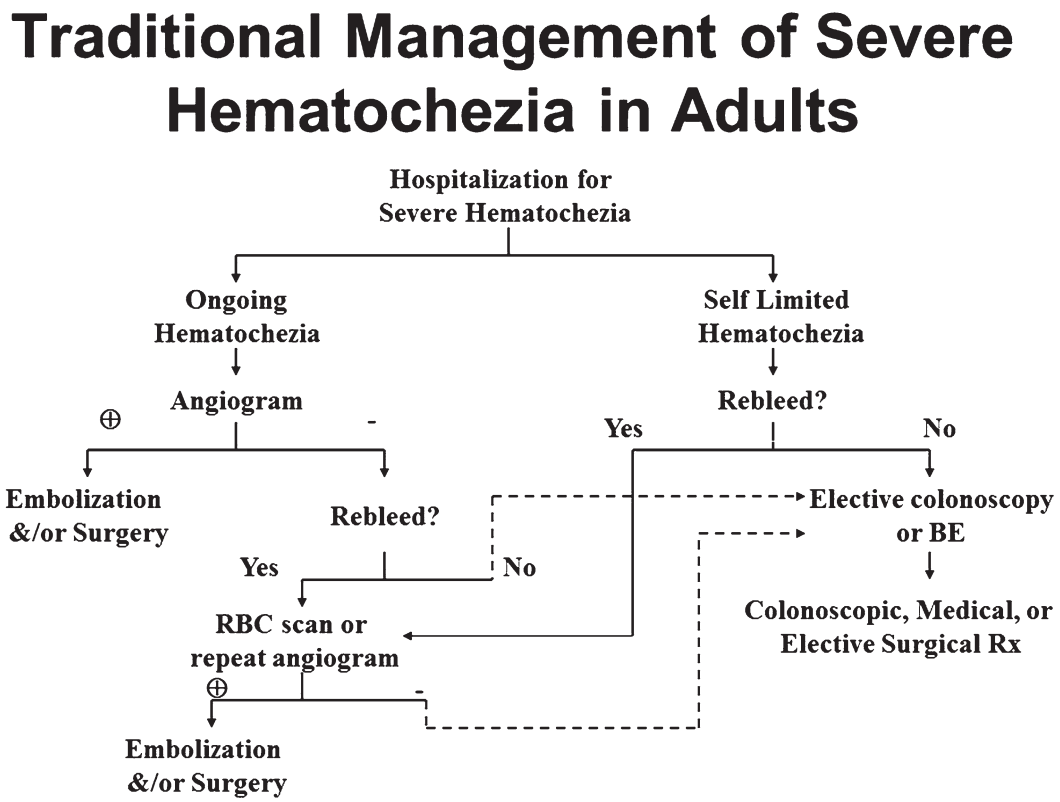

Fig. 23.3 Traditional medical-surgical-angiographic management of severe hematochezia in adults [1, 7, 8, 11, 19]

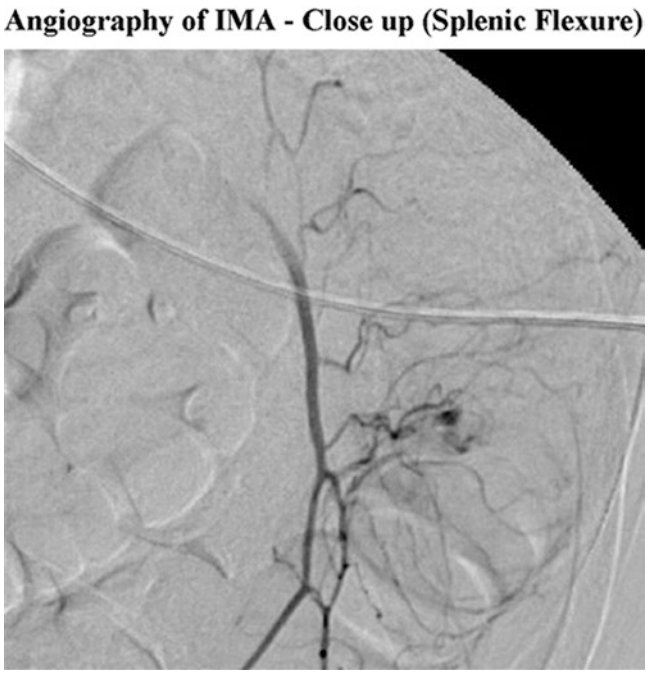

Fig. 23.4 Abdominal angiogram with selective cannulation of the inferior mesenteric artery (IMA) and extravasation of contrast indicating active bleeding. The bleeding site was presumed to be a diverticular hemorrhage near the splenic flexure, and the arteriole was embolized

plications of angiography are also common, about 11% [1, 9, 20, 21]. These include access artery occlusion, clotting, or bleeding; renal insufficiency from the contrast; bowel infarction; and volume overload from the contrast [1, 8, 9].

Our approach for the patient with severe hematochezia is to consider emergency angiography for patients who fail to have a diagnosis made by the urgent colonoscopy/enteroscopy approach and have ongoing or recurrent hematochezia or those with severe ongoing hematochezia and a positive RBC scan (at baseline or early- < 4 h) or in postoperative patients with severe hematochezia who cannot be adequately prepped for urgent colonoscopy. The endoscopic and angiographic examinations are complementary. Refer to Fig. 23.1.

Red Cell Scanning

Technetium-labeled RBC scans have also been used for localization of potential bleeding sites in patients with severe hematochezia [8, 23, 24]. Refer to Fig. 23.5 for a positive early RBC scan in a patient with ongoing GIB bleeding.

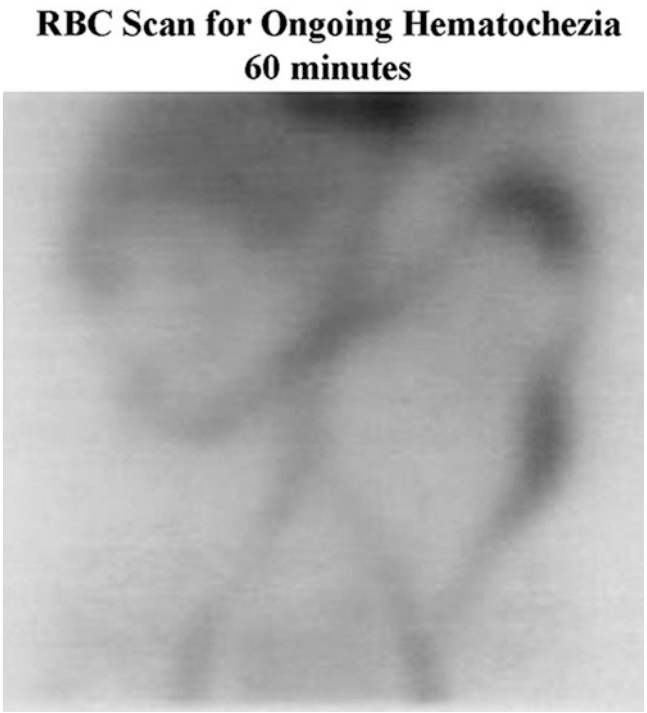

Fig. 23.5 RBC scan at 60 min, performed in a patient with ongoing hematochezia in the hospital. The subsequent angiogram was negative, but there was a clot on a diverticulum found on urgent colonoscopy

The advantages of RBC scanning are that an early study can be done without colon preparation or while the patient with ongoing hematochezia is receiving oral purge for the colonoscopy. The threshold for detection of extravasation into the gut lumen is a 0.1 mL/min bleeding rate, only 20% of the threshold for showing extravasation at angiography. The examination can be repeated, because the technetium label on the RBCs stays active in the vascular space for 24 h. The main disadvantage is that the patients must have active bleeding when the RBC scan is done to show leakage of labeled RBCs into the bowel lumen. Also, whereas early scans (less than 4 h after baseline) may be relatively accurate for a bleeding site localization, delayed scans are notoriously poor for accuracy of localization. Furthermore, specific etiologic (lesion) diagnosis (as opposed to localization) cannot be made, and treatment cannot be administered with RBC scanning. Definitive diagnosis and treatment of the bleeding site will depend on confirmatory endoscopic/colonoscopic procedures, angiography, or surgery. However, RBC scans are utilized in many hospitals as a screen before angiography. If an early RBC scan is positive, then the subsequent yield of abdominal angiography will be higher [1, 8].

We utilize RBC scans in our approach to patients with severe hematochezia. Refer to Fig. 23.1. We recommend early RBC scans (i.e., baseline and up to 1–4 h only) in patients who are hospitalized for severe, ongoing hematochezia, before or after starting the purge or if they rebleed during the hospitalization and no diagnosis or localization has been determined. Even if the RBC scan is positive early, a confirmatory test such as angiography, urgent colonoscopy, push enteroscopy, or deep enteroscopy is recommended before consideration of emergency surgery [8]. Whereas over 75% of patients with an early RBC scan (1–4 h) have effective diagnosis and treatment by surgery, less than 40% of patients with positive delayed scans (12–24 h) have localization by surgery or control of bleeding. Emergency endoscopic hemostasis which can be definitive or allow stabilization of the patient and scheduling of elective surgery may also be feasible [1, 7, 8].

Cost Comparison Versus Urgent Colonoscopy and Randomized Controlled Trials of Traditional Approach to Severe Hematochezia

For patients who have a traditional approach to severe hematochezia, we estimated that the diagnostic yield would be significantly lower, and the incremental cost for patient management would be more than $10,000 per patient two decades ago [8].

Rockey and colleagues performed a randomized prospective study of urgent colonoscopy compared to a traditional approach (as shown in Fig. 23.3) for 100 patients with severe hematochezia [22]. They reported significantly higher rates of definitive diagnosis in the urgent colonoscopy group vs. traditional management group (42% vs. 22%) and lower rates of no source found (4% vs. 24%). However, there were no significant differences in early rebleeding (22% vs. 30%), hospital stay (5.8 vs. 6.6 days), total RBCs transfused (4.2 vs. 5.0 units), surgery (14% vs. 12%), or death from rebleeding (2% vs. 4%). Criticisms of this study are both in design of the study and in technical issues. In the Rockey study, only 4 liters of colon prep were utilized, and consequently many of the preps were suboptimal in the urgent colonoscopy group, new colonic hemostasis techniques (such as combination epinephrine injection and hemoclipping) of focal bleeding sites were not utilized, and test results were not utilized to triage patients to level of care or early hospital discharge [11].

In another recent randomized study of urgent compared to delayed colonoscopy, Laine and Shah reported no differences in major 30-day outcomes including rebleeding, RBCs transfused, hospital days, rates of more testing to make a diagnosis after the colonoscopy, or in estimated hospital charges [25]. However, this study included young low-risk patients, patients with very severe bleeding who would typically require angiography or surgery were not included, and stigmata of hemorrhage were infrequently found (probably related to limiting the amount of prep used to 4 liters) – most diagnoses were “presumptive” and not definitive, several types of lesions were not treated during urgent colonos-

copy (such as bleeding internal hemorrhoids), and the study was stopped prematurely before enrolling the estimated sample size. These limitations significantly limit the clinical relevance, generalizability, and quality of this report compared to other studies by experienced GI hemostasis teams who use more purge solution and have better colon preps, have higher rates of definitive diagnoses, have higher success rates of colonoscopic hemostasis, report significantly better 30-day outcomes, and reduced costs with urgent colonoscopy compared to delayed colonoscopy [11].

Practical Considerations: Angiography or RBC Scanning for Diagnoses

- An angiogram will only be positive for diagnoses and treatment of a bleeding site if there is active bleeding – non-bleeding stigmata cannot be diagnosed.
- RBC scans only localize active bleeding sites, and delayed scans can be very misleading for diagnoses since the blood or clots in the gut move with peristalsis.

Specific Colonic Lesions

Diverticular Hemorrhage

A diverticulum forms when the mucosa of the colon penetrates through an area of weakness in the muscularis and forms a balloon-like structure on the outside of the colonic wall covered by serosa. Hallmarks are of a submucosal artery uniting with a subserosal artery to form an arterial arcade that has bidirectional blood flow. In our studies, stigmata of definitive diverticular hemorrhage are found at either the neck (<50%) or base (>50%). For unknown reasons with diverticular hemorrhage, a rent develops at the neck or the base of the colonic diverticulum eroding into the underlying artery. This can cause sudden and significant colon hemorrhage. Diverticular bleeding is reported to be the most frequent cause for severe hematochezia in the United States, accounting for 20–55% of all cases of lower GI bleeding in adults [1–3, 7, 8, 13, 22]. However, this diagnosis is most often based upon the finding of colonic diverticulosis on some test such as CT scan or colonoscopy and not on stigmata of hemorrhage.

Diverticular bleeding was the cause (including definitive diverticular or presumptive diverticular hemorrhage as defined below) of severe hematochezia in 32.6% of all patients admitted with severe hematochezia in our recently updated CURE Hemostasis cohort study of patients with severe hematochezia [1, 2, 7–9]. However, most patients with colon diverticulosis who presented with severe hematochezia do not have bleeding from diverticulosis. In our series, 45.6% of patients with known colon diverticulosis were found to have bleeding from non-diverticular sources either in the colon or proximal. We refer to them as having "incidental diverticulosis." [9] "Presumptive diverticular bleeding" was diagnosed when no definitive source or other potential sources of hemorrhage on urgent colonoscopy, anoscopy, push enteroscopy, and other imaging including RBC scan, angiography, and/or capsule endoscopy was found. This accounted for the bleeding site in 30.8% of patients with known colonic diverticulosis and severe hematochezia. "Definitive diverticular bleeding" was diagnosed when there was a stigma of recent hemorrhage such as active bleeding, a non-bleeding visible vessel, an adherent clot, or a spot on a diverticulum at urgent colonoscopy. This subgroup accounted for 26.4% of all patients with severe hematochezia and diverticulosis [8, 9] (Fig. 23.6).

Emergency treatment of patients with severe diverticular hemorrhage depends upon the severity of bleeding and local expertise of gastroenterologists, interventional radiologists,

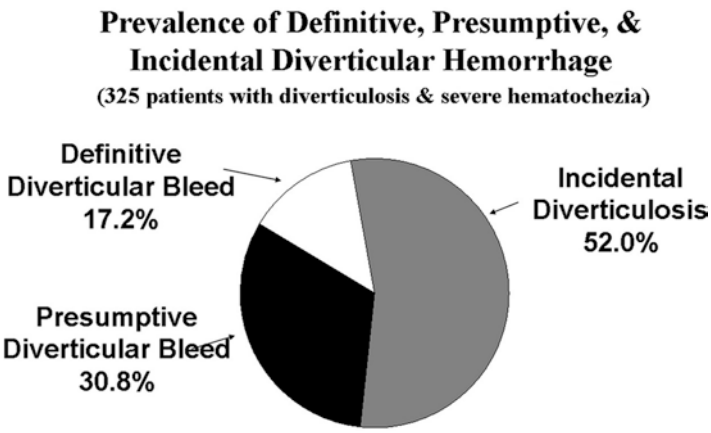

Fig. 23.6 Prevalence of definitive, presumptive, and incidental diverticular hemorrhage in 436 patients with diverticulosis and severe hematochezia [1, 8, 9, 11, 19]

and surgeons. Treatment of bleeding diverticulosis is safe and effective by these experienced teams, including hemostasis focused on the stigma of recent hemorrhage during urgent colonoscopy.

We recently reported about the natural history of definitive diverticular hemorrhage with medical treatment and also results of blood flow monitoring with a Doppler endoscopic probe [26]. For 38 patients studied prospectively after urgent colonoscopy where stigmata of hemorrhage were found but not treated endoscopically, the rates of major rebleeding (and need for intervention) during the next 30 days overall were high (66% and 45%). The 30-day rebleeding (and intervention) rates varied by stigmata with active bleeding, 84%, (58%); non-bleeding visible vessel, 60%, (40%); and adherent clot, 43%, (29%). When arterial blood flow underneath these stigmata of hemorrhage was detected in 92% of another cohort of patients, this could be obliterated by current colonoscopic treatments of the stigmata (hemoclipping in the base of the diverticulum or multipolar probe in the neck), and no patient had rebleeding up to 30 days [26].

Long-term treatment to prevent recurrence of diverticular hemorrhage is highly recommended. Avoidance of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and anticoagulants is the most important for prevention of diverticular and colonic rebleeding. The roles of fiber, control of constipation, and avoidance of nuts and small seeds are controversial. Contrary to common teaching about patients with diverticulosis, Strate et al. recently reported that patients who consumed nuts and seeds in their diet had no more complications of diverticular disease (hemorrhage or diverticulitis), and frequent popcorn eaters had lower rates of diverticulitis than age-matched patients whose diet lacked these foods [27]. Some other studies have reported an association between NSAID's use and diverticular bleeding [28, 29].

We recently reported that patients with documented diverticular hemorrhage based upon urgent colonoscopy (e.g., definitive or presumptive) and long-term follow-up had relatively low rates of recurrent diverticular hemorrhage and very low rates of diverticulitis during long-term follow-up after an initial severe diverticular bleed – less than 1% incidence [30]. The rates of severe colon rebleeding of any type were relatively low, during a median of 5–6 years of follow-up, and were similar for patients treated initially with medical (27% rebled), endoscopic (37% rebled), or surgical therapy (40% rebled). However, the proportion of non-diverticular sources for the rebleeding (as a percentage of all bleeds) varied according to treatment, from 37% (medical) or 59% (endoscopic group) to 75% (surgical group). In other words, at least 35% of all the late rebleeding was from non-diverticular sources of LGI hemorrhage in these patients with documented colon diagnosis of diverticular hemorrhage [30]. During long-term follow-up, death rates were high (about 30%) regardless of treatment during the index diverticula hemorrhage and all were from comorbid conditions and not diverticular hemorrhage. These results indicated that patients with documented diverticular hemorrhage had a relatively benign prognosis and course compared to other patients with severe GI hemorrhage from varices, ulcers, or ischemia [2, 31, 32].

Practical Considerations – Diverticulosis and Hemorrhage

- For patients with stigmata of diverticular hemorrhage, early rebleeding rates are high without endoscopic, angiographic or surgical hemostasis.
- For patients with proven diverticular hemorrhage, stigmata of hemorrhage can be found on urgent colonoscopy in up to 48% of patients.
- For patients with a known diagnosis of colon diverticulosis who are hospitalized for their first episode of severe hematochezia, about 50% are bleeding from a non-diverticular GI source.

Internal Hemorrhoids

Internal hemorrhoids caused severe hematochezia in 10.8% of our patients who were hospitalized [1, 2, 7–9, 12]. Most physicians do not include internal hemorrhoids in the differential diagnosis of severe hematochezia, because the majority of internal hemorrhoidal bleeding is managed as an outpatient by surgeons and is perceived to be intermittent, low grade, and self-limited. However, a significant proportion of patients with internal hemorrhoids have both chronic and acute severe rectal bleeding which have not been commonly recognized. Bleeding internal hemorrhoids constitute a significant public health problem since approximately 10.4 million people suffer from hemorrhoid symptoms annually, prompting 3.5 million physician visits per year [33].

We grade internal hemorrhoids with a slotted anoscope from grade I to IV (refer to Table 23.4), depending on the degree of prolapse through the anal sphincter. Although bleeding may occur from any grade internal hemorrhoid, severe bleeding causing anemia and hospitalization is most often from grade II or III internal hemorrhoids. Patients with drug induced coagulation abnormalities (from NSAIDs, aspi-

Table 23.4 Grades of internal hemorrhoids [34–36]

Grade I: No prolapse below the dentate line
Grade II: Prolapse during defecation with spontaneous reduction
Grade III: Prolapse during defecation requiring manual reduction
Grade IV: Nonreducible prolapse below that dentate line

rin, warfarin, or antiplatelet drugs) or intrinsic coagulopathies (from liver or renal failure or hematologic disorders) may have significant rectal bleeding from smaller grade internal hemorrhoids (grades I or II). Following enemas to clear the distal colon (Fleets® or tap water), bleeding hemorrhoids can be diagnosed with a flexible sigmoidoscope using a retroflexed view, but the internal hemorrhoids are always better visualized with the use of a slotted anoscope [33].

While outpatients with intermittent bleeding from internal hemorrhoids often have cessation of hemorrhage with medical therapy, most hospitalized patients with severe hematochezia require endoscopic therapy or surgery, in our experience [1, 2, 7, 8, 34]. In the past, we have utilized sclerotherapy or anoscopic thermal coagulation (such as with rigid multipolar or heater anoscopic probes) for patients with internal hemorrhoids and hematochezia [33–36]. Recently, we have found rubber band ligation was faster and more efficient particularly for control of severe hematochezia in patients with grade II-IV internal hemorrhoids [37, 38]. We perform urgent rubber banding of bleeding hemorrhoids using a diagnostic size panendoscope and a 4-shot banding device. The technique is similar to banding esophageal or hiatal hernia varices. Concomitant and long-term medical therapy with fiber, stool softeners, and avoidance of aspirin, NSAIDs, and anticoagulants are also highly recommended. Outpatient follow-up and further treatment to completely control bleeding and to reduce the internal hemorrhoids to grade I or less is our routine, and this is highly effective.

Surgical intervention may be indicated for those patients who prefer to have a single procedure despite associated discomfort or those patients with severe rectal bleeding who have failed medical and endoscopic therapy. Surgical hemorrhoidectomy is highly effective in controlling bleeding and eradicating internal hemorrhoids as well as external hemorrhoids [39–41]. However, surgical hemorrhoidectomy is not free of complications [42–45].

Practical Considerations: Internal Hemorrhoids

- Internal hemorrhoids are the third most cause in adult patients hospitalized with severe hematochezia.
- They can be diagnosed by a combination of history, colonoscopy (to exclude other colon causes), and anoscopy.
- Effective treatments are band litigation or bipolar thermal coagulation along with medical therapy, and very few patients require surgery to control active or chronic bleeding.

Ischemic Colitis

Colonic ischemia was responsible for severe hematochezia in 12.2% of our patients hospitalized with hematochezia in our recent reassessment [1, 2, 7–9]. Other series report an incidence of 3–9% of severe lower gastrointestinal bleeding being caused by ischemic colitis [3, 5, 19, 31, 46, 47]. There is usually no identifiable precipitating cause for the acute onset of colonic ischemia. However, many patients with ischemic colitis have underlying atherosclerotic cardiovascular or peripheral occlusive disease. However, ischemic colitis can also be seen with acute myocardial infarction, severe heart failure, hypercoagulable states, vasculitis, sepsis, prolonged strenuous exercise, and some medications such as diuretics [31, 47]. Some patients present with the acute onset of crampy abdominal pain which can be localized in the right lower quadrant, epigastrium, or left lower quadrant depending on the segment of colon involved. However, the pain in severe cases tends to radiate throughout the entire abdomen. The splenic flexure and sigmoid colon, which have poor collateral blood flow (e.g., and are called "watershed areas"), are most often involved [19, 31, 46, 47]. When present, abdominal pain is usually associated with bloody diarrhea. Occasionally, nausea, vomiting, and fever are present. Signs of hypovolemia, tachycardia, and hypotension may be seen in very severe cases of ischemic colitis, but these are most often associated with large vessel stenosis or embolization as seen on surgical services, rather than small vessel disease or hypotension alone without abdominal pain, as more often seen on medical or GI services of hospitalized patients. Physical examination of the abdomen may be normal or have findings such as diffuse abdominal tenderness, hyperactive bowel sounds, or an abdominal bruit (in large vessel stenosis or embolization). No localized peritoneal signs are usually present on medical service patients unless there is frank colonic infarction with involvement of the serosa as more commonly seen on surgical patients. Thumbprinting may be observed on plain abdominal radiographs or CT scans, but this is not a frequent finding in our experience [19, 31, 46, 47]. In many cases of ischemic colitis which we see in elderly patients, only painless hematochezia is noted and no other abdominal symptoms. These medical service patients have mucosal ischemia and ulcerations but usually lack transmural injury or infarction.

Colonoscopy is the best way to make the diagnosis of ischemic colitis of the colon [1, 2, 7, 8, 19, 31, 47]. There is usually segmental involvement consisting of mucosal edema, erythema, friability, mucosal hemorrhages, mucosal necrosis, and ulcerations. Colonic biopsies from the affected and unaffected areas are usually definitive for ischemia. Colonoscopy, stool cultures (and *Clostridium difficile* toxin assay and ova and parasite analysis), and histopathologic findings are useful to differentiate colonic ischemia from inflammatory or infectious colitis.

Treatment is medical therapy and supportive care with intravenous fluids and/or blood transfusions to improve tissue perfusion. Urgent treatment of comorbid conditions is also

warranted, including peripheral or central vascular disease, cardiac arrhythmias, or severe anemia which may have contributed to bowel ischemia. Antibiotics are indicated if fever or sepsis is present. If there is clinical deterioration of the patient with development or peritoneal signs, fever, leukocytosis, or evidence of bowel perforation, surgical intervention with segmental or subtotal colon resection is indicated. Therapeutic colonoscopy plays a limited role in these patients unless a focal ulcer with stigmata of hemorrhage is found at colonoscopy, which is the case in less than 10% of our patients with severe ischemic colitis [1, 2, 7, 8, 19, 31]. In a recent report by our group, the location of the ischemic lesions (ulcers, erosions, and bleeding) in 65 documented cases was 19% rectosigmoid, 49% splenic flexure or descending colon, 16% ascending colon, and 16% both hepatic and splenic flexures [31]. The implication of these data on localization is that a flexible sigmoidoscopy would be adequate for diagnosis and in less than 20% of patients with ischemic colitis documented by urgent colonoscopy. Compared to other colon diagnoses for hematochezia, patients with ischemic colitis had significant higher rates of rebleeding (27.7% vs. 12.6%) and surgery (13.9% vs. 5.6%) and longer hospitalization after diagnosis (11.8 vs 6.5 days). Furthermore, among patients with ischemic colitis, those who first started bleeding after hospitalization for an unrelated medical-surgical problem ("inpatient ischemia") faired much worse than those whose bleeding started before hospitalization ("outpatient ischemia"). Their respective outcomes were in rebleeding (41.4% vs. 16.7%), surgery for bleeding (24.1% vs. 5.6%), deaths (13.8% vs. 2.8%), and both hospital (20.8 vs. 4.8 days) and ICU days (7.6 vs. 0.6 days).

Practical Considerations: Ischemic Colitis

- Ischemic ulcers are the second most common cause in patients with severe hematochezia.
- Most patients seen by gastroenterologists with ischemic colitis have diffuse rather than focal lesions, and these are related to hypoperfusion of the colonic mucosa from comorbidities.
- Those with inpatient development of bleeding have much poorer outcomes than patients whose bleeding starts out of the hospital.

Solitary Rectal Ulcer Syndrome

Rectal ulcers (usually solitary but sometimes multiple) were responsible for 8.5% of the colonic cases of severe hematochezia in our large study [1, 2, 8, 9, 47]. It was the fourth most common colonic cause of severe hematochezia in our large prospective CURE Hemostasis cohort. In contrast to previous series which reported that this syndrome occurs in younger (third and fourth decades of life) patients [48–50], our patients were older, in the sixth and seventh decades of life [47, 51, 52]. This syndrome is more common in women and is characterized by rectal bleeding and mucous discharge in 56–89% of patients [49, 53]. The etiology of this disorder is not completely understood, but prolapse-induced rectal mucosal trauma or ischemia appears to contribute [54]. Our patients usually presented with symptoms of severe constipation and often fecal impaction. Increasingly, inpatients with prolonged hospitalization and inpatient hematochezia represent a large proportion of those with severe rectal ulcer bleeding [51, 52]. Pressure-induced mucosal necrosis in elderly patients with fecal impaction must also be considered. Also, rectal balloons (which are used commonly in ICUs for sick or incontinent patients) are associated with rectal ulcers, often multiple, that bleed. On endoscopy, one or more well-demarcated ulcerations are seen with edematous, erythematous, and nodular borders [51, 52]. Active bleeding or stigmata of recent hemorrhage were found at urgent colonoscopy in most patients with severe hematochezia in our recent studies [51, 52].

Colonoscopic hemostasis of hemorrhage from rectal ulcers consists of coagulation with a large-contact thermal probe or hemoclipping with or without preinjection of epinephrine. Medical management of constipation, adequate nutritional support, and avoidance of anticoagulants, NSAIDs, and antiplatelet drugs are recommended to prevent rebleeding. Surgery is recommended for recurrent, severe bleeding. However, there may be a role for a new, large, over-the-endoscope hemoclip (OVESCO) in patients with severe bleeding, prior to recommending surgery [55].

Practical Considerations: Rectal Ulcers

- Rectal ulcers are the fourth most common cause of severe hematochezia.
- These are more common in inpatients in ICUs or nursing home patients who are bed bound.
- Severe constipation, use of rectal balloons, or anorectal trauma may be associated.
- Acute and chronic bleeding are common and so is slow healing of rectal ulcers.

Delayed Post-polypectomy Hemorrhage

Hemorrhage after an endoscopic polypectomy may occur immediately afterward or may be delayed for hours, days, or rarely weeks [17, 18, 56]. Our focus in this chapter is on delayed severe post-polypectomy hemorrhage resulting in

hospitalization for severe hematochezia. This is defined as occurring one or more days after discharge of the patient from the endoscopy unit after the polypectomy. The incidence of severe delayed post-polypectomy hemorrhage is reported as 1–6% [17, 18, 47, 56, 57]. The variation in these reported rates is most likely a function of study design, patient population (i.e., age, comorbid conditions, use of antiplatelet drugs, or anticoagulants), and configuration and size of index polyps. Because of changes in colonoscopy practices (including performance of more screening colonoscopies for colorectal cancer) and with colonoscopic resection of larger sessile colonic polyps in the last two decades, including piecemeal resection or following submucosal saline injection, delayed post-polypectomy hemorrhage appears to be occurring more frequently [17, 18, 56]. Severe post-polypectomy bleeding was the cause of severe hematochezia in 7.1% of colonic etiologies, in a recent study by the CURE Hemostasis Research Group [1, 2, 9, 57]. The mean size of the polyps was 20 mm in diameter, and most were sessile polyps without carcinoma on histopathology. Delayed hemorrhage occurred a median of 7 days (range 2–73) after polypectomy. Most patients (77%) were men with a mean age of 69 years. The majority (77%) were also consuming aspirin, antiplatelet drugs, or warfarin after polypectomy for comorbid cardiac or vascular conditions. All patients required hospitalization because of severe hematochezia. After colonic purge, urgent colonoscopy revealed ulcerations with a mean diameter of 11 mm at the prior polypectomy sites. Stigmata of hemorrhage on the ulcers included active bleeding in 23%, non-bleeding visible vessel in 23%, clot in 38%, spot in 8%, and clean ulcer in 8%. Ninety-two percent of patients were treated endoscopically, and only one patient rebled. One patient with cancer had surgery, and the remainder was treated medically.

Bleeding occurring immediately after polypectomy is thought to be due to inadequate cauterization of the polyp vessels during polypectomy, whereas delayed post-polypectomy hemorrhage is thought to be due to sloughing of the necrotic, cauterized tissue in the induced ulcer, with exposure of the underlying blood vessel. Intrinsic (from comorbid conditions) or extrinsic coagulopathies (from medications) can aggravate or cause the bleeding by interfering with clotting. The predominance of visible vessels with or without active bleeding or clots indicates an underlying vessel, probably similar to the anatomy of peptic ulcers as defined by Swain [32]. However, to date, there have been no studies reporting on the histology of stigmata of hemorrhage for delayed post-polypectomy colon ulcers, because most are now successfully treated via colonoscopy [17, 18, 47, 56]. Hemostasis is performed with thermal techniques or hemoclipping with or without preinjection with dilute epinephrine around the stigmata of hemorrhage in the post-polypectomy ulcer.

The risk of aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) prior to polypectomy remains a concern. However, according to expert opinion and current guidelines, no significant difference in post-polypectomy bleeding can be expected for those patients consuming these drugs and those who did not before polypectomy [58, 59]. The guidelines from the American Society for Gastrointestinal Endoscopy state that polypectomy in patients consuming standard doses of these drugs, precluding any underlying bleeding disorders, is safe [14]. However, the level of scientific evidence for these guidelines is based on case reports and expert opinion rather than randomized studies. For high-risk patients with coagulopathies, caution is recommended when continuing or resuming aspirin, antiplatelet drugs, and anticoagulants.

Practical Considerations: Delayed Post-polypectomy-Induced Ulcer (PPIU) Hemorrhage

- Delayed PPIU hemorrhage has increased significantly in prevalence as a cause of severe hematochezia over the last two decades.
- This relates to the number of colonoscopies and polypectomies being performed, to right colon location of PPIUs, and to use of antiplatelet and anticoagulant drugs.
- Bleeding occurs about 7 days after polypectomy when the coagulum sloughs off the PPIU exposing a submucosal artery.
- During urgent colonoscopy, there is high prevalence of ulcer stigmata, and it is safe to treat these with hemoclips.

Colonic Angiomas

Colonic angiomas or radiation telangiectasia was the fifth most common colonic cause of severe hematochezia, responsible for 7.2% of the colonic diagnoses [1, 2, 9, 60]. In contrast, the majority of patients we see (70%) with bleeding angiomas present with self-limited intermittent bleeding or occult blood-positive stools and iron-deficiency anemia. These patients are usually hemodynamically stable and can undergo elective colonoscopy in the outpatient setting [60]. A smaller group (30%) of patients with colonic angiomas who more often have coagulopathies present with severe, persistent hemorrhage may be hemodynamically unstable and/or severely anemic and require hospitalization, blood transfusions, and emergency evaluation.

Table 23.5 Comorbid conditions for patients with hemorrhage from colonic angiomas ($N = 108$)

Condition	% of patients
Severe heart disease	46%
Valvular heart disease	29%
Aortic stenosis	16%
Aortic regurgitation	5%
Mitral regurgitation	8%
Chronic renal failure	
Hemodialysis	16%
Cirrhosis	16%
Collagen vascular disorder	5%
Osler-Weber-Rendu syndrome	5%

See Ref. [60]

Practical Considerations: Colon Angiomas and Radiation Telangiectasia

- In elderly patients .with comorbidities and severe hematochezia, right colon angiomas are relatively common as a bleeding site.
- If not too numerous, angiomas can be safely treated with multipolar coagulation (MPEC).
- Radiation telangiectasia after pelvic radiation can cause chronic or acute bleeding, and endoscopic control is feasible with APC or MPEC.

The CURE Hemostasis Research Group randomized 108 prospective patients with bleeding colonic angiomas to colonoscopic treatment with bipolar coagulation (57 patients) or heater probe (51 patients). Most of these patients were elderly (>65 years) and suffered from one or more comorbid conditions (refer to Table 23.5). The mean follow-up of these patients was 2 years which was compared to the 2 years prior to endoscopic treatment in terms of number of bleeding episodes, number of blood transfusions, and hematocrit while on iron and not acutely bleeding [60].

At colonoscopy, most angiomas (85%) were in the right colon [60]. The majority of angiomas (80%) were 5–10 mm in size, 18% were 11–20 mm, and 2% were greater than 20 mm. The mean number of colonoscopies to control bleeding during the follow-up period was 1.4 with a range of 1–4.

Seventy percent of patients had a good outcome with colonic coagulation, experiencing fewer bleeding episodes, requiring fewer blood transfusions, and holding a higher hematocrit during follow-up [60]. Partial colectomies were performed in 18% of patients who had multiple colon angiomas (usually more than 25 in one segment such as the right colon). However, 38% of these operated patients continued to have recurrent bleeding post-hemicolectomy. Complications from colonoscopic coagulation were observed in 5% of patients consisting of delayed hemorrhage due to ulceration (four patients) or post-coagulation syndrome due to full-thickness coagulation (two patients). No perforations occurred. Two of the patients with delayed hemorrhage who had coagulopathies required surgery.

Cost Assessment

A cost analysis, comparing the urgent colonoscopy approach with a traditional medical-surgical-angiographic approach to hematochezia, was previously reported by our group [8]. The urgent colonoscopy group had fewer hospital days, surgeries, and diagnostic tests. The savings based upon 1997 estimates was a mean of $10,065 per patient. Strate and Rockey have also confirmed that early colonoscopy in patients with severe hematochezia results in shorter length of patient hospitalization [61, 62].

Conclusion

Severe hematochezia or lower gastrointestinal bleeding is a frequently encountered medical-surgical problem. The prevalence appears to be increasing because of recent colorectal cancer screening practices and the aging of referral patient populations. Our recommended approach to these patients is for vigorous resuscitation with intravenous fluids and blood transfusions, close monitoring in an intensive care unit or monitored bed unit, bedside evaluation with nasogastric tube lavage for signs of a possible UGI bleeding source, and urgent colonoscopy (or upper endoscopy or small bowel enteroscopy if colonoscopy is negative) following thorough colonic cleansing with a purge via oral or nasogastric tube. Definitive or presumptive diagnosis of the bleeding site can be made with this approach in over 93% of cases. In patients with severe hematochezia, a colonic bleeding site is found in 61.3% of cases. Endoscopic treatment of focal bleeding lesions in the colon or the UGI tract is highly effective and safe in these cases, thereby reducing the need for surgical or angiographic intervention. In patients with a definitive diagnosis and no stigmata of hemorrhage or low-risk stigmata, early diagnosis may also facilitate downgrading the intensity of medical care and/or early discharge from the hospital.

References

1. Jensen DM, Machicado GA. Diagnosis and treatment of severe hematochezia: the role of urgent colonoscopy after purge. Gastroenterology. 1988;95:1569–74.
2. Kovacs TOG, Jensen DM. Gastrointestinal hemorrhage and occult gastrointestinal bleeding. In: Goldman L, Schafer AI, edi-

tors. Goldman – Cecil Medicine. 25th ed. Philadelphia: Elsevier Saunders; 2015. Chapter 135. p. 879–84.
3. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1997;92:419–24.
4. Kollef MH, O'Brian JD, Zuckerman GR, et al. BLEED: a classification tool to predict outcomes in patients with acute upper and lower gastrointestinal hemorrhage. Crit Care Med. 1997;25:1125–32.
5. Peura DA, Lanza FL, Gostout CJ, et al. The American College of Gastroenterology bleeding registry: preliminary findings. Am J Gastroenterol. 1997;92:924–8.
6. Velayos FS, Williamson A, Sousa KH, et al. Early predictors of severe lower gastrointestinal bleeding and adverse outcomes: a prospective study. Clin Gastroenterol Hepatol. 2004;2:485–90.
7. Kovacs TOG, Jensen DM. Upper or small bowel hemorrhage presenting as hematochezia. Tech Gastrointest Endosc. 2001;3:206–15.
8. Jensen DM, Machicado GA. Colonoscopy for diagnosis and treatment of severe lower gastrointestinal bleeding: routine outcomes and cost analysis. Gastrointest Endosc Clin N Am. 1997;7:477–98.
9. Jensen DM, Machicado GA, Jutabha R, Kovacs TOG. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. N Engl J Med. 2000;342:78–82.
10. Tarone RE, Blot WJ, McLaughlin JR. Non-selective, non-aspirin, non-steroidal anti-inflammatory drugs and gastrointestinal bleeding relative and absolute risk estimates from recent epidemiological studies. Am J Ther. 2004;11:17–25.
11. Jensen DM. Management of patients with severe hematochezia – with all current evidence available. Am J Gastroenterol. 2005;100: 2403–6.
12. Cuellar RE, Gavaler JS, Alexander JA, et al. Gastrointestinal tract hemorrhage. The value of a nasogastric aspirate. Arch Intern Med. 1990;150:1381–4.
13. Rathgaber SW, Wick TM. Colonoscopy completion and complication rates in a community gastroenterology practice. Gastrointest Endosc. 2006;64:556–62.
14. Eisen GM, Baron TH, Dominitz JA, et al. Guideline on the management of anticoagulation and antiplatelet therapy for endoscopic procedures. Gastrointest Endosc. 2002;55:775–9.
15. Levin TR, Zhao W, Conell C, et al. Complications of colonoscopy in an integrated health care delivery system. Ann Intern Med. 2006;145:880–6.
16. Dominitz JA, Eisen GM, Baron TH, Goldstein JL, et al. Complications of colonoscopy. Gastrointest Endosc. 2003;57:441–5.
17. Metz AJ, Bourke MJ, Moss A, Williams SJ, Swan MP, Byth K. Factors that predict bleeding following endoscopic mucosal resection of large colonic lesions. Endoscopy. 2011;43:506–11.
18. Liaquat H, Rohn E, Rex DK. Prophylactic clip closure reduced the risk of delayed post-polypectomy hemorrhage: experience in 277 clipped large sessile or flat colorectal lesions and 247 control lesions. Gastrointest Endosc. 2013;77:401–7.
19. Savides TJ, Jensen DM. Endoscopic therapy for severe gastrointestinal bleeding. Adv Intern Med. 1995;40:243–71.
20. Athanasoulis CA. Therapeutic applications of angiography. N Engl J Med. 1980;302:1117–25.
21. Smith TP. Angiographic diagnosis and endovascular management of non-variceal gastrointestinal hemorrhage. Gastroenterol Clin N Am. 2005;34:735–52.
22. Green BT, Rockey DC, Portwood G. Urgent colonoscopy for evaluation and management of acute lower gastrointestinal hemorrhage: a randomized controlled trial. Am J Gastroenterol. 2005;100:2395–402.
23. Beam P, Persad R, Wilson N, et al. 99m-technetium-labeled red blood cell scintigraphy as an alternative to angiography in the investigation of gastrointestinal bleeding: clinical experience in a district general hospital. Ann R Coll Surg Engl. 1992;74:192–9.
24. Hunter JM, Pezim ME. Limited value of technetium 99 labeled red cell scintigraphy in localization of lower gastrointestinal bleeding. Am J Surg. 1991;159:503–6.
25. Laine L, Shah A. Randomized trial of urgent vs. elective colonoscopy in hospitalized patients for lower GI bleeding. Am J Gastroenterol. 2010;105:2636–41.
26. Jensen DM, Ohning GV, Kovacs TOG, Jutabha R, Ghassemi KA, Dulai GS, Machicado GA. Natural history of definitive diverticular hemorrhage based on stigmata of recent hemorrhage and colonoscopic Doppler blood flow monitoring for risk stratification and definitive hemostasis. Gastrointest Endosc. 2016;83:416–23.
27. Strate LL, Liu YL, Syngal S, Giovannucci EL. Nut, corn, and popcorn consumption and the incidence of diverticular disease. JAMA. 2008;300:907–14.
28. Aldoori WH, Giovannucci EL, Rimm EB, et al. Use of acetaminophen and nonsteroidal anti-inflammatory drugs: a prospective study and the risk of symptomatic diverticular disease in men. Arch Fam Med. 1998;7:255–60.
29. Laine L, Connors LG, Reicin A, et al. Serious lower gastrointestinal clinical events with non-selective NSAID or coxib use. Gastroenterology. 2003;124:288–92.
30. Ohning GV, Jensen DM, Kovacs TOG, Ghassemi KA, Jutabha R, Machicado GA, Dulai G, Sedarat A. Long-term outcomes in patients with diverticular hemorrhage based upon initial diagnosis with urgent colonoscopy and different treatments. Am J Gastroenterol. 2016;111(Supplement 1):S74: # 157.
31. Chavalitdhamrong D, Jensen DM, Kovacs TOG, Dulai G, Jutabha R, Ohning GV, Machicado GA. Ischemic colitis is a common cause of severe hematochezia and patient outcomes are worse than other colonic diagnoses. Gastrointest Endosc. 2011;74:852–7.
32. Swain CP, Storey DW, Bown SG, et al. Nature of the bleeding vessel in recurrently bleeding gastric ulcers. Gastroenterology. 1986;90:595–608.
33. Johanson JF. Hemorrhoids. In: Digestive diseases in the United States: epidemiology and impact, NIH publication 94–1447. Washington DC: US Government Printing Office; 1994. p. 273–98.
34. Jutabha R, Miura-Jutabha C, Jensen DM. Current medical, anoscopic, endoscopic and surgical treatments for bleeding internal hemorrhoids. Tech Gastrointest Endosc. 2001;3:199–205.
35. Randall GM, Jensen DM, Machicado GA, et al. Prospective randomized comparative study of bipolar versus direct cost electrocoagulation for treatment of bleeding internal hemorrhoids. Gastrointest Endosc. 1994;40:403–10.
36. Jensen DM, Jutabha R, Machicado GA, et al. Prospective randomized comparative study of bipolar electrocoagulation versus heater probe for treatment of chronically bleeding internal hemorrhoids. Gastrointest Endosc. 1997;46:435–43.
37. Pfenninger JL. Modern treatments for internal hemorrhoids. BMJ. 1997;314:1211–2.
38. Su MY, Chin CT, Wu CS, Ho YP, Lien SM, Tung SY, Chen PC. Endoscopic hemorrhoidal ligation of symptomatic internal hemorrhoids. Gastrointest Endosc. 2003;58:871–4.
39. Senagore A, Mazier WT, Luchtefeld MA, et al. Treatment of advanced hemorrhoidal disease: a prospective, randomized comparison of cold scalpel vs contact Nd:YAG laser. Dis Colon Rectum. 1993;36:1042–9.
40. Andrews BJ, Layer OT, Jackson BT, et al. Randomized trial comparing diathermy hemorrhoidectomy with the scissor dissection Milligan-Morgan operation. Dis Colon Rectum. 1993;36:580–3.
41. Hodgson WJ, Morgan J. Ambulatory hemorrhoidectomy with CO2 laser. Dis Colon Rectum. 1995;38:1265–9.
42. Rosen L, Sipe P, Stasik JJ, et al. Outcome of delayed hemorrhage following surgical hemorrhoidectomy. Dis Colon Rectum. 1993;36:743–6.
43. Eu KW, Tech TA, Seow-Choen F, et al. Anal stricture following haemorrhoidectomy: early diagnosis and treatment. Aust N Z J Surg. 1995;65:101–3.

44. Parickh SR, Molinelli B, Dailey TH. Liver abscess after hemorrhoidectomy. Report of two cases. Dis Colon Rectum. 1994;37:185–9.
45. Shanmugan V, Thaha MA, Rabindranath KS, Campbell KL, Steale RJ, Loudon MA. Systematic review of randomized trials comparing rubber band ligation with excisional hemorrhoidectomy. Br J Surg. 2005;92:1481–7.
46. Zuckerman GR, Prakash C. Acute lower intestinal bleeding. Gastrointest Endosc. 1999;49:228–38.
47. Gralnek IM, Jensen DM. An assortment of colonic lesions that present with severe hematochezia. Tech Gastrointest Endosc. 2001;3:216–20.
48. Madigan MR, Morson BC. Solitary ulcer of the rectum. Gut. 1969;10:871–81.
49. Tjandra JT, Fazio VW, Church JM, et al. Clinical conundrum of solitary rectal ulcer. Dis Colon Rectum. 1992;35:227–34.
50. Sharara AI, Azar C, Amr SS, et al. Solitary rectal ulcer syndrome: endoscopic spectrum and review of the literature. Gastrointest Endosc. 2005;62:755–62.
51. Kanwal F, Jutabha R, Dulai D, Jensen DM. Major stigmata of hemorrhage on rectal ulcers and outcomes in patients with severe hematochezia. Gastrointest Endosc. 2003;57:462–8.
52. Jensen DM, Kovacs TOG, Jutabha R, Ohning GV, Dulai GS, Machicado GA. Rectal ulcers causing severe hematochezia: update on diagnosis, hemostasis, healing, and outcomes. Gastrointest Endosc. 2007;65:AB258:T1434.
53. Niv Y, Bat L. Solitary ulcer syndrome: clinical endoscopic and histopathological spectrum. Am J Gastroenterol. 1986;81:486–91.
54. Levine DS. “solitary” rectal ulcer syndrome. Gastroenterology. 1987;92:243–53.
55. Mönkemüller K, Peter S, Toshniwal J, Popa D, Zabielski M, Stahl RD, Ramesh J, Wilcox CM. Multipurpose use of the ‘bear claw’ (over-the-scope-clip system) to treat endoluminal gastrointestinal disorders. Dig Endosc. 2014;26:350–7.
56. Rex DK, Lewis BL, Waye JD. Colonoscopy and endoscopic therapy for delayed post-polypectomy hemorrhage. Gastrointest Endosc. 1992;38:127–9.
57. Ohning GV, Ghassemi KA, Jensen DM, Kovacs TOG, Machicado GA, Dulai GS, Jutabha R. Doppler ultrasound probe (DUP) detection of arterial blood flow in severe delayed post-polypectomy induced ulcer hemorrhage (PPIUH): relationship to stigmata & implications for primary prevention. Gastrointest Endosc. 2013;77:AB162.
58. Yousfi M, Gostout CJ, Baron TH, et al. Postpolypectomy lower gastrointestinal bleeding: potential role of aspirin. Am J Gastroenterol. 2004;99:1785–9.
59. Hui AJ, Wong RM, Ching JY, et al. Risk of colonoscopic polypectomy bleeding with anti-coagulants and antiplatelet agents: analysis of 1657 cases. Gastrointest Endosc. 2004;59:44–8.
60. Machicado GA, Jensen DM. Bleeding colonic angiomas and radiation telangiectasias: endoscopic diagnosis and treatment. Tech Gastrointest Endosc. 2001;3:185–91.
61. Schmulewitz N, Fisher DA, Rockey DC. Early colonoscopy for acute lower GI bleeding predicts shorter hospital stay: a retrospective study of experience in a single center. Gastrointest Endosc. 2003;58:841–6.
62. Strate LL, Orav EJ, Syngal S. Early predictors of severity in acute lower intestinal tract bleeding. Arch Intern Med. 2003;163:838–43.

Endotherapy of Leaks and Fistula

24

V.K. Rai, Usha Goenka, and M.K. Goenka

Introduction

Gastrointestinal leaks and fistula involve the disruption of the gastrointestinal wall. The gastrointestinal fistula was first reported in the 1800s, and despite significant advances, the management of gastrointestinal fistula remains a challenge. Historically, the majority of fistulae result from surgical procedures, and the surgeon often makes the initial diagnosis. However, with the advancement in endoscopic procedures and introduction of new invasive techniques in gastroenterology such as endoscopic submucosal dissection, endoscopic mucosal resection, endoscopic necrosectomy, and cyst drainage, many cases of leaks and fistulae are now encountered by gastroenterologists. Surgery has traditionally been the primary option for the management of gastrointestinal fistulae and was associated with high morbidity and mortality [1]. Recently, endoscopic therapy along with interventional radiology has taken a prominent role in the management of these complicated cases. With the improvement in flexible endoscopic technology and development of new endoscopic devices, endoscopists are expanding their role in the management of gastrointestinal fistulae. Endoscopically deployable stents, endoscopic suturing devices, through-the-scope (TTS) and over-the-scope (OTS) clips, sealants, fistula plugs, and vacuum sponges are among the few technologies that are currently being used to treat fistulae. These therapies spare many patients going for surgical repair of these defects. The optimum management of leaks and fistula usually requires a multidisciplinary approach. In this chapter, the emerging role of endoscopy in the management of gastrointestinal fistulae has been discussed.

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Definition and Classification

Fistulae are broadly classified into internal and external fistulae. Internal fistulae have communication between the gastrointestinal epithelium and the peritoneal space, retroperitoneal space, thorax, or another internal area, whereas external fistulae have communication between the gastrointestinal epithelium and skin [2]. Fistulae are also classified based on etiology, anatomy, and fluid output (low output is <500 mL/day, and high output is >500 mL/day) [3]. Although the terminology of perforation, fistula, and leaks appears similar, all these terms are fundamentally different. Perforation refers to the acute full-thickness defect in the gastrointestinal tract, whereas leaks are defined as the disruption of surgical anastomosis leading to fluid collection [4]. The term fistula usually means an abnormal communication between two epithelialized surfaces [4]. Table 24.1 enumerates the various causes of gastrointestinal leaks and fistulae [5–10].

Gastrointestinal Perforations

Gastrointestinal perforation is a medical emergency, and the success of its treatment depends on its early diagnosis and triage of the patient to endoscopic or surgical management. The initial crucial steps in its medical management include proper positioning of the patient to reduce

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Table 24.1 Etiology of gastrointestinal leaks and fistula

Diagnostic endoscopy, colonoscopy, and ERCP procedures having high risk of leaks and fistula
Dilatation: bougie, balloon achalasia polypectomy/EMR/ESD ampullectomy
Appendicular abscess and pancreatic necrosis drainage, POEM
Postsurgical anastomotic dehiscence, Boerhaave's syndrome
Diverticulitis
PEG and feeding tubes, foreign body and trauma

EMR endoscopic mucosal resection, *ESD* endoscopic submucosal dissection, *POEM* peroral endoscopic myotomy, *PEG* percutaneous endoscopic gastrotomy, *ERCP* endoscopic retrograde cholangiopancreaticography

intraluminal content leakage and contamination, initiation of parenteral broad-spectrum antibiotics, and intensive cardiopulmonary monitoring [11]. In case a perforation is detected during an endoscopic procedure, efforts should be made for its immediate endoscopic closure. Careful endoscopic assessment of the defect before an intervention is vital in determining the feasibility of endoscopic closure. Insufflation of carbon dioxide instead of room air during endotherapy is essential as carbon dioxide gets absorbed quickly. This will avoid further expansion of perforation and minimize peritonitis. The endoscopist should also assess the size, the edge of the defect, and any potential source of bleeding. Moreover, the endoscopic closure can be achieved by using various methods and devices, and the corresponding endoscopic techniques vary depending on the location, size of the defect, and timing of recognition. In most cases, surgical intervention is required for a failed endoscopic closure of a perforation. In addition, asymptomatic perforations that have been recognized 24 h or more after the procedure can be managed conservatively. The serious consequences of gastrointestinal tract perforations include abdominal compartment syndrome, severe subcutaneous emphysema, tension pneumothorax, tension pneumoperitoneum, and peritonitis. Tension pneumothorax and tension pneumoperitoneum can be managed by immediate needle decompression. It is well known that extraluminal air does not mean that surgery is needed, especially when carbon dioxide is used, and the volume of extraluminal air is usually not proportional to the size of the gastrointestinal perforation. Subcutaneous emphysema may require emergency endotracheal intubation to prevent airway obstruction. Peritonitis requires an emergency surgical evaluation for possible lavage and closure. Radiologic examinations should be performed so as to confirm perforation closure after endotherapy. Contrast studies with water-soluble agents are useful, but computed tomography (CT) not only confirms the leak but can also detect extraluminal air, fluid collections, and other complications. Hence, a CT scan is preferred in most cases for confirming perforation closure.

Practical Considerations

- Gastrointestinal perforation is a medical emergency.
- Perforation that is detected during an endoscopic procedure requires an immediate endoscopic closure.
- Insufflation of carbon dioxide instead of room air is essential as carbon dioxide gets absorbed quickly.
- Asymptomatic perforations recognized 24 h or less after the procedure can be managed conservatively.
- Extraluminal air does not mean an immediate surgery especially when carbon dioxide is used.
- CT scan is preferred as it not only confirms the leak but can also detect extraluminal air, fluid collections, and other complications.

Gastrointestinal Leaks and Fistulae

Inflammatory or malignant processes can cause an acute and chronic fistula, but one of its commonest causes is an anastomotic leak after gastrointestinal surgery. Leaks are responsible for significant morbidity and high mortality, especially when the treatment is delayed [12]. Early presentation of leaks of gastrointestinal tract includes features of systemic inflammatory response syndrome and can have a septic shock in a short time [13]. Upper gastrointestinal radiography with water-soluble contrast (e.g., Gastrografin) or preferably a CT scan can confirm the leakage. Endoscopy allows visualization of the lumen defect and its size and can help in choosing the appropriate endoscopic modality. The location of the fistula orifice should be marked by injecting methylene blue through an external catheter for accurate localization of orifice at the time of endotherapy.

The most appropriate treatment for gastrointestinal leaks remains controversial. Some authors suggest aggressive therapy with surgical reoperation or endotherapy, while others recommend conservative treatment. However, the conservative therapy is associated with a prolonged hospital stay, increased costs, and a mortality rate of up to 60% [13]. The current established endoscopic management of leaks and fistulae includes metal stent placement, endoclipping, application of tissue sealants, and suturing devices. There are certain guiding principles for the proper use of these techniques; tissue sealants and clip application are considered for small defects, while endoscopic stent placement should be used for defects involving 30–70% of the lumen circumference. Large defects should ideally be treated surgically.

Practical Considerations

- Gastrointestinal surgery is the most common cause for fistula.
- Fistula orifice should be marked by injecting methylene blue through an external catheter for accurate localization of the orifice at the time of endotherapy.
- The current established endoscopic treatment of leaks and fistulae includes metal stent placement, endoclipping, application of tissue sealants, and suturing devices.
- Tissue sealants and clip application are considered for small defects, while endoscopic stent placement should be used for defects involving 30–70% of the lumen circumference. Large defects require surgery.

Approach to Management

The aim of endoscopic therapy is to provide a barricade to the flow of luminal contents across the defect by applying various devices like stents, clips, etc. Table 24.2 lists the various techniques used for endotherapy of leaks and fistulae. Regardless of the techniques used, there are a few guiding principles in the management of leaks and fistula that are applicable to all patients. Almost all patients require multidisciplinary involvement with a team dealing in endoscopy, surgery, interventional radiology, critical care, and nutrition. In addition, the definition and delineation of the site of the leak are also critical. This is often done by contrast radiology studies or endoscopy tattooing by methylene blue or India ink. If a fluid collection or cavity exists, drainage by large-bore percutaneous catheter before endoscopic closure should be considered to prevent sepsis. The careful evaluation of the state of the tissue surrounding the leak/fistula helps in choosing modalities of endoscopic technique and associated accessories for the approximation of edges. In most cases, a combination of different techniques is required for successful closure of leaks and fistulae. For example, an esophagogastric fistula may be best managed with fibrin glue injection and endoscopic clip closure, followed by esophageal stent placement over the fistula site to divert the luminal stream. The adequacy of the closure should be studied ideally at the time of the procedure, after the closure, and during follow-up to confirm continued integrity. This can be accomplished by oral water-soluble contrast radiography or CT scan as well as by clinically measuring the percutaneous drain output over time.

Table 24.2 Techniques for endotherapy of gastrointestinal leaks/fistula

Diversion
Enteral covered stents
Closure
Endoclips: through the scope (TTS) and Ovesco endoscopic suture
Sealant: fibrin, cyanoacrylate glue

Practical Considerations

- All patients require multidisciplinary involvement.
- Delineation of the site of the leak is important by contrast radiology studies or endoscopic tattooing by methylene blue or India ink.
- If a fluid collection or cavity exists, drainage by large-bore percutaneous catheter before endoscopic closure should be considered to prevent sepsis.

Through-the-Scope Clips

Endoclips, which are more popular for controlling gastrointestinal bleeding, can also be used for closing the gastrointestinal wall defect [14]. Endoclips can either be TTS clips, where the clips are on an applicator and introduced through the biopsy channel of the endoscope, or the recently available OTS clips, which are mounted on a cap fixed to the scope tip similar to variceal band ligator device. The TTS clips and their delivery systems are available from different manufacturers and differ in their size and mechanical properties. The most commonly used TTS clips are Quick clip (Olympus, America Inc., Center Valley, PA, United States), Instinct clip (Cook Medical Inc., Bloomington, IN, United States), and Resolution clip (Boston Scientific Inc., Natick, United States). The clips with rotatable and reopenable properties are particularly useful in disrupted tissue for precise application of clips. Although TTS clips have been used for luminal defects <2 cm in size, this technique is less effective for defects >1 cm, and thus, a combined technique using an endoloop and TTS clips or omental patching with TTS clip or OTS clips is more preferred. The application of the clip is difficult in inflamed or indurated tissue, which is often noted in chronic defects. Therefore, the suction or abrasion of edges with argon plasma coagulation is useful before clip deployment so that the edges of the defect are approximated securely.

TTS clips have been used to close fistula and leaks located in the esophagus, stomach, as well as colon [15, 16]. Most of these studies involve a small number of patients, and large series have been reported for the results of clips to close the leaks following endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR). Minami et al., in a series of 117 patients with gastric leak following EMR, showed a success rate of 98.3% with TTS clips [17]. Jeon et al. also reported the successful management of 39

patients with perforations following ESD by using endoclips [18]. The overall success rate is higher for esophagus and stomach and somewhat moderate for colonic leaks probably due to the ease of applicability of clips in the former location [18]. Thus, clips should be preferred over stents if the leak is located in proximal or distal esophagus as well as stomach [19].

Practical Considerations

- TTS clips have been used for luminal defects <2 cm in size; this technique is less effective for defects >1 cm.
- Clips should be preferred over stents if the leak is located in proximal or distal esophagus as well as stomach.

Over-the-Scope Clips

The OTS clips can close the full thickness of open defects of up to 2–3 cm. The design of the device is fundamentally different from that of the TTS clips. The advantage of OTS over TTS clips is their ability to close chronic leaks and fistulae even in the case of inflamed or fibrotic tissue surrounding the defect. This is possible due to the greater compressive strength and tissue capture of the OTS devices [20, 21]. Two commercially available OTS clip systems are the Ovesco clip (Ovesco Endoscopy AG, Tübingen, Germany) and the Padlock clip (Aponos Medical Corp., Kingston, New Hampshire). The OTS clip system comprises a transparent applicator cap with a mounted OTS clip, thread, thread retriever, and a hand wheel for clip release. The transparent applicator cap is mounted on the tip of the endoscope with the clip in a bent shape. The clip is made of a biocompatible material, Nitinol, which has shape memory and can regain its original shape after deployment. The caps are available in three different sizes according to the size of the commercially available endoscopes: 11 mm, 12 mm, and 14 mm. The clips are also available in three sizes adapted to the cap sizes. Anchor and twin graspers are sometimes used for larger and chronic defects, where the anchor can pull the defective mucosa into the OTS cylinder while the twin grasper reduces the gap of the defect. However, one should be careful to avoid capturing twin grasper or anchor while releasing the clip. A duodenal fistula closed by OTS is shown in Fig. 24.1. Voermans et al. reported a success rate of 89% with OTS clips in 36 patients with iatrogenic perforations (esophageal, 5; gastric, 6; duodenal, 12; colonic, 13) [16]. A large multicenter retrospective study by Chavez et al. involved 188 patients with gastrointestinal leaks and fistula treated with OTS clips [22]. OTS was used as primary treatment in 97 patients and as rescue therapy in 64 patients. The success rate was 75% in the first group and 47% in the second group. The result was better for perforation (95%) and leaks (80%) compared to fistula (45%), probably due to less fibrotic edges in perforation [22]. In addition, there is no reported risk of peritoneal dissemination or tumor recurrence after the usage of endoclips for perforations following ESD or EMR performed for early cancers.

Practical Considerations

- The advantage of OTS over TTS clips is their ability to close chronic leaks and fistulae even in case of inflamed or fibrotic tissue surrounding the defect.

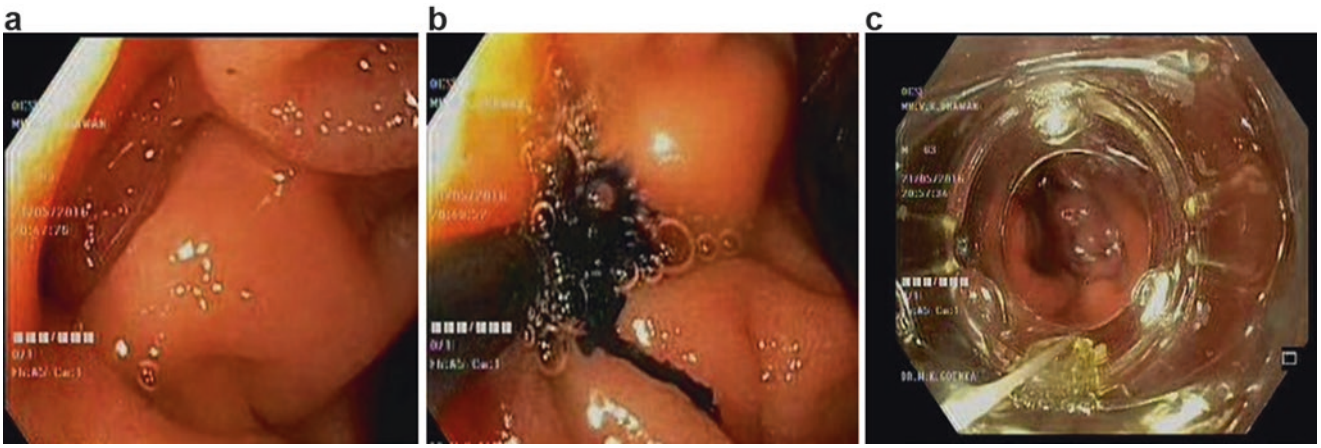

Fig. 24.1 Duodenal fistula closure by over-the-scope clip (OTS). (**a**) Endoscopic appearance of duodenal fistula; (**b**) fistula site marked by India ink; (**c**) OTS closed the fistula

Endoscopic Suturing System

Endoscopic suturing techniques allow for the closing of larger defects. The OverStitch Endoscopic Suturing System (Apollo Endosurgery, Austin, Tex) has been approved for clinical use [23]. This device requires a double-channel therapeutic endoscope and consists of three main components: the end cap, the needle driver handle, and an anchor exchange catheter. The end cap is mounted on the distal tip of the endoscope just as the OTS clip. The OverStitch Endoscopic Suturing System can apply both interrupted and continuous stitches without having to remove the device [24].

Endoscopic suturing can be used to close both acute perforations and chronic fistulae. Two studies have demonstrated a high rate of primary closure of gastro-gastric fistulae after bariatric surgery [25, 26]. However, the long-term results of large (> 2 cm) chronic fistula closure with this technique are not satisfactory. The tissue must be sufficiently healthy and strong to hold the sutures and not tear or incise when the sutures are cinched, and the tissue is pulled for apposition.

The currently available systems have evolved greatly during the past decade, but further refinement is necessary to improve the technical feasibility of the procedure for most therapeutic endoscopists and to allow for the greater application of use.

Practical Considerations

- The suturing system requires a double-channel therapeutic endoscope and consists of three main components: the end cap, the needle driver handle, and an anchor exchange catheter.

Self-Expanding Metal and Plastic Stents

The fundamental role of the stent in the management of gastrointestinal leaks and fistula is to cover the region of leakage so that gastrointestinal secretions and food particles could be diverted away from the point of defects, leading to the natural healing of the defects. Therefore, covered stents are used for endotherapy of leaks and fistula. However, the major limitation with covered stents is their tendency for migration, which occurs in at least 25% of patients [27, 28]. The increased motility of the lower gastrointestinal tract may cause easy stent migration both distally and proximally. Therefore, the stents are usually used for the closure of leaks and fistula only in the upper gastrointestinal tract. Moreover, stent placement is usually performed over a wire under fluoroscopic guidance. This can be particularly difficult in the left colon. The major advantage of stent placement is the immediate control of leaks and allowing early enteral feeding. Postoperative leaks after esophagectomy and gastrectomy occur in approximately 7–8% of cases when performed for the treatment of esophageal or gastric cancer [29]. Leak rates after bariatric surgical procedures appear to be less and reported up to 5.2% of patients undergoing Roux-en-Y bypass and 2.4% after sleeve gastrectomy [30]. Langer et al. first described their experience by using the Polyflex SEPS (Boston Scientific Inc., Marlborough, MA) for patients with leaks after esophagectomy [31]. However, this technique did not become popular because of the difficulty in its deployment due to the need for pre-deployment assembly, stiffness of the stent, and large-sized delivery catheter. To circumvent these issues, partially covered self-expanding metal stents (PCSEMS) were introduced, but they also had shortcomings of difficult subsequent stent removal because of growth of tissue at the proximal and distal uncovered portions. In a series of 56 patients reported by Bakken et al., 22 had an esophageal FCSEMS inserted for a leak/fistula [32]. The stent migration rate was 28%, but all of the stents were successfully retrieved. Seven of the 22 patients (32%) showed initial improvement in their leak. The closure of esophageal fistula by the fully covered metal stent is shown in Fig. 24.2.

A recent study identified four factors that significantly reduced the effectiveness of therapy [33]: (1) leak located in the proximal esophagus, (2) esophageal injury longer than 6 cm, (3) stent traversing gastroesophageal junction, and (4) anastomotic leak associated with a more distal leak. The optimal diameter of the stent depends on the localization of gastrointestinal disruption. Generally, the stents for cervical leaks should have a smaller diameter (18–23 mm) than those for postgastrectomy leaks (21–25 mm) to avoid excessive tracheal compression and foreign body sensation. The stents should be removed within 6–8 weeks when healing of the disruption is confirmed by water-soluble contrast examination, endoscopy, and resolution of clinical symptoms.

Practical Considerations

- Covered stents are used for endotherapy of leaks and fistula.
- The major limitation with covered stents is their tendency for migration.

Tissue Sealants

Tissue sealants have been used for more than 20 years with good results for gastrointestinal disruptions. The most commonly used tissue sealants are biologic (fibrin) glue and cyanoacrylate [34, 35]. The sites of application mostly include

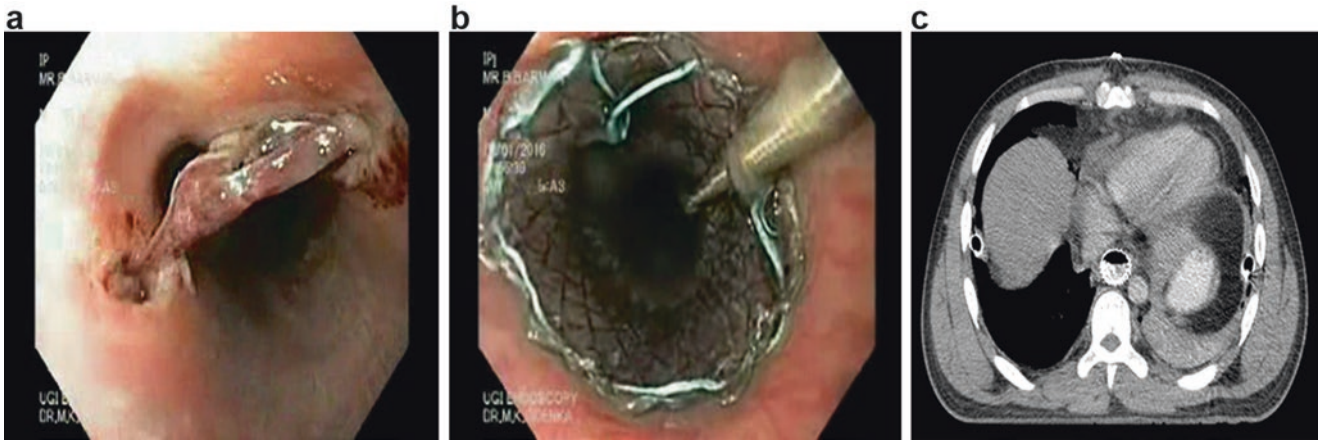

Fig. 24.2 Esophageal traumatic fistula. (**a**) Endoscopic image of two esophageal fistulae. (**b**) Fistulous opening closed by fully covered metal stents. (**c**) CT image showing fistulae closed by stent

endoscopically accessible areas of post-anastomotic leakage or after bariatric surgical procedures. Typically, the mucosa around the opening of the fistula is de-epithelialized with the aim of development of reactive inflammatory response around the opening, leading to complete sealing. The application of the tissue sealant should be performed with a double-lumen catheter inserted down the working channel of the endoscope [33, 34]. Once applied, the cyanoacrylate polymerizes after contact with moisture, causing tissue necrosis and an inflammatory response. Glue has antibacterial properties, so it can also be applied to an infected site. High-output gastrointestinal fistulae are less likely to successfully close with the use of tissue sealant alone, and thus, a combination therapy using clips or covered stents is usually required. For larger openings, it has been observed that the filling of gaps with Vicryl mesh plugs or soft tissue grafting material such as Surgisis (Cook Inc., West Lafayette, IN) before glue injection has better long-term success [36]. For upper gastrointestinal fistulae with a large diameter, Böhm et al. reported promising results by combining Vicryl mesh and fibrin glue [37].

Practical Considerations

- Glue has antibacterial properties, so it can also be applied to an infected site.

Other Techniques

The Amplatzer Septal Occluder (AGA Medical Group, Plymouth, MN) has been developed for the closure of atrial septal defects but has also been used off-label to close gastrointestinal fistulae [38]. Gastric leaks and esophagotracheal fistulae have been successfully closed with this cardiac septal defect occluder. The device consists of two self-expandable disks made of Nitinol® mesh covered by polyester fabric, connected by a short waist that has various diameters.

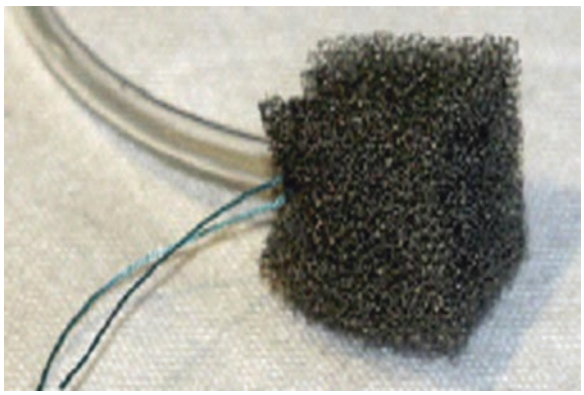

Fig. 24.3 Vacuum-assisted device

Endoscopic vacuum-assisted closure (EVAC) by Endo-Sponge (Fig. 24.3) is a minimally invasive method to treat anastomotic leakage following rectal surgery [39]. The sponge allows a gentle, continuous suction over all tissues in contact with the sponge surface and provides drainage with a gradual reduction in the size of the wound cavity [40]. Table 24.3 summarizes the success rates of different commonly used techniques.

Conclusion

The appropriate management of patients with gastrointestinal leaks, fistulae, and perforations requires multidisciplinary coordination among the gastroenterologist, surgeon, and radi-

Table 24.3 Summary of studies on outcome of endoscopic technique of leaks and fistulae

Ref.	Modality used	Technical success (%)	Complication (%)
Freeman et al. [27]	SEPS	100	24
Van Heel et al. [41]	SEMS/SEPS	100	33
Schimdt et al. [42]	SEMS/CLIPS	100	NA
D'Cunha et al. [43]	SEMS/CLIPS	95	13
Biancari et al. [44]	Stents + clips	100	25
Schweigert et al. [45]	SEMS/SEPS	100	85
Heits et al. [46]	Vacuum therapy	100	20
Biancari et al. [47]	SEMS/clips	100	34

NA not available, *OTSC* over-the-scope clip, *SEMS* self-expandable metal stent, *SEPS* self-expandable plastic stent

ologist. The increasing number of complex endoscopic procedures with a high risk of perforation and the increasing incidence of leakage associated with bariatric operations necessitate minimally invasive treatment of these complications. TTS, endoscopic suturing devices, stents, sealants, fistula plugs, vacuum-assisted devices, and OTS have been shown to be effective modalities. The treatment of acute small-size defects is more effective than the treatment of chronic and large defects. Hybrid therapy with a combination of surgery and endoscopic techniques is also a promising technique.

References

1. Schecter WP, Hirshberg A, Chang DS, et al. Enteric fistulas: principles of management. J Am Coll Surg. 2009;209(4):484–91.
2. Falconi M, Pederzoli P. The relevance of gastrointestinal fistulae in clinical practice: a review. Gut. 2001;49(suppl 4):iv2.
3. González-Pinto I, González EM. Optimising the treatment of upper gastrointestinal fistulae. Gut. 2001;49(suppl 4):iv21.
4. Kumar N, Thompson CC. Endoscopic therapy for postoperative leaks and fistulae. Gastrointest Endosc Clin N Am. 2013;23:123–36.
5. Baron TH, Gostout CJ, Herman L. Hemoclip repair of a sphincterotomy-induced duodenal perforation. Gastrointest Endosc. 2000;52:566–8. [PMID: 11023583].
6. Kim HS, Lee DK, Jeong YS, Kim KH, Baik SK, Kwon SO, Cho MY. Successful endoscopic management of a perforated gastric dysplastic lesion after endoscopic mucosal resection. Gastrointest Endosc. 2000;51:613–5. [PMID: 10805857].
7. Rosés LL, Ramirez AG, Seco AL, Blanco ES, Alonso DI, Avila S, Lopez BU. Clip closure of a duodenal perforation secondary to a biliary stent. Gastrointest Endosc. 2000;51:487–9. [PMID: 10744829].
8. Cipolletta L, Bianco MA, Rotondano G, Marmo R, Piscopo R, Meucci C. Endoscopic clipping of perforation following pneumatic dilation of esophagojejunal anastomotic strictures. Endoscopy. 2000;32:720–2. [PMID: 10989998].
9. Jacobson BC, Briggs DR, Carr-Locke DL. Endoscopic closure of a colovesical fistula. Gastrointest Endosc. 2001;54:248–50. [PMID: 11474404].
10. Van Bodegraven AA, Kuipers EJ, Bonenkamp HJ, Meuwissen SG. Esophagopleural fistula treated endoscopically with argon beam electrocoagulation and clips. Gastrointest Endosc. 1999;50:407–9. [PMID: 10462666].
11. Paspatis GA, Dumonceau JM, Barthet M, Meisner S, Repici A, Saunders BP, Vezakis A, Gonzalez JM, Turino SY, Tsiamoulos ZP, Fockens P, Hassan C. Diagnosis and management of iatrogenic endoscopic perforations: European Society of Gastrointestinal Endoscopy (ESGE) position statement. Endoscopy. 2014;46:693–711. [PMID: 25046348].
12. Abou Rached A, Basile M, El Masri H. Gastric leaks post sleeve gastrectomy: review of its prevention and management. World J Gastroenterol. 2014;20:13904–10.
13. Csendes RS, Burdiles P, Burgos AM, Maluenda F, Diaz JC. Conservative management of anastomotic leaks after 557 open gastric bypass. Obes Surg. 2005;15:1252–6.
14. Gevers AM, De Goede E, Simoens M, Hiele M, Rutgeerts P. A randomized trial comparing injection therapy with hemoclip and with injection combined with hemoclip for bleeding ulcers. Gastrointest Endosc. 2002;55(4):466–9.
15. Binmoeller KF, Grimm H, Soehendra N. Endoscopic closure of a perforation using metallic clips after snare excision of a gastric leiomyoma. Gastrointest Endosc. 1993;39:172–4. [PMID: 8495838].
16. Voermans RP, Le Moine O, von Renteln D, Ponchon T, Giovannini M, Bruno M, Weusten B, Seewald S, Costamagna G, Deprez P, Fockens P. Efficacy of endoscopic closure of acute perforations of the gastrointestinal tract. Clin Gastroenterol Hepatol. 2012;10:603–608. [PMID: 22361277]. https://doi.org/10.1016/j.cgh.2012.02.005.
17. Minami S, Gotoda T, Ono H, Oda I, Hamanaka H. Complete endoscopic closure of gastric perforation induced by endoscopic resection of early gastric cancer using endoclips can prevent surgery (with video). Gastrointest Endosc. 2006;63:596–601. [PMID:16564858].
18. Jeon SW, Jung MK, Kim SK, Cho KB, Park KS, Park CK, Kwon JG, Jung JT, Kim EY, Kim TN, Jang BI, Yang CH. Clinical outcomes for perforations during endoscopic submucosal dissection in patients with gastric lesions. Surg Endosc. 2010;24:911–916. [PMID: 19789921]. https://doi.org/10.1007/s00464-009-0693-y.
19. Fischer A, Schrag HJ, Goos M, von Dobschuetz E, Hopt UT. Nonoperative treatment of four esophageal perforations with hemostatic clips. Dis Esophagus. 2007;20:444–8. [PMID: 17760660].
20. Surace M, Mercky P, Demarquay JF, et al. Endoscopic management of GI fistulae with the over-the-scope clip system (with video). Gastrointest Endosc. 2011;74(6):1416–9.
21. Von Renteln D, Denzer UW, Schachschal G, Anders M, Groth S, Rösch T. Endoscopic closure of GI fistulae by using an over-the-scope clip (with videos). Gastrointest Endosc. 2010;72(6):1289–96.
22. Chavez YH, Kratt T, Law JK, Arezzo A, Sharaiha RZ, Poley JW, Kahaleh M, Thompson CC, Ryan MB, Choksi N, Elmunzer BJ, Gosain S, Goldberg EM, Modayil RJ, Stavropoulos S, Schembre D, Dimaio CJ, Chandrasekhara V, Hasan M, Varadarajulu S, Hawes R, Gomez V, Woodward TA, Cohen SR, Fluxa F, Vleggaar FP, Raju GS, Khashab M. A large international multicenter experience with an over-the- scope clipping device for endoscopic Management of Gastrointestinal Perforations, fistulae, and leaks in 188 patients. Gastrointest Endosc. 2013;77:AB148.
23. Watson RR, Thompson CC. Applications of a novel endoscopic suturing device in the GI tract [abstract]. Gastrointest Endosc. 2011;73(4):AB105.
24. Bonin EA, Wong Kee Song LM, Gostout ZS, Bingener J, Gostout CJ. Closure of a persistent esophagopleural fistula assisted by a novel endoscopic suturing system. Endoscopy. 2012;44(Suppl 2 UCTN):E8–E9. [PMID: 22396292]. https://doi.org/10.1055/s-0031-1291494.
25. Fernandez-Esparrach G, Lautz DB, Thompson CC. Endoscopic repair of gastrogastric fistula after roux-en-Y gastric bypass: a less-invasive approach. Surg Obes Relat Dis. 2010;6(3):282–8.
26. Kantsevoy SV, Thuluvath PJ. Successful closure of a chronic refractory gastrocutaneous fistula with a new endoscopic suturing device (with video). Gastrointest Endosc. 2012;75:688–690. [PMID: 21762902]. https://doi.org/10.1016/j.gie.2011.04.031.

27. Freeman RK, Ascioti AJ, Wozniak TC. Postoperative esophageal leak management with the Polyflex esophageal stent. J Thorac Cardiovasc Surg. 2007;133:333–8.
28. Eloubeidi MA, Talreja JP, Lopes TL, et al. Success and complications associated with placement of fully-covered removable self-expandable metal stents for benign esophageal diseases. Gastrointest Endosc. 2011;73:673–81.
29. Lang H, Piso P, Stukenborg C, et al. Management and results of proximal anastomotic leak in a series of 1114 total gastrectomies for gastric cancer. Eur J Surg Oncol. 2000;26:168–71.
30. Morales MP, Miedema BW, Scott JS, et al. Management of postsurgical leaks in the bariatric patient. Gastrointest Endosc Clin N Am. 2011;21:295–304.
31. Langer FB, Wenzl E, Prager G, et al. Management of postoperative esophageal leaks with the Polyflex self-expanding covered plastic stent. Ann Thorac Surg. 2005;79:398–403.
32. Bakken JC, Wong Kee Song LM, de Groen PC, et al. Use of a fully covered self-expandable metal stent for the treatment of benign esophageal diseases. Gastrointest Endosc. 2010;72:712–20.
33. El Hajj II, Imperiale TF, Rex DK, et al. Treatment of esophageal leaks, fistulae, and perforations with temporary stents: evaluation of efficacy, adverse events, and factors associate with successful outcomes. Gastrointest Endosc. 2014;79:589–98.
34. Rábago LR, Ventosa N, Castro JL, Marco J, Herrera N, Gea F. Endoscopic treatment of postoperative fistulas resistant to conservative management using biological fibrin glue. Endoscopy. 2002;34:632–8. [PMID: 12173084]
35. Pramateftakis MG, Vrakas G, Kanellos I, Mantzoros I, Angelopoulos S, Eleftheriades E, Lazarides C. Endoscopicapplication of n-butyl-2-cyanoacrylate on esophagojejunal anastomotic leak: a case report. J Med Case Rep. 2011;5:96. [PMID:21392389]. https://doi.org/10.1186/1752-1947-5-96.
36. Tringali A, Daniel FB, Familiari P, et al. Endoscopic treatment of recalcitrant esophageal fistula with new tools: stents, Surgisis and nitinol staples. Gastrointest Endosc. 2010;72:647–50.
37. Bohm G, Mossdorf A, Klink C, et al. Treatment algorithm for postoperative upper gastrointestinal fistulas and leaks using combined vicryl plug and fibrin glue. Endoscopy. 2010;42:599–602.
38. Repici A, Presbitero P, Carlino A, Strangio G, Rando G, Pagano N, Romeo F, Rosati R. First human case of esophagus-tracheal fistula closure by using a cardiac septal occluder (with video). Gastrointest Endosc. 2010;71:867–869. [PMID: 20185124]. https://doi.org/10.1016/j.gie.2009.08.036.
39. Holle G, Riedel K, von Gregory H, Gazyakan E, Raab N, Germann G. Vacuum-assisted closure therapy. Current status and basic research [in German]. Unfallchirurg. 2007;110(6):490–504.
40. Weidenhagen R, Gruetzner KU, Wiecken T, Spelsberg F, Jauch KW. Endoscopic vacuum-assisted closure of anastomotic leakage following anterior resection of the rectum: a new method. Surg Endosc. 2008;22(8):1818–25.
41. Van Heel NC, Haringsma J, Spaander MC, Bruno MJ, Kuipers EJ. Short-term esophageal stenting in the management of benign perforations. Am J Gastroenterol. 2010;105:1515–1520. [PMID: 20234349]. https://doi.org/10.1038/ajg.2010.104.
42. Schmidt SC, Strauch S, Rösch T, Veltzke-Schlieker W, Jonas S, Pratschke J, Weidemann H, Neuhaus P, Schumacher G. Management of esophageal perforations. Surg Endosc. 2010;24:2809–2813. [PMID: 20428896]. https://doi.org/10.1007/s00464-010-1054-6.
43. D'Cunha J, Rueth NM, Groth SS, Maddaus MA, Andrade RS. Esophageal stents for anastomotic leaks and perforations. J Thorac Cardiovasc Surg. 2011;142:39–46.e1. [PMID: 21683837]. https://doi.org/10.1016/j.jtcvs.2011.04.027.
44. Biancari F, Gudbjartsson T, Mennander A, Hypén L, SalminenP KK, Viktorzon M, Böckelman C, Tarantino E, Tiffet O, Koivukangas V, Søreide JA, Viste A, Bonavina L, Vidarsdottir HH, Saarnio J. Treatment of esophageal perforation in octogenarians: a multicenter study. Dis Esophagus. 2014;27:715–718. [PMID: 24118339]. https://doi.org/10.1111/dote.12148.
45. Schweigert M, Beattie R, Solymosi N, Booth K, Dubecz A, Muir A, Moskorz K, Stadlhuber RJ, Ofner D, McGuigan J, Stein HJ. Endoscopic stent insertion versus primary operative management for spontaneous rupture of the esophagus (Boerhaave syndrome): an international study comparing the outcome. Am Surg. 2013;79:634–40. [PMID: 23711276].
46. Heits N, Stapel L, Reichert B, Schafmayer C, Schniewind B, Becker T, Hampe J, Egberts JH. Endoscopic endoluminal vacuum therapy in esophageal perforation. Ann Thorac Surg. 2014;97:1029–1035. [PMID: 24444874]. https://doi.org/10.1016/j.athoracsur.2013.11.014.
47. Biancari F, Saarnio J, Mennander A, Hypén L, Salminen P, Kuttila K, Victorzon M, Böckelman C, Tarantino E, Tiffet O, Koivukangas V, Søreide JA, Viste A, Bonavina L, Vidarsdóttir H, Gudbjartsson T. Outcome of patients with esophageal perforations: a multicenter study. World J Surg. 2014;38:902–909. [PMID: 24174169]. https://doi.org/10.1007/s00268-013-2312-2.

25 The Role of Chromoendoscopy and Enhanced Imaging Techniques in Inflammatory Bowel Disease Colorectal Cancer Colonoscopy Surveillance

Rotimi Ayoola, Monica Mohanty, Jai Eun Lee, and Humberto Sifuentes

Introduction

Patients with a long-standing ulcerative colitis (UC) and extensive Crohn's disease (CD) colitis have an approximately twofold higher risk of developing colorectal cancer [1–4]. Increased duration of disease, greater extent of colonic involvement, concomitant primary sclerosing cholangitis, and an increasing degree of histologic inflammation contribute to the level of colorectal cancer risk [1, 5–8]. Sporadic colorectal cancers develop after the accumulation of key mutations in an adenoma-carcinoma sequence. In inflammatory bowel disease (IBD), colorectal cancers develop in the background of chronic inflammation and regeneration. This chronic inflammation is hypothesized to be the key factor in the pathogenesis of IBD colorectal cancer causing increased oxidative stress; promoting repeated cycles of injury, regeneration, and repair; and finally accelerating the accumulation of key mutations [9]. In comparison to sporadic colorectal cancers, p53 mutations occur in the early stages of IBD-related colon cancer [10]. Long-standing inflammation results in dysplastic colonic tissue that is often multifocal and diffuse and thus difficult to identify by standard means.

A majority of gastrointestinal professional societies have recommended colonoscopy for the surveillance of patients with IBD [11–15]. Despite surveillance, IBD patients with colitis continue to be at risk for colorectal cancer secondary to missed and unrecognized dysplastic lesions at colonoscopy. Recent studies have demonstrated a high number of interval cancers in IBD patients, where colorectal cancers are diagnosed within the period after a screening/surveillance examination and before the date of the next recommended surveillance examination [16]. In a St. Mark's UC surveillance program lasting three decades, colorectal cancers were identified in 12.3% of the 600 patients (74 neoplasms including 30 colorectal cancers). More than 50% of the colorectal cancers were considered to be interval colorectal cancers [17].

In addition to the importance of missed lesions, other factors can play a role in interval cancers in patients with IBD: incompletely resected lesions, more aggressive tumor biology, or noncompliance to surveillance recommendations. Missed lesions are significant as two-thirds of the dysplastic lesions identified in IBD patients on colonoscopy have a non-polypoid (superficial elevated, completely flat, or depressed) shape [18]. The growth pattern of these subtle dysplastic lesions is often multifocal and diffuse, and thus its detection may not be optimal with the use of traditional white light colonoscopy.

Until recently, the random sampling of mucosa throughout the colon has been the primary method of surveillance. This approach to colonoscopy surveillance in IBD has been ineffective, time-consuming, and expensive and has a low diagnostic yield. According to the latest studies, most dysplastic lesions are visible to careful endoscopic inspection [19]. It has now been shown that most IBD-related dysplasia is "visible" by using modern endoscopic examination and the so-called invisible dysplasia is relatively uncommon [20]. This has led to a more focused approach in surveillance colonoscopy, mainly targeted biopsies of any mucosal abnormalities using chromoendoscopy (CE) and other enhanced imaging techniques including high-definition endoscopy, confocal laser endomicroscopy, endocytoscopy, and molecular imaging.

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Practical Considerations

It has now been shown that most IBD-related dysplasia is "visible" by using modern endoscopic examination and the so-called invisible dysplasia is relatively uncommon.

Terminology

The SCENIC consensus statement (endorsed by the American Gastroenterological Association and American Society for Gastrointestinal Endoscopy) on surveillance and management of dysplasia in IBD has been proposed to simplify the current endoscopic classification of dysplastic lesions found in patients with IBD [13, 14]. It has now been determined that the terms dysplasia-associated lesion or mass (DALM), adenoma-like, and non-adenoma-like should be abandoned. Descriptive phrases, modified from the Paris classification, have now been recommended (Table 25.1) [13, 14]. This revised Paris classification should be used to classify lesions as polypoid (pedunculated, sessile) and non-polypoid (superficially elevated, flat, depressed). In addition, it should also be applied to endoscopic features such as location of the lesion within or outside an area of known colitis, borders (distinct or indistinct), and the presence of ulceration within the lesion (Table 25.1). The SCENIC international consensus suggests that the term endoscopically resectable should indicate that (1) distinct margins of the lesion could be identified, (2) the lesion appears to be completely removed on visual inspection after endoscopic resection, (3) histologic examination of the resected specimen is consistent with complete removal, and (4) biopsy specimens taken from mucosa immediately adjacent to the resection site are free of dysplasia on histologic examination [13, 14]. On the other hand, dysplastic lesions that are not endoscopically resectable based on their unfavorable endoscopic features should be referred for surgical management.

Practical Considerations

The term endoscopically resectable should indicate that (1) distinct margins of the lesion could be identified, (2) the lesion appears to be completely removed on visual inspection after endoscopic resection, (3) histologic examination of the resected specimen is consistent with complete removal, and (4) biopsy specimens taken from mucosa immediately adjacent to the resection site are free of dysplasia on histologic examination.

Table 25.1 SCENIC classification for IBD-related dysplasia using modified Paris classification [13, 14]

Term	Definition
Visible dysplasia	Dysplasia identified on target biopsies from a lesion visualized at colonoscopy
Polypoid	Lesion protruding from the mucosa into the lumen ≥2.5 mm
Pedunculated	Lesion attached to the mucosa by a stalk
Sessile	Lesion not attached to the mucosa by a stalk: entire base is contiguous with the mucosa
Non-polypoid	Lesion with little (< 2.5 mm) or no protrusion above the mucosa
Superficial elevated	Lesion with protrusion <2.5 mm above the lumen (less than the height of the close cup of a biopsy forceps)
Flat	Lesion without protrusion above the mucosa
Depressed	Lesion with at least a portion depressed below the level of the mucosa
General descriptors	
Ulcerated	Ulceration (fibrinous-appearing base with depth) within the lesion
Border	
Distinct border	Lesion's border is discrete and can be distinguished from surrounding mucosa
Indistinct border	Lesion's border is not discrete and cannot be distinguished from surrounding mucosa
Invisible dysplasia	Dysplasia identified on random (nontargeted) biopsies of colon mucosa without a visible lesion

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High-Definition Endoscopy

Over the last 10 years, various advanced endoscopic imaging techniques have been introduced into our endoscopic practice. Most recently, high-definition (HD) endoscopes have been developed that produce signal images with resolutions that range from 850,000 pixels to 2 million pixels with a wider field of vision (170°) [21]. By contrast, standard-definition (SD) endoscopes produce signal images with resolutions of 100,000–400,000 pixels and a field of view of 130° [21]. HD colonoscopies have superior resolution than SD colonoscopies, and this increased resolution likely improves the detection of subtle dysplastic lesions. In patients with IBD, dysplastic lesions develop as flat lesions as opposed to protruding lesions in the intestinal lumen. A recent retrospective study based on 369 patients with long-standing colonic IBD HD colonoscopy detected significantly more adenomas especially within flat or right-sided lesions, as compared to SD colonoscopy [22]. The adjusted prevalence ratio of detecting dysplastic lesions on targeted biopsies was calculated as 2.99 for HD colonoscopy [22]. Additionally, HD colonoscopy does not require additional time or skills (Table 25.2).

Table 25.2 Suggested step for implementation of chromoendoscopy into endoscopic practice

Equipment	
Colonoscope	High-definition colonoscope, monitor, and cables
Accessories	Apply dye via: Water-jet channel by using water pump attached to the endoscope activated via foot pedal or spray catheter: length 240 cm, endoscope accessory channel 2.8 mm
Contrast agent	Indigo carmine, 5-mL ampule (0.8%) Methylene blue, 10-mL ampule (1%)
Procedure and protocol	
Time allotment	Consider doubling colonoscopy time slot initially during the learning curve period
Standard operating procedure	Complete colonoscopy to cecum Lavage with water and suction during intubation
	Prepare dye solution during insertion for application via the foot pump or spray Indigo carmine (0.03%): mix two 5-mL ampules of 0.8% indigo carmine with 250-mL water Methylene blue (0.04%): mix one 10-mL ampule of 1% methylene blue with 240-mL water
	If using a foot pump: once the cecum is intubated, the water irrigation can be exchanged with the contrast solution. Apply the dye solution in a circumferential technique while withdrawing the colonoscope. Direct spray to the antigravity side
	If using a spray catheter: the dye spray catheter is inserted into the biopsy channel; the catheter tip should protrude 2–3 cm from the endoscope. Apply dye solution segmentally by using a rotational technique while withdrawing the colonoscope to cover the surface mucosa with dye
	Suction any excess solution after approximately 1 min to aid mucosal visualization
	Focus on 20–30-cm segments sequentially with reinsertion of the endoscope to the proximal extent of each segment before slow withdrawal and mucosal visualization
	Targeted dye spray for suspicious lesions: Prepare more concentrated dye solution for application Indigo carmine (0.13%): mix one 5-mL ampule of 0.8% indigo carmine with 25-ml water Methylene blue (0.2%): mix one 10-mL ampule of 1% methylene blue with 40-mL water Spray about 30 mL directly from a 60-mL syringe through the biopsy channel
	Remove endoscopically resectable suspicious lesions by using polypectomy or endoscopic mucosal resection
	Do target biopsies of any unresectable abnormality visualized through chromoendoscopy to diagnose dysplasia
	Do biopsies of flat area surrounding lesions to assess for dysplasia
	Consider tattoo of suspicious dysplastic lesions arising from flat mucosa or not amenable to complete removal
	Recommendation regarding the need to perform random, nontargeted biopsies for detection of dysplasia vary
	If biopsies for dysplasia are not done, two random biopsies in every bowel segment are commonly recommended to document microscopic disease activity

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Practical Considerations

HD colonoscopies have superior resolution than SD colonoscopies, and this increased resolution likely improves the detection of subtle dysplastic lesions.

Chromoendoscopy

Chromoendoscopy uses a dye solution of either methylene blue or indigo carmine applied onto colonic mucosa to enhance contrast during surveillance colonoscopy. These dyes enhance lesion detection and discrimination by defining the mucosal surface and light-absorptive patterns. Methylene blue is an absorptive stain that stains the normal absorptive epithelium of the small intestine and colon, and the absence of staining indicates the presence of metaplastic, neoplastic, or inflammatory change. It typically requires 60 seconds before adequate staining is achieved. Indigo carmine, on the other hand, is a contrast stain that is a nonabsorbed dark bluish dye that highlights mucosal pits, grooves, erosions, depressions, and subtle colonic contour irregularities and allows better distinguishing of borders, depth, and surface topography of lesions [23]. Chromoendoscopy is a safe procedure, and the stains are considered nontoxic at the concentrations normally used [24]. Methylene blue may cause a harmless, transient blue-green discoloration of the urine and feces.

A tandem colonoscopy study by Rutter and colleagues documented a dysplasia detection rate per patient of 7% following targeted biopsies in chromoendoscopy (9 dysplastic lesions in 7 of 100 patients) and 2% in standard colonoscopy (2 dysplastic lesions in 2 of 100 patients) [25]. In a meta-analysis of eight clinical trials of surveillance colonoscopy, chromoendoscopy detected a significantly greater proportion of patients with dysplasia in comparison with white-light colonoscopy (RR 1.8 [95% CI, 1.2–2.6] and absolute risk increase, 6% [95% CI, 3–9%]) [13, 14]. Deepak and colleagues recently showed an incremental diagnostic yield of chromoendoscopy and outcomes in IBD patients with a history of colorectal dysplasia on white-light endoscopy, most of which were amenable to endoscopic treatment [26]. Overall, these studies consistently show that chromoendoscopy is the optimal surveillance technique for detecting dysplasia in patients with IBD.

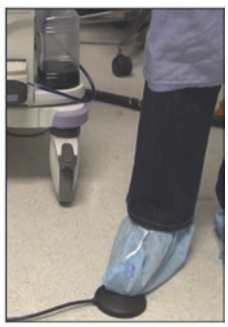
As recommended by the SCENIC international consensus statement, chromoendoscopy is the preferred method of surveillance in IBD patients but has not been broadly implemented. Potential barriers include lack of training in chromoendoscopy, increased time required, and lack of reimbursement despite extra time. The extra time to perform chromoendoscopy has been estimated to be 11 min from several tertiary centers and 18 min from a single community-based practice. In terms of costs associated with chromoendoscopy, a recent study evaluated whether it is cost-effective and found that it was not only more effective but also less costly compared to conventional white-light endoscopy with four-quadrant random biopsies taken every 10 cm [27].

Practical Considerations

Chromoendoscopy is the optimal surveillance technique for detecting dysplasia in patients with IBD.

Chromoendoscopy Technique

The chromoendoscopy technique requires an excellent bowel preparation, and the entire mucosa should be free of mucus, blood, and stool. The exam should be performed when the disease is in remission to avoid and minimize potential misdiagnosis between inflammatory changes and dysplasia [28]. Consideration should be taken to increase or double colonoscopy time slot initially during the learning curve period. Prior to starting the procedure, a total of 250 L of diluted dye (methylene blue, 0.04–0.1%, or indigo carmine, 0.03–0.1%) is prepared (Fig. 25.1). A 0.04% solution of methylene blue can be achieved by taking a 1%, 10-ml ampule and mixing it with 240 ml of water; a 0.03% solution of indigo carmine

Purpose	Technique	Method	Dilution*	Color	
Lesion detection	Pan chromo-endoscopy	Water jet channel using auxiliary foot pump or biopsy channel using spray catheter	Indigo carmine (0.8%, 5ml ampule): 2 ampules + 250ml water (0.03%) Methylene blue (1%, 10ml ampule): 1 ampule + 240ml water (0.04%)		
Lesion characterization and delineation of borders	Targeted chromo-endoscopy	Syringe spray through biopsy channel	Indigo carmine (0.8%, 5ml ampule): 1 ampule + 25ml water (0.03%) Methylene blue (1%, 10ml ampule): 1 ampule + 40ml water (0.2%)		

*Various dilutions ranging from 0.03-0.2% of Indigo carmine and methylene blue have been reported for panchromoendoscopy.

Fig. 25.1 Chromoendoscopy technique (Reprinted from Laine et al. [13, 14]. Copyright (2015), with permission from Elsevier). * Various dilutions ranging from 0.03% to 0.2% of Indigo carmine and methylene blue have been reported for panchromoendoscopy

can be prepared by taking two 0.08%, 5-ml ampules and mixing it with 250 ml of water. Colonic accessories that should be at hand are based on preference and include water-jet channel by using water pump attached to the endoscope activated via foot pedal or spray catheter (length 240 cm, endoscope accessory channel 2.8 mm).

During insertion it is recommended to lavage and suction small amounts of debris or fluid. Once the cecum is reached, either methylene blue or indigo carmine is sprayed; approximately 250 ml of diluted dye is sprayed circumferentially throughout the colon. Once the excess fluid is suctioned, the mucosa is carefully evaluated. Efficient spraying is applied by directing the dye to the antigravity side of the colon [28]. During withdrawal focus is given to 20–30 cm of colon at a time with reinsertion of the endoscope to the proximal extent of each segment before slow withdrawal and mucosal visualization. During inspection, careful attention is made to areas that appear to be different from surrounding background in color, pattern, or level. When being completed for IBD surveillance, random biopsies for dysplasia are not needed [29]. If biopsies for dysplasia are not completed, typically two random biopsies in every bowel segment are recommended to document microscopic disease activity.

Practical Considerations

During inspection with chromoendoscopy, careful attention is made to areas that appear to be different from surrounding background in color, pattern, or level.

Confocal Laser Endomicroscopy

Confocal laser microscopy (CLE) is a relatively new novel tool that permits in vivo microscopic evaluation of colonic mucosa. It emits a low-power blue laser light onto tissue, which is reflected from the tissue and refocused on the detection system by the same lens, leading to microscopic imaging at 1000-fold magnification in real time [30]. There are currently two different FDA-approved devices: (1) a probe-based CLE system that can be advanced through the accessory channel of a standard endoscope (pCLE, Cellvizio, Mauna Kea Technologies, Paris, France) and (2) an integrated device where the CLE probe is integrated into the distal end of a high-resolution endoscope ("integrated," iCLE; Pentax, Tokyo, Japan). Currently only the Cellvizio system is commercially available.

A systematic review and meta-analysis evaluating the efficacy of CLE for discriminating colorectal neoplasia including patients with IBD concluded that CLE is comparable to colonoscopy histopathology in diagnosing colorectal neoplasia [31]. For real-time CLE, endoscopy-based systems had better sensitivity (0.97 vs. 0.82, $p < 0.0001$) and specificity (0.99 vs. 0.82, $p < 0.0001$) than probe-based system [31]. The role of CLE for the assessment of mucosal inflammation, for prediction of therapeutic response, and for cancer surveillance in IBD has been recently reviewed in a systematic review, and it was found that CLE can be used to reliably assess macro- and microscopic inflammatory activity in IBD patients and to obtain optical biopsies in real time [32]. Overall, while promising, further studies are needed to further validate the accuracy and clinical application of this technology.

Practical Considerations

Confocal laser microscopy (CLE) is a relatively new novel tool that permits in vivo microscopic evaluation of colonic mucosa.

Endocytoscopy

Similar to CLE, endocytoscopy aims to enable real-time microscopic imaging of mucosa in vivo. An endocytoscopy system is manufactured by Olympus (Tokyo, Japan) and uses contact light microscopy with a fixed-focus, high-power objective lens to allow in vivo microscopic imaging of the GI tract with up to 1390-fold magnification [33]. The main difference between CLE and endocytoscopy is that endocytoscopy is based solely on high-level magnification using optical lenses, and there is no confocal plane; hence, only the very superficial layer of the mucosa can be imaged. There is limited data on the assessment of mucosal inflammation in IBD with endocytoscopy. However, one recent study did report that they were able to demonstrate that endocytoscopy can be used not only for the determination of mucosal inflammation but also for the identification and visualization of single inflammatory cells [34]. Endocytoscopy allowed to reliably distinguish single inflammatory cells, namely, neutrophilic, basophilic, and eosinophilic granulocytes and lymphocytes [34]. Potential clinical applications for endocytoscopy require further studies to validate its use in IBD.

Practical Considerations

Similar to CLE, endocytoscopy allows in vivo microscopic imaging of the GI tract.

Molecular Imaging

The novel field of "molecular imaging" or "in vivo immunohistochemistry" involves the application of fluorescent antibodies in conjunction with in vivo imaging such as CLE or endocytoscopy to allow the visualization and quantification of biochemical structures or process on the molecular level in real time. In a landmark phase 1 clinical trial, a fluorescein isothiocyanate (FITC)-labeled anti-TNF antibody was manufactured and topically applied during endoscopy to inflamed mucosa of IBD patients that were naïve to anti-TNF antibody treatment [35]. Topical antibody administration in 25 patients with Crohn's disease led to detection of intestinal membrane-bound TNF (mTNF) during CLE. The amount of intestinal mTNF was quantified via CLE, and interestingly, patients with high numbers of mTNF cells showed a higher short-term response rate (92%) at week 12 upon subsequent anti-TNF therapy as compared to patients with low amounts of mTNF cells (15%). The clinical response in patients with high amounts of intestinal mTNF cells was sustained over a follow-up period of 1 year and was associated with mucosal healing observed at follow-up colonoscopy [35]. This landmark study was the first to provide real-world evidence that molecular imaging with fluorescent antibodies has the potential to predict therapeutic responses to biological treatment and can be used for personalized medicine in IBD.

Practical Considerations

The novel field of "molecular imaging" or "in vivo immunohistochemistry" involves the application of fluorescent antibodies in conjunction with in vivo imaging such as CLE or endocytoscopy to allow the visualization and quantification of biochemical structures or process on the molecular level in real time.

Conclusions

In summary, the role of chromoendoscopy and enhanced imaging techniques in IBD colorectal cancer colonoscopy surveillance has placed more emphasis on high visual inspection of colonic mucosa. As stated in the SCENIC guidelines, chromoendoscopy with targeted biopsies can improve endoscopic detection and management of visible dysplastic colorectal lesions in IBD patients, compared with conventional white-light colonoscopy with random biopsy. Image enhanced technologies such as high-definition endoscopy and chromoendoscopy can improve the detection of non-polypoid dysplastic lesions in daily clinical practice. Recent developments in optical biopsy techniques with CLE and endocytoscopy have allowed us to microscopically assess colonic mucosa in real time, but overall while promising additional studies are needed to validate their use in IBD. Lastly, rapidly evolving molecular imaging technologies appear promising and have the potential to predict therapeutic responses to biological treatment thus providing a personalized medical approach.

References

1. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut. 2001;48(4):526–35.
2. Friedman S, Rubin PH, Bodian C, Goldstein E, Harpaz N, Present DH. Screening and surveillance colonoscopy in chronic crohn's colitis. Gastroenterology. 2001;120(4):820–6.
3. Friedman S, Rubin PH, Bodian C, Harpaz N, Present DH. Screening and surveillance colonoscopy in chronic crohn's colitis: results of a surveillance program spanning 25 years. Clin Gastroenterol Hepatol. 2008;6(9):993–8. quiz 953-4.
4. Jess T, Rungoe C, Peyrin-Biroulet L. Risk of colorectal cancer in patients with ulcerative colitis: a meta-analysis of population-based cohort studies. Clin Gastroenterol Hepatol. 2012;10(6):639–45.
5. Soetikno RM, Lin OS, Heidenreich PA, Young HS, Blackstone MO. Increased risk of colorectal neoplasia in patients with primary sclerosing cholangitis and ulcerative colitis: a meta-analysis. Gastrointest Endosc. 2002;56(1):48–54.
6. Rutter M, Saunders B, Wilkinson K, et al. Severity of inflammation is a risk factor for colorectal neoplasia in ulcerative colitis. Gastroenterology. 2004;126(2):451–9.
7. Rubin DT, Huo D, Kinnucan JA, et al. Inflammation is an independent risk factor for colonic neoplasia in patients with ulcerative colitis: a case-control study. Clin Gastroenterol Hepatol. 2013;11(12):1601–8.e1-4.
8. Krugliak Cleveland N, Colman RJ, Rodriquez D, et al. Surveillance of IBD using high definition colonoscopes does not miss adenocarcinoma in patients with low-grade dysplasia. Inflamm Bowel Dis. 2016;22(3):631–7.
9. Itzkowitz S. Colon carcinogenesis in inflammatory bowel disease: applying molecular genetics to clinical practice. J Clin Gastroenterol. 2003;36(5 Suppl):S70–4. discussion S94-6.
10. Brentnall TA, Crispin DA, Rabinovitch PS, et al. Mutations in the p53 gene: an early marker of neoplastic progression in ulcerative colitis. Gastroenterology. 1994;107(2):369–78.
11. Annese V, Daperno M, Rutter MD, et al. European evidence based consensus for endoscopy in inflammatory bowel disease. J Crohns Colitis. 2013;7(12):982–1018.
12. Farraye FA, Odze RD, Eaden J, et al. AGA medical position statement on the diagnosis and management of colorectal neoplasia in inflammatory bowel disease. Gastroenterology. 2010;138(2):738–45.
13. Laine L, Kaltenbach T, Barkun A, et al. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. Gastrointest Endosc. 2015;81(3):489–501.e26.
14. Laine L, Kaltenbach T, Barkun A, et al. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. Gastroenterology. 2015;148(3):639–651.e28.

15. Leighton JA, Shen B, Baron TH, et al. ASGE guideline: endoscopy in the diagnosis and treatment of inflammatory bowel disease. Gastrointest Endosc. 2006;63(4):558–65.
16. Sanduleanu S, Kaltenbach T, Barkun A, et al. A roadmap to the implementation of chromoendoscopy in inflammatory bowel disease colonoscopy surveillance practice. Gastrointest Endosc. 2016;83(1):213–22.
17. Rutter MD, Saunders BP, Wilkinson KH, et al. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. Gastroenterology. 2006;130(4):1030–8.
18. Jaramillo E, Watanabe M, Befrits R, Ponce de Leon E, Rubio C, Slezak P. Small, flat colorectal neoplasias in long-standing ulcerative colitis detected by high-resolution electronic video endoscopy. Gastrointest Endosc. 1996;44(1):15–22.
19. Rubin DT, Rothe JA, Hetzel JT, Cohen RD, Hanauer SB. Are dysplasia and colorectal cancer endoscopically visible in patients with ulcerative colitis? Gastrointest Endosc. 2007;65(7):998–1004.
20. Soetikno R, Sanduleanu S, Kaltenbach T. An atlas of the non-polypoid colorectal neoplasms in inflammatory bowel disease. Gastrointest Endosc Clin N Am. 2014;24(3):483–520.
21. Technology Committee ASGE. High-definition and high-magnification endoscopes. Gastrointest Endosc. 2014;80(6):919–27.
22. Subramanian V, Ramappa V, Telakis E, et al. Comparison of high definition with standard white light endoscopy for detection of dysplastic lesions during surveillance colonoscopy in patients with colonic inflammatory bowel disease. Inflamm Bowel Dis. 2013;19(2):350–5.
23. Bartel MJ, Picco MF, Wallace MB. Chromocolonoscopy. Gastrointest Endosc Clin N Am. 2015;25(2):243–60.
24. ASGE Technology Committee, Wong Kee Song LM, Adler DG, et al. Chromoendoscopy. Gastrointest Endosc. 2007;66(4):639–49.
25. Rutter MD, Saunders BP, Schofield G, Forbes A, Price AB, Talbot IC. Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis. Gut. 2004;53(2):256–60.
26. Deepak P, Hanson GJ, Fletcher JG, et al. Incremental diagnostic yield of chromoendoscopy and outcomes in inflammatory bowel disease patients with a history of colorectal dysplasia on white-light endoscopy. Gastrointest Endosc. 2016;83(5):1005–1012.
27. Konijeti GG, Shrime MG, Ananthakrishnan AN, Chan AT. Cost-effectiveness analysis of chromoendoscopy for colorectal cancer surveillance in patients with ulcerative colitis. Gastrointest Endosc. 2014;79(3):455–65.
28. Soetikno R, Subramanian V, Kaltenbach T, et al. The detection of nonpolypoid (flat and depressed) colorectal neoplasms in patients with inflammatory bowel disease. Gastroenterology. 2013;144(7):1349–52. 1352.e1–6.
29. van den Broek FJ, Stokkers PC, Reitsma JB, et al. Random biopsies taken during colonoscopic surveillance of patients with longstanding ulcerative colitis: low yield and absence of clinical consequences. Am J Gastroenterol. 2014;109(5):715–22.
30. Neumann H, Kiesslich R, Wallace MB, Neurath MF. Confocal laser endomicroscopy: technical advances and clinical applications. Gastroenterology. 2010;139(2):388–92. 392.e1–2.
31. Su P, Liu Y, Lin S, et al. Efficacy of confocal laser endomicroscopy for discriminating colorectal neoplasms from non-neoplasms: a systematic review and meta-analysis. Color Dis. 2013;15(1):e1–12.
32. Rasmussen DN, Karstensen JG, Riis LB, Brynskov J, Vilmann P. Confocal laser endomicroscopy in inflammatory bowel disease--a systematic review. J Crohns Colitis. 2015;9(12):1152–9.
33. Neumann H, Fuchs FS, Vieth M, et al. Review article: in vivo imaging by endocytoscopy. Aliment Pharmacol Ther. 2011;33(11):1183–93.
34. Neumann H, Vieth M, Neurath MF, Atreya R. Endocytoscopy allows accurate in vivo differentiation of mucosal inflammatory cells in IBD: a pilot study. Inflamm Bowel Dis. 2013;19(2):356–62.
35. Atreya R, Neumann H, Neufert C, et al. In vivo imaging using fluorescent antibodies to tumor necrosis factor predicts therapeutic response in crohn's disease. Nat Med. 2014;20(3):313–8.

Ultrasound-Guided/Ultrasound-Assisted Percutaneous Liver Biopsy

26

Roopjeet K. Bath and George Y. Wu

Introduction

Much progress has been made in the development of noninvasive tests for evaluation of liver inflammation and fibrosis. However, histological assessment continues to provide valuable diagnostic and prognostic information that cannot be obtained in any other way. With the use of imaging guidance, liver biopsy remains a safe and invaluable tool for the clinical evaluation of liver disease. This chapter will discuss the indications and contraindications for liver biopsy, provide detailed instructions and technical tips, and offer practical information for safe and effective performance of ultrasound (US)-guided percutaneous liver biopsy.

Indications

The primary indication for liver biopsy is to provide diagnostic information when all other tests have failed to provide a diagnosis. It can also be helpful in assessing mild to moderate fibrosis [1]. Indications and contraindications are shown in Table 26.1 [2].

Unexplained elevations in liver enzymes and hepatomegaly are common indications. Diagnoses that may only be made by histological examination include intrahepatic cholestatic liver disease, steatohepatitis, drug-induced liver disease, autoimmune hepatitis, and neoplastic lesions. In addition, liver biopsy provides diagnostic value in less common diseases such as Wilson's disease, alpha antitrypsin-1 deficiency, congenital metabolic storage diseases, mucopolysaccharidosis, hemochromatosis, granulomatous disease, amyloidosis, and other infiltrative diseases [3].

Liver biopsy can provide direct information on the grade and stage of liver disease and can assist in treatment selection [2]. It is particularly useful when diseases coexist and where staging may govern the aggressiveness of management [4]. Sequential biopsies may offer information on the progression of disease as in cases of liver transplantation where the etiology of graft dysfunction is unclear [3].

Although liver biopsy is not indicated for the diagnosis of hepatocellular carcinoma that has typical imaging features, for those cases where imaging characteristics are atypical, biopsy can still be helpful [1, 4]. Many nonmalignant focal liver lesions such as hemangioma, focal nodular hyperplasia, and cysts also have characteristic findings on imaging studies or serological markers for diagnosis, making these modalities preferred over liver biopsy [3]. However, when there is doubt, and especially if growth rates are uncharacteristically rapid, liver biopsy may be helpful.

Contraindications

Contraindications for percutaneous liver biopsy include those that may increase the risk for post-procedure bleeding as well as conditions that may make the performance of the procedure unsafe. Absolute contraindications include severe coagulopathy, an uncooperative patient, impaired mental status, infection of the hepatic bed, or extrahepatic biliary obstruction with cholangitis [3]. PT, INR, and platelet count results should be routinely obtained within a week of the procedure [3]. It is recommended that the prothrombin time (PT) be less than 3–5 s prolonged and the international normalized ratio (INR) be less than 1.6 [4, 5]. Additionally, the

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Table 26.1 Various options for liver biopsy

Approach	Description	Indications	Performed by
Transthoracic, palpation/ percussion guided	The biopsy site is determined by manual palpation of the liver edge and percussion during exhalation	Uncommon. The use of ultrasound provides reliable, noninvasive beneficial guidance	Gastroenterologist/ hepatologist
Transthoracic, ultrasound assisted	The biopsy site is confirmed by ultrasound before the biopsy	No contraindications to blind biopsy. Simple and cost-effective approach	Gastroenterologist/ hepatologist
Transthoracic, ultrasound guided	The needle and biopsy placement is guided in real time by ultrasound	The presence of focal lesions identified by prior imaging studies. Prior abdominal surgery with adhesions	Radiologist
Subcostal ultrasound assisted/ guided	The same procedures as above except from a subcostal approach rather than transthoracic	Hepatomegaly that extends below the costal margin	Radiologist
Transjugular or transvenous	The biopsy is approached either through the jugular or femoral vein using fluoroscopy	Coagulopathy, ascites, morbid obesity, vascular hepatic lesions, fulminant hepatic failure, indication for concomitant procedure (e.g., TIPS)	Interventional radiologist
Laparoscopic/surgical	The biopsy is approached via laparoscopy and surgical excision	Suspected metastases, unexplained ascites staging of hepatocellular carcinoma, large biopsy required	Surgeon

platelet count should be greater than 60,000–80,000, and there should be no recent NSAID or anticoagulant use or severe illness [3, 4]. Recommendations on the management of anticoagulation to permit liver biopsy are presented later in this chapter. Relative contraindications include a difficult body habitus (i.e., morbid obesity) or ascites, in which cases a transjugular biopsy approach is preferred. Previous surgery in the area with the possible presence of adhesions is also a relative contraindication. Possible vascular lesions, hemangiomas, amyloidosis, and hydatid disease are also relative contraindications to a percutaneous approach [3]. The AASLD guidelines recommend that patients on chronic hemodialysis should be dialyzed prior to liver biopsy, and heparin should be avoided if possible. DDAVP (desmopressin) can also be considered, although appears to be unnecessary in patients on stable dialysis regimens.

The American College of Physicians and Patient Care Committee of American Gastroenterological Association recommend that patients live within a 30 mile radius of the procedure site, be accompanied by a chaperone that can supervise them for the 24 h following the procedure, and should be directly observed for 6 h post-biopsy at the procedure center where there is access to appropriate treatment for major complications [6]. Most centers have a 2–4 h direct observation period after the procedure [7].

Anticoagulation/Antiplatelet Management

All antiplatelet medications (e.g., aspirin, clopidogrel, IIb/IIIa receptor antagonists, and NSAIDs) should be discontinued at least 7–10 days prior to liver biopsy and may be restarted 48–72 h after liver biopsy [3].

All anticoagulant medications should be discontinued prior to liver biopsy. Warfarin should be stopped at least 5 days prior, and heparin should be discontinued at least 12–24 h prior. Warfarin can be restarted the day following liver biopsy [3].

Management of the newer anticoagulant therapies, including direct thrombin inhibitors and factor Xa inhibitors, can be extrapolated from guidelines on perioperative management of these agents in high-bleeding-risk settings [8].

Practical Considerations

- Remember the indications and contraindications for the liver biopsy.
- Hemodialysis patients should get their dialysis prior to the liver biopsy, and heparin should be avoided if possible.
- Patients should live within a 30 mile radius of the procedure site and should be accompanied by a chaperone.
- All antiplatelet medications (e.g., aspirin, clopidogrel, IIb/IIIa receptor antagonists, and NSAIDs) should be discontinued at least 7–10 days prior to liver biopsy.

Procedure Technique: Percutaneous Ultrasound-Assisted Liver Biopsy

After obtaining informed consent, a thorough explanation of the procedure including what the patient may expect to feel at each step is valuable in allaying fear and anxiety. Particular

attention should be devoted to peri- and post-procedural pain concerns.

Percutaneous liver biopsy can be performed using several different needle types, each of which has individual advantages and disadvantages as shown in Table 26.2. The needle type should be selected according to the suspected disease process as well as relevant patient risk factors [9]. While some institutions use reusable needles, commercial kits and guns are so convenient and reliable that at most institutions, the latter have largely supplanted the former. Regardless of the type of needle used, certain supplies are required as shown in Fig. 26.1. These include sterile gloves, a straight edge, a specimen container with formalin, and a typical liver biopsy kit with either a Jamshidi needle (Fig. 26.2) or a Menghini needle (Fig. 26.3a). A liver biopsy gun is shown in Fig. 26.3b. An extra bottle of 10 ml of 1% lidocaine is useful in ensuring adequate local anesthesia.

Table 26.2 Percutaneous biopsy needles

	Suction	Cutting
Types	Jamshidi, Klatskin, Menghini	Tru-Cut, Vim-Silverman
Advantages	Good sample size	Smaller sample size, no fragmentation
Disadvantages	Fragmentation	Risk of bleeding

Biopsy with a Jamshidi-Menghini Needle Kit

The patient is placed supine with the right side of the body placed at the edge of the procedure table. The right arm is placed with the hand behind the head or the neck with slight torsion of the thorax to the left. The legs and hips are then pivoted approximately 15 degrees toward the left. These positional maneuvers widen the right intercostal spaces. In females with substantial breast tissue, the right breast may interfere by overlapping the optimal biopsy site. In such cases, to free the area, a drape is securely taped to the base of the breast (Fig. 26.4a), and tension is applied to the caudal end of the drape to move the breast cephalad until the site is clear. To maintain tension, the drape is then anchored to the patient's gown or other convenient immobile objects with a clip or clamp (Fig. 26.4b). The liver and right thoracic area are palpated and percussed at the eight to tenth intercostal spaces along the mid-axillary line (Fig. 26.5a). The patient is instructed to inhale followed by full exhalation, with a two to three 3 s hold at full expiration (Fig. 26.5b). The point of maximum dullness during full expiration is determined. This preliminary site is marked as a potential biopsy location (Fig. 26.5c). Ultrasound is used to visualize the liver, gallbladder, and kidney. To do this, a 19 kHz handheld probe is most convenient. The probe is glided over areas of interest

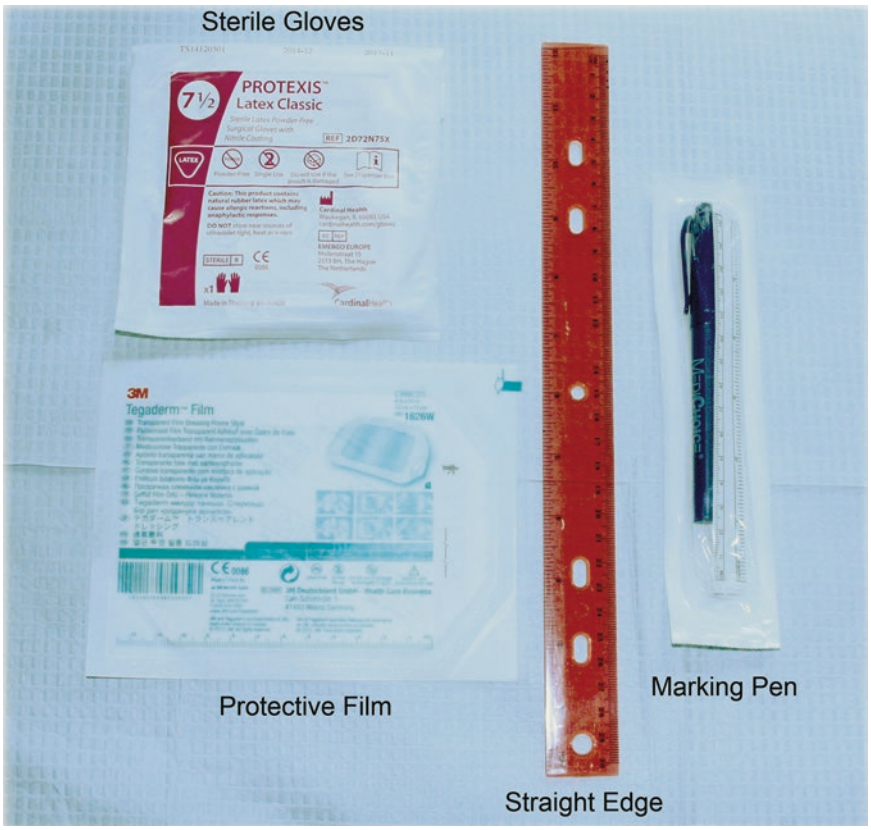

Fig. 26.1 Preparatory materials for percutaneous liver biopsy. plastic ruler, sterile gloves, surgical marker, sterile plastic site covering

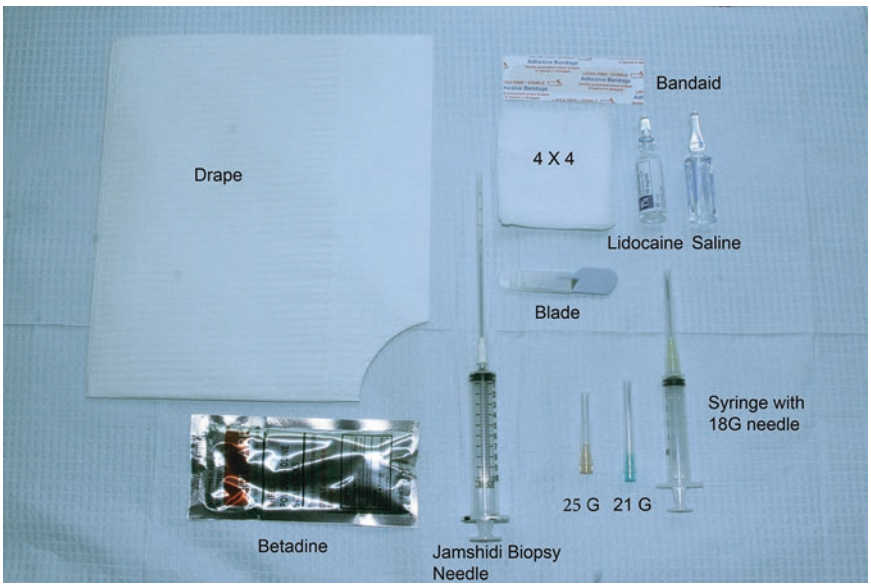

Fig. 26.2 Jamshidi (Menghini) liver biopsy kit. Jamshidi (Menghini) needle 9.8 cm, 17 G (1.47 mm) beveled tip, #11 surgical scalpel, normal saline 5 mL, alternate specimen container, lidocaine 1% 5 mL, 25 G needle, 22 G needle, 18 G needle, sterile gauze

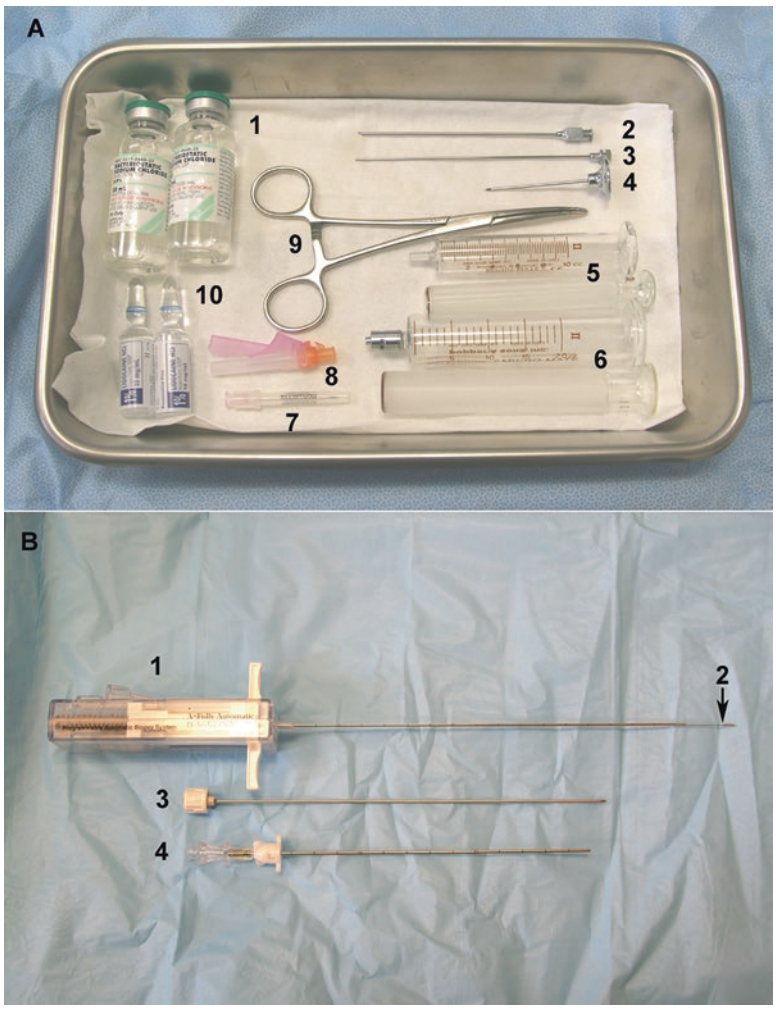

Fig. 26.3 (**a**) Menghini liver biopsy kit. (*1*) Bacteriostatic sodium chloride 60 mL; (*2*) Menghini needle, 7.0 cm, 16 G (1.65 mm) beveled tip; (*3*) stylette; (*4*) trocar; (*5*) syringe for anesthesia; (*6*) syringe for biopsy; (*7*) 20 G needle; (*8*) 25 G needle; (*9*) forceps; (*10*) lidocaine 1% 10 mL. (**b**) Liver biopsy gun. (*1*) Liver biopsy gun, 18 G, (*2*) biopsy cutting site, (*3*) trocar, (*4*) sheath

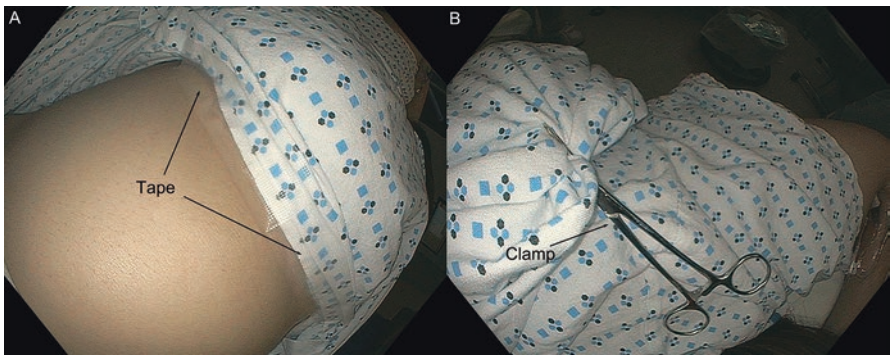

Fig. 26.4 A method to free the proposed biopsy site from an overlapping breast. (**a**) A drape is place over the breast and securely taped to the base of the breast (**b**) tension applied to the opposite end of the drape to move the breast cephalad until the site is clear. To maintain tension, the drape is then anchored to the patient's gown or other convenient immobile objects with a clip or clamp

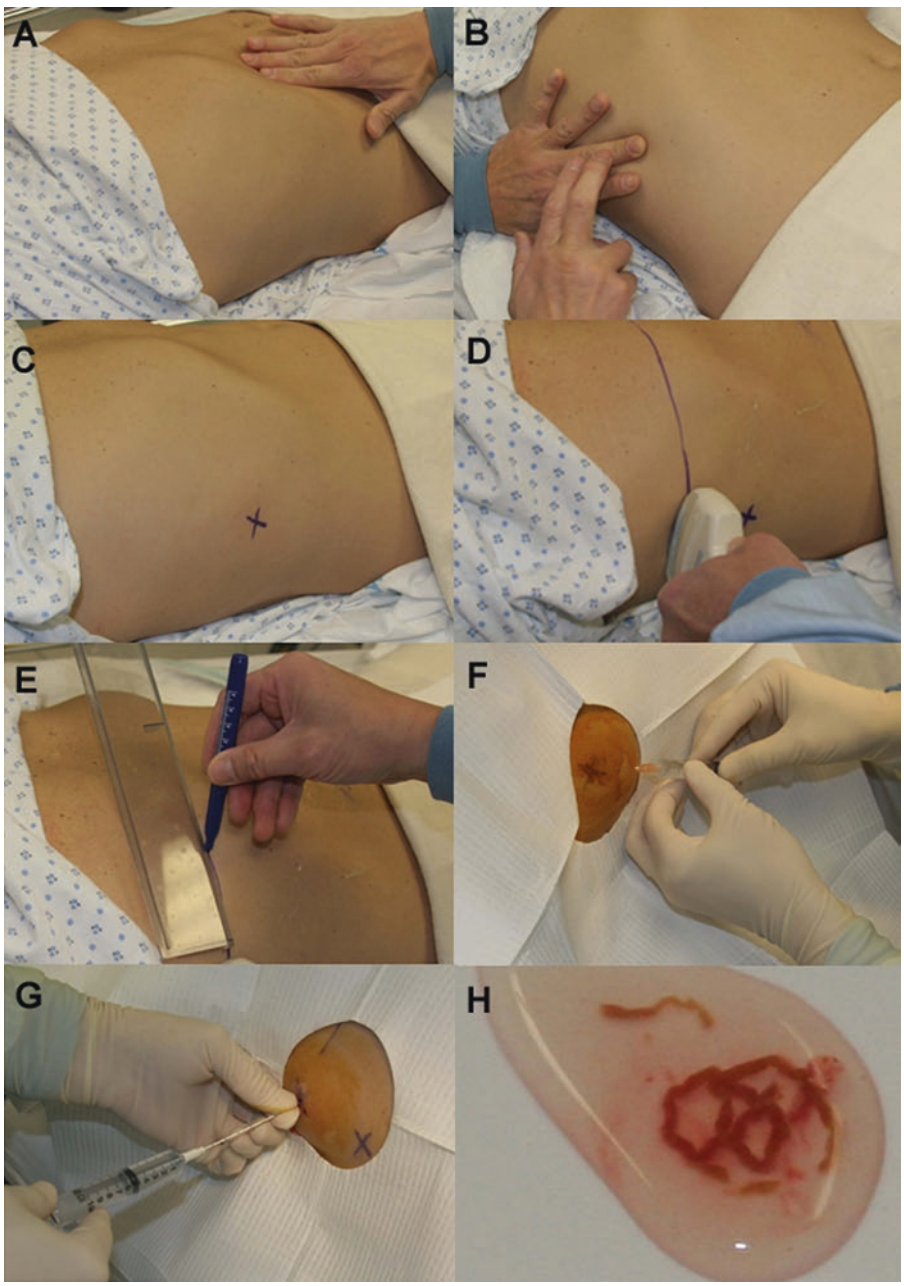

Fig. 26.5 Percutaneous liver biopsy with ultrasound assistance. (**a**) Palpation, (**b**) percussion, (**c**) marking potential site, (**d**) ultrasound examination of biopsy path,* (**e**) marking direction of biopsy, (**f**) administration of anesthesia, (**g**) insertion of biopsy needle, (**h**) sample of liver biopsy in saline (*see Fig. 26.6, e.g., of ultrasound images)

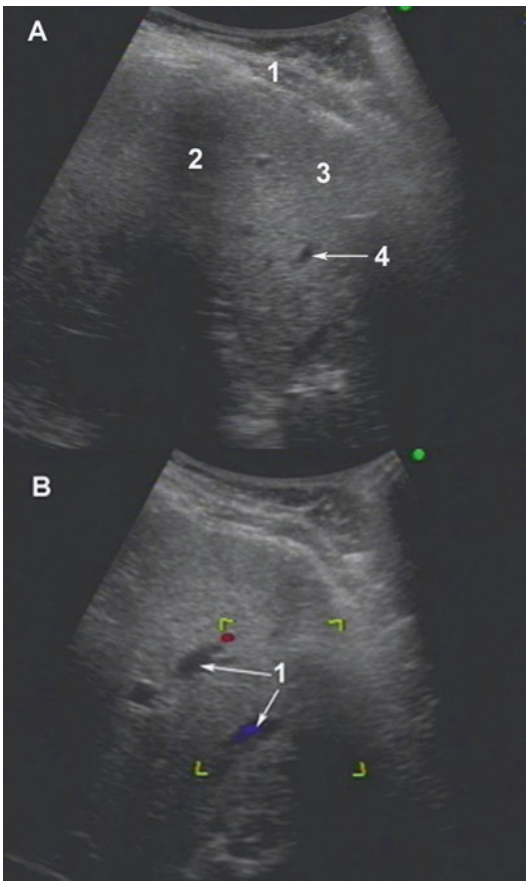

Fig. 26.6 (**a**) B-mode ultrasound image of target area for liver biopsy. (*1*) Glisson's capsule, (*2*) rib shadow, (*3*) liver, (*4*) blood vessel or bile duct. (**b**) Doppler mode ultrasound image of target area for liver biopsy. (*1*) Hepatic blood vessels. Doppler mode can be used to differentiate between blood vessels (*red* and *blue* structures) and bile ducts (no color)

including the site of preliminary mark (Fig. 26.5d). The gallbladder and kidney should be identified and made certain that the structure is distant (not visible with the probe held in the direction of the biopsy) from the potential biopsy site at full expiration. The site of the maximum diameter of the liver is determined and marked if different from the preliminary mark (Fig. 26.6a). Doppler imaging at the site allows avoidance of large peripheral hepatic vessels and bile ducts (Fig. 26.6b). Both the B-mode and Doppler images can be captured for the medical record. The puncture site is selected in the inferior portion of the intercostal space to avoid the intercostal nerves and vessels. With the ultrasound probe in place, a straight edge is placed over the chest, and a line is drawn from the mark along the direction of the ultrasound beam (Fig. 26.5e), to delineate the optimal direction of the biopsy needle.

The ultrasound jelly is removed, and an antiseptic solution is applied to the marked site. A sterile drape is placed and taped in place over the surgical field, aligning a prominent crease in the paper with site and line drawn based on the ultrasound imaging. Local anesthesia, 1% lidocaine, is injected tangential to the skin with a 25 G needle infiltrating intradermally to raise a bleb and then aiming perpendicular to the skin penetrating 2–3 mm at a time progressively deeper into the subcutaneous tissue and intercostal muscles to anesthetize the path of entry (Fig. 26.5f). The needle is changed to a 21 G needle, and the process is repeated injecting approximately 2.5 ml in the process. If blood is obtained during the infiltration, it usually indicates that the surface of the liver has been reached. The needle should be withdrawn and the angle changed to 15 degrees from perpendicular aiming caudad, and another 2.5 ml should be injected in an attempt to spray the Glisson's capsule. Satisfactory infiltration is the key to minimizing discomfort of the liver biopsy. There should be little hesitation to use more than 5 ml of lidocaine provided in the kit, in order to ensure proper anesthesia especially in individuals who are obese or more sensitive to pain. A number 11 surgical blade is used to make a 1–2 mm nick in the skin at the site for introduction of the biopsy needle.

The biopsy device is prepared by removing the biopsy needle from the syringe and aspirating 3–4 ml of sterile saline into the barrel. Then, the biopsy needle is replaced securely. This is important as some manufacturing defects result in an inability to securely attach the needle to the syringe. This can result in premature separation of the needle and barrel during withdrawal of the needle from the body.

To perform the biopsy, the needle shaft is held with one hand, and the needle is slowly advanced 1–2 mm at a time through the chest wall (Fig. 26.4g), until the penetration of the peritoneum is felt. A small amount of saline is expressed through the needle to confirm the position of the needle in the peritoneum and to flush out any tissue present in the needle. If the needle is in the peritoneum, little resistance will be felt, and the saline will be expelled easily. If resistance is felt, it may indicate that the needle is at or in the liver edge or still in the chest wall. In this case, the needle should be withdrawn slightly and saline again injected. If resistance to injection is still felt, the needle should be advanced slowly until the peritoneum is pierced and the injection procedure repeated. Once it is certain that the needle is in the peritoneum, suction is applied to the syringe and locked or held in a way to maintain vacuum. One hand holds the needle with the thumb and fingers at the desired depth of insertion, and the other hand adjusts the direction, making sure that the needle is aimed along the crease of the drape and that the needle is levelled to the table. The patient is instructed to inhale fully, then exhale fully, and hold exhalation until directed otherwise. At full exhalation held for 1–2 s, the needle is rapidly inserted into the liver along the marked direction in an even and fluid motion, followed by rapid withdrawal all occurring in about 1 s. The sample is expelled into a clean flat surface of the kit and carefully placed into a screw-capped container

containing 10% neutral buffered-formalin (Fig. 26.4h). A typical sample will be 2.5–4 cm in length.

For ultrasound-guided biopsies, sterile jelly and a probe covered with sterile plastic are used and held by an assistant while the biopsy is performed. The optimal location is determined, and the site is anesthetized with lidocaine as described above.

As soon as possible after the biopsy, the patient should be bandaged and instructed to assume a right lateral decubitus position and remain in that position for 2–4 h to minimize bleeding. Blood pressure, pulse, heart rate, and symptoms are monitored frequently, for example, every 15 min for the first hour, every 30 min for the second hour, and then hourly until discharge [10]. If stable after 3 h of observation, the patient can be discharged. At home, patients are instructed to remain at bed rest for the remainder of the day in the right lateral decubitus position as much as possible. The day after the procedure, patients can perform their usual activities but should avoid intense exercise and heavy lifting. Prescription narcotics can be used, but if the procedure is performed properly and local anesthesia is adequate, this is rarely necessary. NSAIDS or anticoagulants should be avoided for at least 48 h.

The ideal size of a liver biopsy specimen has been shown to be approximately 3.0 cm in length, although adequate sizes have been reported to range between 1 and 3 cm [2, 3]. The diameter should be between 1.2 and 2 mm, and the sample should include at least 6–8 portal triads. This represents 1/50,000 of the adult liver size [2, 9]. Sampling error has been shown to approach 20–30% [1]. This can be decreased by taking samples from different lobes, although this is rarely done in clinical practice. Note that staging and grading of chronic viral hepatitis has been shown to require a minimum of 2 cm in biopsy length with at least 11 portal triads [11].

Alternate Devices

A Menghini needle kit (Fig. 26.3a) is used following the same procedure as with the Jamshidi needle kit, with two exceptions. The first is that the Jamshidi has a lock to maintain vacuum in the syringe. This allows for a more controlled grip on the needle shaft and syringe when taking the biopsy. The second is that the Jamshidi needle is designed to prevent aspiration of the sample into the barrel of the syringe and, thus, ensures easy removal of the sample from the needle. With the Menghini needle, the biopsy sample is retained either within the needle or within the barrel of the syringe. Depending on its location, the sample can be poured out from the syringe after removing the plunger or can be pushed out of the needle using the stylette. Sometimes, it is difficult to retrieve the sample from the syringe barrel. For this reason, some Menghini needle kits supply a blunt stopper to be inserted into the proximal end of the needle before taking the biopsy to prevent the sample from entering the barrel of the syringe.

Liver Biopsy Gun

Radiologists often use a liver biopsy gun (Fig. 26.3b) for ultrasound-guided biopsies. The biopsy gun is best used for sampling focal rather than generalized liver lesions. The gun allows multiple passes to be completed at low risk until an adequate sample is obtained, and guide devices are available to maintain the gun in a particular position for sampling specific lesions. The biopsy gun technique is similar to the procedure described above, with the exception of the use of real-time ultrasound and a slightly different method of entry and biopsy. After preparation and local anesthesia, a 17 G needle is inserted into the sheath and twisted to lock into place. The sheath and needle are inserted percutaneously into the liver and guided to the appropriate depth by ultrasound. The 17 G needle is removed, while the sheath is held carefully in position. The biopsy gun is loaded to engage the 18 G needle and then is inserted into the sheath with the bevel of the needle facing toward the ultrasound probe. The tip of the bevel is visualized on ultrasound to confirm appropriate placement within the liver. The biopsy gun trigger is pressed and the biopsy is taken. The gun is removed keeping the sheath held in place. The sample is removed and visualized, and if inadequate, the gun can be reinserted to obtain another sample. Once an adequate sample is obtained, the sheath can be removed and the patient prepared for recovery.

Complications

Most complications from percutaneous liver biopsy occur shortly after the procedure. The overall rate of major or life-threatening complications has been reported to be between 0.09 and 2.3% [12]. This rate has been shown to be dependent on the experience and training of the operator [13]. Sixty-one percent of complications occur in the first 2 h, and 96% occur in the first 24 h [14]. One to 3% of patients are hospitalized for an adverse event, most commonly for vasovagal hypotension or post-procedure pain [2]. The most common complication of the procedure is pain. Pain is usually described as a dull ache in the right upper quadrant of the abdomen or in the right shoulder. It typically lasts less than 2 h and responds to analgesics [15]. Moderate or severe pain should raise suspicion for bleeding or biliary leak and indicates the need for further investigation through ultrasound or abdominal CT with contrast.

Bleeding is the most significant complication of liver biopsy and may be subcapsular, intrahepatic, free intraperitoneal hemorrhage or hemobilia. Most severe bleeding occurs within 4 h but may occur up until 1 week after the procedure [16]. Risk factors for severe hemorrhage include older age, more than three biopsy passes, or the presence of cirrhosis or liver cancer [14]. Signs of severe bleeding include abdominal pain and hemodynamic instability. It should be managed with aggressive fluid support and blood transfusions as needed. Vascular embolization and surgical repair are treatment options if the bleeding continues [2]. Percutaneous liver biopsy poses a risk of death, mainly due to bleeding, with a reported mortality rate of approximately 1/10,000 [3].

Additional complications include gall bladder puncture or bile leak, pneumothorax, hemothorax, bowel or kidney perforation, and infection [2]. Biliary leak is usually minor but may require surgery if severe. Pneumothorax or hemothorax may require chest tube drainage. Bowel perforation carries the risk of infection and may require the use of antibiotics. These complications can usually be managed expectantly and supportively. Close observation is required to monitor the need for rapid intervention [3].

Costs

Examples of costs for various methods of liver biopsy are presented in Table 26.3. Percutaneous liver biopsy is the least expensive method comparatively. Additionally, ultrasound guidance has been shown to be both beneficial [17] and cost-effective [18] when performing percutaneous liver biopsies. These figures should be considered examples of relative costs of the different methods rather than typical charges as these will vary considerably between institutions.

Table 26.3 An example of costs[a] of various methods of liver biopsy

Approach	Physician's fees	Hospital fees	Total
Percutaneous US guided/assisted	$1,030[b]	$823[c]	$1,853
Transjugular/ transvenous	$1,355	S596	$1,951
Laparoscopic	$1,635	$1,113[d]	$2,748
Open surgical wedge	$1,885	$596	$2,481

[a]These figures should be considered examples of relative costs of the different methods rather than typical charges because these will vary considerably among institutions.
[b]Includes ultrasound reading fee of $145.
[c]Fees are per 30 min of GL suite time.
[d]Fees are per 30 min of OR time.

Practical Considerations and Conclusion

- Liver biopsy continues to be indicated in cases where noninvasive testing is inconclusive or when histologic information or chemical analysis is required.
- Absolute contraindications to percutaneous liver biopsy include severe coagulopathy, uncooperative patient, or serious illness. Relative contraindications include a difficult body habitus, presence of abdominal adhesions, or known vascular hepatic lesions.
- All antiplatelet medications (e.g., aspirin, clopidogrel, IIb/IIIa receptor antagonists, and NSAIDs) should be discontinued at least 7–10 days prior to liver biopsy and may be restarted 48–72 h after liver biopsy.
- All anticoagulant medications should be discontinued prior to liver biopsy. Warfarin should be stopped at least 5 days prior, and heparin should be discontinued at least 12–24 h prior. Warfarin can be restarted the day following liver biopsy.
- Complications of percutaneous liver biopsy usually occur shortly following the procedure and include pain, bleeding, and nearby visceral organ damage.

References

1. Campbell MS, Reddy KR. The evolving role of liver biopsy. Aliment Pharmacol Ther. 2004;20:249–59.
2. Bravo AA, Sheth SG, Chopra SC. Liver biopsy. N Engl J Med. 2001;344(7):495–500.
3. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD. Liver biopsy, AASLD position paper. Hepatology. 2009;49(3):1017–44.
4. Siegel CA, Suriawinata AA, Silas AM, Van Leeuwen DJ. Liver biopsy 2005: when and how? Cleve Clin J Med. 2005;72(3):199–201.
5. Thampanitchawong P, Piratvisuth T. Liver biopsy: complications and risk factors. World J Gastroenterol. 1999;5:301–4.
6. Jacobs WH, Goldberg SB. Statement on outpatient percutaneous liver biopsy. Dig Dis Sci. 1989;34:322–3.
7. Howard R, Karageorge G, van Harselaar K, Bell M, Basford P, Schultz M, et al. Post-procedure surveillance in liver biopsy: how long is long enough? N Z Med J. 2008;121(1280):8–14.
8. Lip GYH, Douketis JD. Perioperative management of patients receiving anticoagulants. In: LLK L, editor. UpToDate. Waltham: UpToDate. Accessed on 28 Feb 2016.
9. Sporea I, Popescu A, Sirli R, et al. World J Gastroenterol. 2008;14(21):3396–402.
10. Arora G. Percutaneous liver biopsy. eMedicine. 5 Apr 2009. Percutaneous Liver Biopsy Technique. Updated: Oct 12, 2015. Author: Gaurav Arora, MD, MS; Chief Editor: Kurt E Roberts, MD

11. Guido M, Rugge M. Liver biopsy sampling in chronic viral hepatitis. Semin Liver Dis. 2004;24:89–97.
12. Adams T, Lewis JH. Percutaneous liver biopsy. Clin Perspect Gastroenterol. 2002;2:117–21.
13. Froehlich F, Lamy O, Fried M, Gonvers JJ. Practice and complications of liver biopsy. Results of a nationwide survey in Switzerland. Dig Dis Sci. 1993;38(8):1480–4.
14. Piccinino F, Sagnelli E, Pasquale G, Giusti G. Complications following percutaneous liver biopsy: a multicentre retrospective study on 68,276 biopsies. J Hepatol. 1986;2:165–73.
15. Montalto G, Soresi M, Carroccio A, et al. Percutaneous liver biopsy: a safe outpatient procedure? Digestion. 2001;63:55–60.
16. Terjung B, Lemnitzer I. Bleeding complications after percutaneous liver biopsy, an analysis of risk factors. Digestion. 2003;67:138–45.
17. Lindor KD, Bru C, Jorgensen RA, et al. The role of ultrasonography and automatic-needle biopsy in outpatient percutaneous liver biopsy. Hepatology. 1996;23:1079–83.
18. Younossi ZM, et al. Ultrasound-guided liver biopsy for parenchymal liver disease: an economic analysis. Dig Dis Sci. 1998;43(1):46–50.

27 Instruments and Accessories for Endoscopic Retrograde Cholangiopancreatography (ERCP)

Jai Eun Lee and Sumanth Daram

Background

Since its inception in 1968, endoscopic retrograde cholangiopancreatography (ERCP) has advanced as an important diagnostic and therapeutic procedure for patients with various benign and malignant pancreatic and biliary tract diseases. ERCP is a widely practiced procedure in hospitals across the world. Successful and safe practice of ERCP requires not only well trained and experienced endoscopists but also a team of dedicated nurses and technicians. The endoscopist should have a solid fundamental knowledge of the indications, unique features, safety, and complications of individual instruments and accessories utilized in the procedure. This chapter aims to provide the most up-to-date information on essential equipment for ERCP. This information includes equipment's usage, different available types, advantages and disadvantages of various features, and safety.

Instruments and Accessories

Endoscopes

For diagnostic and therapeutic ERCP procedures, a side-viewing duodenoscope is routinely used in adult patients as well as pediatric patients weighing over 10 kg. The therapeutic duodenoscopes have an elevator which allows for different maneuvers to cannulate the papilla. Also, they have a large working channel with diameter of 4.2 mm which can be used for large accessory devices. In some cases, this feature facilitates simultaneous use of two guidewires/catheters [2]. The smaller-caliber diagnostic duodenoscope also has an elevator, but the working channel is smaller at 2.8 mm/3.2 mm. Smaller pediatric duodenoscopes available with a 2.0-mm channel may be necessary in case of examination of neonates. At the time of publication, to the authors' best knowledge, the diagnostic and neonatal duodenoscopes are no longer commercially available. Standard forward-viewing endoscopes such as gastroscopes, colonoscopes, and enteroscopes (with or without balloon/device assistance) may occasionally be used to accomplish ERCP in patients with surgically altered anatomy such as those resulting from a Whipple procedure, Roux-en-Y gastric bypass, or Billroth II gastrectomy; these endoscopes facilitate intubation of the afferent loop [10].

Practical Considerations

- Diagnostic and neonatal duodenoscopes are no longer commercially available.
- Forward-viewing endoscopes such as gastroscopes, colonoscopes, and enteroscopes (with or without balloon/device assistance) may need to be used to accomplish ERCP in surgically altered anatomy.

Contrast Agents

The contrast media currently used for ERCP are all hydrophilic benzoic acid derivatives and can be grouped into four different categories including ionic monomer, ionic dimer, nonionic monomer, and nonionic dimer. The media can also be classified as either high-osmolality contrast media (HOCM) or low-osmolality contrast media (LOCM). These two types appear to produce similar image quality [19]. Because of its low cost, high-osmolality contrast media have become the standard agent for ERCP [17]. The injection technique affects the quality of image, while the contrast media viscosity influences the ease of injection through

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small-diameter catheters [20]. For image of strictures and pancreatic duct anatomy, full-strength contrast can give a better quality. In contrast, for small stones within large ducts, dilute contrast may be better. Diluting contrast, however, has potential disadvantages of increased volumes needed and introduction of air during syringe changes. For potential safety of use, low-osmolality media had been proposed as safer option. This is based on the theory that reduced osmotic fluid shifts across ductal mucosa and pancreatic acini lead to a lesser magnitude of increase in intraductal pressures. This proposed advantage of low-osmolality media has not been supported by studies with evidence for advocating the use of low-osmolality agents to decrease ERCP complications. The rise in serum iodine concentration with injection of contrast media during ERCP is about 1/100 of intravenous administration [18]. The systemic iodine load from diagnostic ERCP is about 0.6% of that from coronary angiograms [21]. In studying the risk of post-ERCP pancreatitis comparing HOCM with LOCM, a meta-analysis showed no statistically significant difference [11].

Adverse reactions to contrast media in ERCP are categorized to either idiosyncratic or non-idiosyncratic [9]. Acute reactions can be rated minor, intermediate/moderate, or severe with the minor reactions being mostly self-limiting and not requiring therapy, intermediate reactions responding well to supportive care, and severe reactions requiring immediate resuscitative efforts [22]. There can be delayed reactions seen between 1 h and 7 days after the contrast injection. The incidence of delayed reactions is between 2 and 8% [22]. LOCM has lower prevalence of intravenous contrast media reaction than HOCM [26].

In terms of prophylaxis against adverse reactions to contrast exposure during ERCP procedures, there is no evidence-based standard of practice. Hence, current clinical practices follow recommendations for intravenous contrast media [20]. One survey done with 42 physicians showed that 8% of physicians had personal experience with a suspected contrast media reaction at ERCP and 83% used prophylaxis in patients with a prior reaction or food allergies [8]. The American College of Radiology recommends several regimens for prophylaxis for reactions to intravenous contrast media; however, these have not been studied for ERCP. Following are frequently used regimens: (1) prednisone, 50 mg by mouth at 13 h, 7 h, and 1 h before contrast media, plus 50-mg diphenhydramine intravenously, intramuscularly, or by mouth 1 h before the contrast injection and (2) methylprednisolone, 32 mg by mouth 12 h and 2 h before contrast medium injection with an antihistamine that can be added similar to regimen 1 [3]. While there are no definitive guidelines backed by high-quality evidence, various prophylactic regiments are routinely used prior to ERCP in patients with history of previous reaction to intravascular contrast agents. Not uncommonly, prophylaxis is administered to patients with no prior reaction to intravascular contrast media who are thought to be at increased risk (e.g., shellfish allergy). A large-scale prospective study reported extremely low incidence of adverse reaction to HOCM injected during ERCP procedure without prophylactic premedication. The incidence was low even in patients with prior severe reaction to intravascular contrast agents, suggesting that the use of prophylactic regiments prior to ERCP appears to be unnecessary [9]. In their practice, the authors do not routinely premedicate patients with history of allergy to intravenous contrast agents. In summary, in spite of the absence of evidence that exposure to contrast media during ERCP is associated with significant incidence of adverse effects, isolated individual cases cannot be ruled out. Therefore, awareness of this possibility and close monitoring of the patient preparedness for emergency therapy are necessary [20].

Practical Considerations

- High-osmolality contrast media (HOCM) and low-osmolality contrast media (LOCM) produce similar image quality.
- For image of strictures and pancreatic duct anatomy, full-strength contrast can give a better quality.
- Risk of post-ERCP pancreatitis comparing HOCM with LOCM has been shown to be identical in a meta-analysis.
- LOCM has lower prevalence of intravenous contrast media reaction than HOCM.
- In the context of adverse reactions to contrast agents, the use of prophylactic regiments prior to ERCP appears to be unnecessary; no definitive evidence-based guidelines exist.

Cannulation Devices

Standard Cannulation Catheters

In diagnostic and therapeutic ERCP procedures, selective cannulation of the duct of interest is one of the major steps. Various instruments have been developed to better facilitate this step, especially selective common bile duct cannulation. The standard cannulation catheters are generally made of Teflon material and available in different tip sizes and configurations, lengths, and number of available lumens. The most common choice for standard ERCP cannulation catheters is 5–7 Fr in caliber, with tips that usually taper to 3–5 Fr. The tips can be straight, tapered, or rounded in configuration. These catheters allow for up to a 0.035-in. guidewire [2].

Cannulation catheters are available in single-, double-, and triple-lumen types with the double-lumen and triple-lumen types having an advantage of contrast injection without

removal of the guidewire. The contrast material can be injected through one lumen via a Luer lock connection on the catheter handle, while the guidewire can be passed through the other lumen. In triple-lumen catheters, two ports are designed for contrast material injection with the third port for the guidewire. Another design with a Tuohy-Borst adapter gives a similar advantage with the adapter as a common port for both contrast material injection and guidewire passage [15]. For better facilitation of biliary cannulation or selective entry into either the right or left hepatic duct, the Swing-tip catheter (Olympus America Inc., Central Valley, Pa.) may be helpful. With this type of cannulation catheters, the cannula tip can be bent in either the up-down or left-right directions [2]. The cannulation of minor papilla can be approached with various cannulation devices including standard cannulation catheters, smaller-tipped devices, or special blunt-tipped needle catheters specifically designed for minor papilla cannulation. The smaller-tipped devices are ultra-tapered tip catheters with or without a 0.018- or 0.021-in. hydrophilic guidewire [15]. A comprehensive list of available cannulation catheters is featured in ASGE's technology status evaluation report on ERCP cannulation and sphincterotomy devices.

Sphincterotomes (Papillotomes)

Designed for biliary sphincterotomy, a sphincterotome features an electrosurgical cutting wire at the distal end of a Teflon catheter with a monopolar power source connected to the catheter (Fig. 27.1). The catheter contains the wire with 2–3 cm of exposed wire exiting at a variable distance from the tip [2]. A retractable plunger on the control handle of the sphincterotome gives the ability to flex the catheter tip upward while pulling on the cutting wire. This flexion of the catheter tip allows aligning the cutting wire and maintaining contact of the wire with the papilla. The manipulation of the sphincterotome tip by the cutting wire also facilitates alignment of the tip in the proper axis for cannulation of the duct. Sphincterotomes

Fig. 27.1 Sphincterotomes (Permission for use granted by Cook® Medical, Bloomington, Indiana)

are being increasingly used as the primary biliary cannulation device since sphincterotomy is performed in many of the ERCP procedures. The ability to flex the sphincterotome thereby varying the angle of cannulation enhances the ability to achieve successful deep cannulation of the duct of interest. Randomized trials have been performed comparing cannulation using the standard cannulation catheters versus using the sphincterotomes. The studies have shown the cannulation rate of 84–97% with sphincterotomes compared to rate of 62–67% with standard cannulation catheters [24] [6].

The sphincterotomes are available in different tip configurations and lengths as well as in double-lumen or triple-lumen devices. The tip lengths, which can range from 3 to 20 mm, indicate the distance between the distal end of the sphincterotome and the distal attachment of the cutting wire. The cutting wire length ranges from 15 to 35 mm with a monofilament configuration. There are some sphincterotomes available with an insulating sleeve on the proximal half of the cutting wire. This feature facilitates prevention of short-circuiting of the power in case the wire is in contact with the endoscope and of causing inadvertent thermal injury of the overhanging duodenal mucosa during the sphincterotomy. There are also some hybrid sphincterotomes available with a built-in, 11.5-mm stone extraction balloon (Stonetome, Boston Scientific) [15]. ASGE's technology status evaluation report on ERCP cannulation and sphincterotomy devices shows a list of available sphincterotomes and precut devices.

In contrast to the single-lumen device, the double-lumen and triple-lumen devices offer different advantages for performing cannulation and therapeutic interventions. The double-lumen device allows for either injection of contrast or introduction of guidewire [15]. With an additional port, the triple-lumen device facilitates injection of contrast while keeping the guidewire in place. For the cutting wire, there are various generator currents available including cutting, auto-cut, coagulation, and blended. Limited data have shown a lower risk of post-ERCP pancreatitis with the use of a pure cutting current. Pure cutting current is also often used for pancreatic sphincterotomy due to reduced risk of pancreatic duct injury and subsequent stenosis. Using an auto-cut mode is thought to reduce the risk of procedure-related bleeding as well as to eliminate the "zipper-cut" phenomenon [2].

Surgically Altered Anatomy

Performing ductal cannulation in patients with surgically altered anatomy due to prior surgeries including Billroth II or Roux-en-Y can be challenging. It requires passing through an afferent limb to reach the ampulla. In a study of cannulation and papillotomy in 24 patients with previous Billroth II gastrectomy, a wire-guided Billroth II papillotome which was designed with a cutting wire in the opposite direction compared to the standard sphincterotomes was used. This

study demonstrated that the papillotomy was successful using the guidewire Billroth II papillotome without complications [27]. Another study examined using an S-shaped sphincterotome for patients with previous Billroth II or Roux-en-Y reconstruction. A modified catheter with the cutting wire that winds around the catheter at a pivotal point between the catheter's proximal and distal holes was used. This allows the catheter tip to be forced into an S shape when the wire is pulled [13]. Another special tool for these challenging cases with altered anatomy is a rotatable sphincterotome. One case series with limited sample size of patients with bile duct stones and previous Billroth II gastrectomy attempted sphincterotomy using a rotatable papillotome with 89% success rate [16].

Access Papillotomy Catheters (Precut)

Access (precut) papillotomy may be performed by incising the papilla after a failed attempt at deep ductal cannulation using the standard methods. One of the common devices used for a precut papillotomy is a needle-knife catheter with a retractable electrosurgical cutting wire (Fig. 27.2). The needle-knife catheters are available in different tip lengths and single-, double-, or triple-lumen configurations. Once the catheter is passed through the endoscope and is placed in the position in the lumen, the wire can be projected forward from the distal end of the catheter using the control handle. The endoscopist can cut the targeted tissue with the exposed needle, which is in contact with the mucosa, while activating the electrosurgical current and manually moving the catheter and the endoscope [15]. An Erlangen-type papillotome which is similar to the standard traction-type sphincterotome can be used to perform access papillotomy. This device has an ultrashort, 5-mm-long, monofilament cutting wire with less than 1-mm catheter tip distal to the wire [15].

Another instrument for access papillotomy is a catheter with a small scissor cutting mechanism at its tip. The papillotomy is performed with the lower blade placed into the papillary orifice and closing the scissor with the control handle. One small case series showed that in 8 of 12 patients, scissor precut facilitated common bile duct cannulation when used if at least four attempts to cannulate the common bile duct with standard methods were unsuccessful. No complications were reported in this study [12].

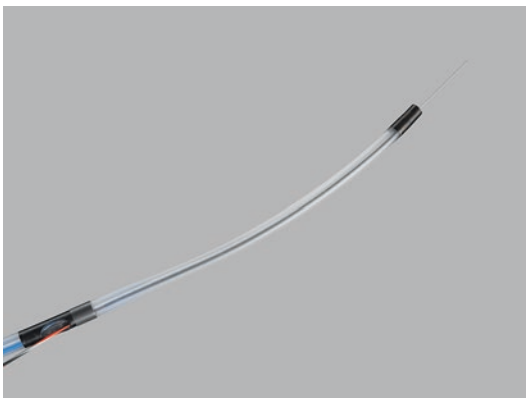

Fig. 27.2 Needle knife (Permission for use granted by Cook® Medical, Bloomington, Indiana)

Practical Considerations

- Cannulation catheters are available in single-, double-, and triple-lumen types.
- Studies have shown the cannulation rate of 84–97% with sphincterotomes compared to rate of 62–67% with standard cannulation catheters.
- Using an auto-cut mode for sphincterotomy is thought to reduce the risk of intraprocedural bleeding as well as to eliminate the "zipper-cut" phenomenon.
- Billroth II papillotome, S-shaped papillotome, and a rotatable papillotome are available to facilitate selective ductal cannulation in patients with altered surgical anatomy.

Guidewires

During diagnostic and therapeutic ERCP procedures, guidewires are important tools for achieving selective biliary, pancreatic, cystic, or intrahepatic duct access as well as antegrade passage during combined "rendezvous" procedures [25]. They are often times useful not only for sphincterotomy but also necessary for traversing strictures, stricture dilation, cytology tissue sampling, and stent placement. The choice of guidewires can depend on the type of maneuvers to be accomplished during the procedure. Gaining access through tight strictures in the biliary ducts or pancreatic ducts can be better supported by the guidewires with slippery and flexible leading tips. On the other hand, for advancing devices including biliary stents, the guidewires that are more stiff and taut are better suited while minimizing lateral deviation and maintaining the forward axial transmission of forces [2].

Currently, different guidewires are available in various materials, lengths, diameters, and designs for ERCP procedures. The guidewire configurations can be either straight or angled with J-shaped tips. For the guidewire designs, there are three general types including monofilament wires, coiled wires, and coated/sheathed wires. The monofilament guidewires are made of stainless steel and designed for rigidity. The coiled guidewires have an inner monofilament core for stiffness and an outer spiral coil made of stainless steel for flexibility. In addition, most of the coiled guidewires are

coated with Teflon, which minimizes resistance while facilitating traversing tortuous strictures. Lastly, other coated or sheathed wires can be made up of a monofilament core of stainless steel or nitinol and an outer sheath of Teflon, polyurethane, or another polymer [2].

The diameters for the guidewires range from 0.018 to 0.035 in., and the lengths can be from 260 to 480 cm with the ones longer than 400 cm mainly used for "long-length" exchange of devices [14] [2]. The guidewires are available in various types such as conventional, completely hydrophilic, or combination (hybrid) wires. The data regarding relative efficacy of specific type of wires are limited [2].

Maintaining the wire position is essential while performing different maneuvers safely with over-the-wire devices including dilators and stents. This can be achieved with using the wires with graduated or continuous markings for visual endoscopic measurement or movement detection and with stabilizing the proximal end of the wire on an immobile accessory device [2].

Pancreatic and Biliary Stents

For evaluation and treatment for biliary and pancreatic ducts, either plastic or metal stents are available and can be used therapeutically for obstructed bile ducts or pancreatic ducts, or for ductal leakage, or to prevent post-ERCP pancreatitis. Following is an overview of different aspects of plastic stents and metal stents.

Plastic Stents

Plastic stents made mainly composed of polyethylene or Teflon and radiopaque with additional markers either proximally or distally on some. Diameter for plastic biliary stents ranges from 5 to 12 Fr, while the length ranges from 1 to 18 cm. Some of the stents with large diameter require a larger accessory channel on the endoscope, specifically a 3.7-mm channel for 10-Fr stents and a 4.2-mm channel for 11.5-Fr or larger caliber stents. Plastic biliary stents are available in various configurations, including pigtail stents and flanged stents (Fig. 27.3). There are single or double pigtail stents with either one or both ends coiled and side holes along the curved pigtail [23]. Double pigtail configuration helps with preventing both proximal and distal migration. The stents with this configuration are frequently used for difficult bile duct stones or hilar strictures which have higher rate of stent migration. Straight "Amsterdam"-type stents are also available and frequently used for biliary drainage [2].

Plastic pancreatic stents are mainly made of polyethylene materials. The diameter of the stents ranges from 3 to 11.5 Fr, and the length ranges from 2 to 25 cm. There are various configurations available with straight, curved, wedge, or single pigtail designs [23]. The choice of the stents with particular designs depends mostly on the desired duration of the stent. Most of the stents have a type of mechanism to prevent internal migration. The stents with an internal flange may be used for the purpose of prolonged stenting, while the ones with no internal flange may be used for short-term stenting leading to spontaneous migration, such as when used for prophylaxis against post-ERCP pancreatitis. Different ways to improve stent patency have been studied in the past. Studies show that a straight configuration can be helpful, while others including eliminating side holes, changing stent material, or coating the inner surface with a hydrophilic substance have not been proven to be successful [4] [7]. The stents can be removed using a number of different tools including snares, baskets, and foreign body forceps. Stents with large diameter greater than 10 Fr can be removed with a standard polypectomy snare. A foreign body forceps or standard biopsy forceps can be used to remove small 3- or 5-Fr pancreatic stents [2].

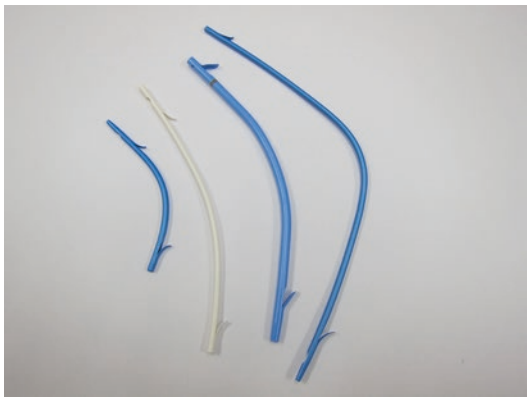

Fig. 27.3 Various biliary and pancreatic stents

Self-Expandable Metal Stents

Self-expandable metal stents (SEMS) with generally larger diameter than the plastic stents offer advantage of prolonged stent patency and reduction of recurrent obstruction. While SEMS conventionally were used in patients with a known diagnosis of malignancy, there has been increasing usage of SEMS for benign indications including refractory/persistent benign biliary strictures and for novel indications such as the creation of a choledochoduodenostomy or hepaticogastrostomy. The metal alloys used for the metal stents allow for radial expansile force while providing flexibility to conform to the duct. The diameters for the SEMS range from 6 to 10 mm with the lengths ranging from 4 to 12 cm [23]. There are three different types of SEMS available including uncovered, partially covered, or fully covered types. Material such as polytetrafluoroethylene, polytetrafluoroethylene/fluorinated ethylene propylene, or silicone membranes is used to make the coverings. The endoscopist can make selective

choices for which type of SEMS to use depending on the clinical situation of each case. For the removal of the stents, a snare or a foreign body retrieval forceps can be used to remove fully covered or some partially covered SEMS [2]. On the other hand, uncovered stents can be difficult to remove in case of tumor ingrowth or benign tissue hyperplasia [5].

Stone Extraction Devices

Two main basic stone extraction devices including extraction balloon catheters and basket catheters are used for stone extraction. After endoscopic sphincterotomy or balloon dilation of the ampulla, the common bile duct stones can be extracted using either of these devices. The balloon catheters and baskets have different structural and functional features unique to each one. The extraction balloon catheters have a round balloon near the tip, which can be inflated with air to preset sizes, and they can have either triple lumen or double lumen (Fig. 27.4). Triple-lumen balloon catheters which have different lumens for air for balloon inflation, guidewire, and contrast injection are more recently available [1]. The port for contrast material injection can be either proximal or distal to the balloon position in different extraction balloon catheters. Confirmation of duct clearance during a balloon sweep and occlusion cholangiogram is commonly performed using an extraction balloon which has the contrast material port distal to the balloon. However, having the contrast injection port proximal to the balloon position can facilitate stone visualization during extraction and evaluation of distal duct anatomy [1]. Most commonly, these extraction balloons are used to pull out stones and sludge from the biliary and pancreatic ducts into the small bowel. During this process, "balloon sweep," the balloon catheter is advanced over the guidewire, the balloon is inflated proximal to the stone, and then the catheter is pulled with the inflated balloon. Before advancing the balloon catheter in the duct, the balloon should be tested to ensure correct inflation [2]. Although extraction balloons are widely used, there is not much research data comparing different balloons and their efficacy [1].

Metal wire baskets are other most commonly used device for stone extraction and are available in different sizes and configurations. A Dormia basket is a common configuration, which has four wires radially at 90° intervals (Fig. 27.5). Spiral baskets and flower baskets are the other two configurations involving more than four wires and used for retrieving smaller stone fragments. Some basket devices are compatible with lithotripsy. Both extraction balloons and basket devices are generally safe in practice although there should be caution against excessive force, which can increase the risk of complications including bleeding and perforation. In comparison to extraction balloons, use of wire baskets carries risk of having the basket trapped in the duct by capturing stones that are too large for extraction. This complication is a rare medical emergency which may require rescue lithotripsy among other various endoscopic or surgical managements [1].

Final Words

- ERCP is a very commonly performed procedure worldwide.
- The armamentarium for successful and safe performance of ERCP is extensive.
- Physicians performing ERCP should be well versed with various types of available accessories and gear themselves for newer ones as they become available.

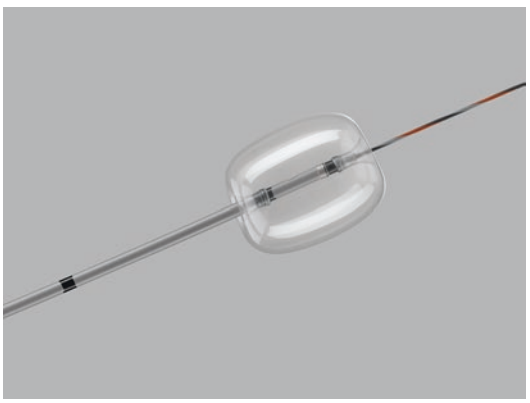

Fig. 27.4 Extraction balloons (Permission for use granted by Cook® Medical, Bloomington, Indiana)

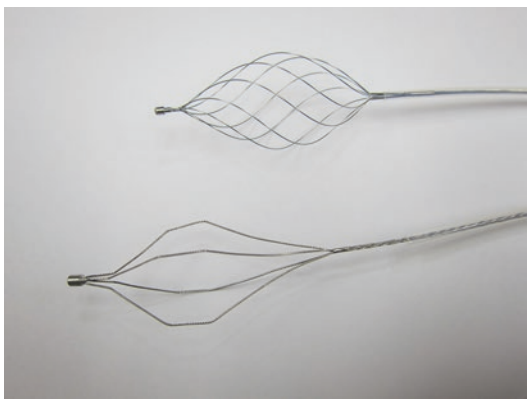

Fig. 27.5 Memory Basket® Eight Wire and Memory Basket® Soft Wire by Cook® Medical (Permission for use granted by Cook® Medical, Bloomington, Indiana)

References

1. Adler DG, et al. Biliary and pancreatic stone extraction devices. Gastrointest Endosc. 2009;70(4):603–609.
2. Ahlawat SK, Al-Kawas FH. Endoscopes, guidewires and accessories. In: ERCP s.l. Philadelphia: Elsevier; 2008. p. 31–42.
3. American College of Radiology Committee on Drugs and Contrast Media. Manual on contrast media. 5.0 ed. Reston: ACR; 2004.
4. Catalano MF, et al. "Tannenbaum" teflon stents versus traditional polyethylene stents for treatment of malignant biliary stricture. Gastrointest Endosc. 2002;55(3):354–8.
5. Cheng JL, et al. Endoscopic palliation of patients with biliary obstruction caused by nonresectable hilar cholangiocarcinoma: efficacy of self-expandable metallic Wallstents. Gastrointest Endosc. 2002;56(1):33–9.
6. Cortas GA, Mehta SN, Abraham NS, Barkun AN. Selective cannulation of the common bile duct: a prospective randomized trial comparing standard catheters with sphincterotomes. Gastrointest Endosc. 1999;50(6):775–9.
7. Costamagna G, et al. Hydrophilic hydromer-coated polyurethane stents versus uncoated stents in malignant biliary obstruction: a randomized trial. Gastrointest Endosc. 2000;51(1):8–11.
8. Draganov PV, Cotton PB. Iodinated contrast sensitivity in ERCP. Am J Gastroenterol. 2000;95(6):1398–401.
9. Draganov PV, Forsmark CE. Prospective evaluation of adverse reactions to iodine-containing contrast media after ERCP. Gastrointest Endosc. 2008;68(6):1098–101.
10. Enestvedt BK, et al. Devices and techniques for ERCP in the surgically altered GI tract. Gastrointest Endosc. 2016;83(6):1061–1075.
11. George S, et al. Role of osmolality of contrast media in the development of post-ERCP pancreatitis: a metaanalysis. Dig Dis Sci. 2004;49(3):503–8.
12. Heiss FW, Cimis RSJ, MacMillan FPJ. Biliary sphincter scissor for precut access: preliminary experience. Gastrointest Endosc. 2002;55(6):719–22.
13. Hintze RE, Veltzke W, Adler A, Abou-Rebyeh H. Endoscopic sphincterotomy using an S-shaped sphincterotome in patients with a Billroth II or Roux-en-Y gastrojejunostomy. Endoscopy. 1997;29(2):74–8.
14. Jacob L, Geenen JE. ERCP guidewires. Gastrointest Endosc. 1996;43(1):57–60.
15. Kethu SR, et al. ERCP cannulation and sphincterotomy devices. Gastrointest Endosc. 2010;71(3):434–45.
16. Kim GH, et al. Endoscopic removal of bile-duct stones by using a rotatable papillotome and a large-balloon dilator in patients with a Billroth II gastrectomy. Gastrointest Endosc. 2008;67(7):1134–8.
17. Kimmey MB, et al. Technology assessment status evaluation. Radiographic contrast media used in ERCP. Gastrointest Endosc. 1996;43(2):647–51.
18. Mann K, et al. Systemic iodine absorption during endoscopic application of radiographic contrast agents for endoscopic retrograde cholangiopancreaticography. Eur J Endocrinol. 1994;130(5):498–501.
19. Martin DF, et al. Diagnostic quality in endoscpic retrograde cholangiopancreatography: comparison between lodiaxol and lopromide. Endoscopy. 2000;32(10):783–7.
20. Mishkin D, et al. ASGE technology status evaluation report: radiographic contrast media used in ERCP. Gastrointest Endosc. 2005;62(4):480–4.
21. Monig H, et al. Iodine absorption in patients undergoing ERCP compared with coronary angiography. Gastrointest Endosc. 1999;50(1):79–81.
22. Morcos SK, Thomsen HS. Adverse reactions to iodinated contrast media. Eur Radiol. 2001;11(7):1267–75.
23. Pfau PR, et al. Pancreatic and biliary stents. Gastrointest Endosc. 2013;77(3):319–27.
24. Schwacha H, et al. A sphincterotome-based technique for selective transpapillary common bile duct cannulation. Gastrointest Endosc. 2000;52(3):387–91.
25. Somogyi L, et al. Guidewires for use in GI endoscopy. Gastrointest Endosc. 2007;65(4):571–6.
26. Valls C, Andia E, Sanchez A, Moreno V. Selective use of low-osmolality contrast media in computed tomography. Eur Radiol. 2003;13(8):2000–5.
27. Wang YG, et al. A new guide wire papillotome for patients with Billroth II gastrectomy. Endoscopy. 1996;28(2):254–5.

Minor Papilla Cannulation and Endotherapy

28

Alexander Larson and Bret T. Petersen

Introduction

Most efforts to perform pancreatography for assessment of leaks, constriction, filling defects, or irregularity due to chronic pancreatitis are pursued through the major papilla at the ampullary junction with the bile duct. Endoscopic cannulation of the minor papilla is performed (a) when symptoms or imaging studies warrant attempts to diagnose and potentially treat anatomic variations of the pancreatic ductal system and (b) when access to the ventral duct at the major papilla fails or is inadequate to accomplish diagnostic or therapeutic goals in the upstream main duct. The normal development of pancreatic ductal anatomy occurs during the eighth week of gestation with the fusion of the ventral and dorsal pancreas and their respective ducts, resulting in formation of the main pancreatic duct which drains from the dorsal body and tail through the ventral duct of Wirsung in the head to the major papilla and the duodenum. The short segment of dorsal duct extending from the junction between the dorsal and ventral ducts at approximately the genu to the minor papilla becomes the accessory duct or duct of Santorini. The accessory duct and the minor papilla may be patent or only vestigial, without an appreciable lumen.

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Indications

Diagnosis and Therapy for Anatomic Variants in Ductal Anatomy

Several anatomic variants in ductal anatomy can develop within the pancreatic head in the course of embryogenesis. Some of them have been held responsible for clinical symptoms of acute recurrent or chronic pancreatitis. The most common variant is pancreas divisum, which results from complete or partial failure of fusion between the dorsal and ventral ducts, yielding separate duodenal drainage of the dorsal and ventral sectors, through the minor and major papillae, respectively (Fig. 28.1a, b). This anatomic variation occurs in approximately 10% of the general population, though rates vary among ethnic groups worldwide, ranging from 3 to 22% [1, 2]. Of those with pancreas divisum, 15% express the incomplete variation characterized by a very diminutive ductal connection between the dorsal and ventral pancreatic ducts. The majority of patients with pancreas divisum are asymptomatic, though approximately 5% experience recurrent mild to severe pancreas-type pain, recurrent acute pancreatitis, or dorsal chronic obstructive pancreatitis.

The etiology of clinical syndromes commonly attributed to anomalous ductal anatomy is presumed to be increased pressure within the dorsal duct as a result of normal active secretion meeting resistance to flow at the smaller caliber of the minor papilla. The infrequency of symptoms among patients with pancreas divisum suggests other factors may contribute to the development of recurrent pancreatitis and pain. Possible contributing cofactors include associated minor papilla stenosis, alcohol toxicity, autoimmune pancreatitis, and genetic mutations. At least one allele for a CFTR mutation has been noted in 10–20% of patients with pancreas divisum who experience recurrent pancreatitis [3]. Additionally, patients in this cohort have been identified to carry a higher frequency of SPINK1 mutation than is found

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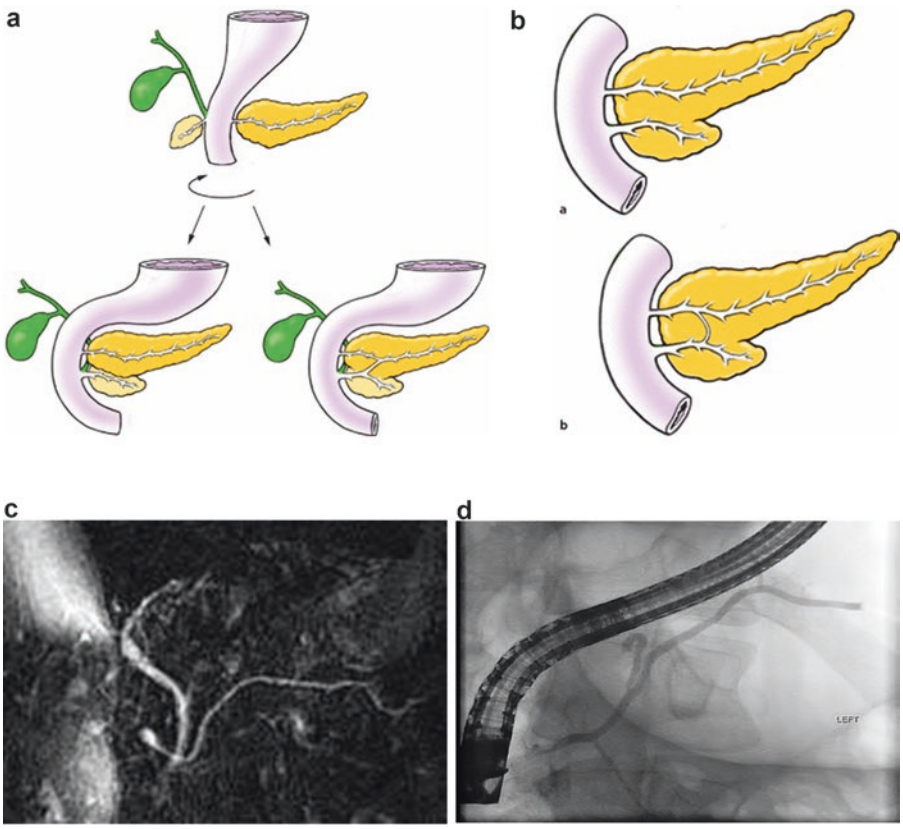

Fig. 28.1 (**a**) Graphic of normal pancreatic duct formation, (**b**) graphic of pancreas divisum, (**c**) MRCP of pancreas divisum with demonstration of Santorinicele, (**d**) ERCP via minor papilla demonstrating dorsal duct in pancreas divisum

in healthy controls [4]. The occurrence of pancreatitis among patients with these genetic mutations is not universal; hence, they are often referred to as enabling factors rather than causative factors. These findings suggest that symptomatic pancreas divisum is a multifactorial process. Whether therapeutic efforts directed predominantly at the ductal anatomy are efficacious remains controversial.

Pancreas divisum may be suspected or recognized incidentally during abdominal cross-sectional imaging or endoscopic retrograde cholangiopancreatography for other conditions, or it can be identified by intent when evaluating causes for the conditions noted above. Dominant dorsal duct drainage via the minor papilla may be suspected during any cross-sectional imaging modality, including computed tomography, magnetic resonance imaging (MRI), MR cholangiopancreatography (MRCP) (Fig. 28.1c), and endoscopic ultrasonography (EUS).

Secretin-enhanced MRCP (S-MRCP), with reported sensitivity, specificity, positive predictive, and negative predictive values of 73%, 97%, 82%, and 95%, respectively, is the preferred imaging technique for identification of this anatomic variant [5]. Timed early and delayed S-MRCP imaging of the dorsal duct subsequent to secretin administration has been studied as a means of characterizing whether a given patient with this common anatomic variant demonstrates physiologic changes that might correlate with symptoms [6, 7]. Ductal dilation is a normal response following secretin or meal stimulation. Prolonged ductal dilation beyond statistical norms suggests greater resistance to outflow than is seen in most patients without outflow obstruction. A completely normal timed S-MRCP argues against intervention for presumed obstruction.

A Santorinicele, or cystic dilation at the junction of the accessory duct of Santorini and the duodenum, may also lead to symptoms related to hindered outflow (Fig. 28.1c). A Santorinicele is predominantly symptomatic in the setting of pancreas divisum. This structure is usually evident by EUS or pancreatography via MRCP or ERCP. Therapy generally employs minor papilla sphincterotomy [8–10]. Yet another cause of focal obstruction to drainage at the minor papilla is focal neoplasia at its junction with the duodenal wall.

After imaging has confirmed pancreas divisum in patients with recurrent pancreatitis or severe episodes of pancreas-type pain, endoscopic retrograde cholangiopancreatography (ERCP) (Fig. 28.1c) with minor papilla endoscopic sphincterotomy is often considered as a means to decrease the trans-papillary pressure gradient, thus promoting drainage of the dorsal or main pancreatic ductal system. Pancreatography via the major papilla will demonstrate a tiny to medium-sized ventral system (Fig. 28.2b) without flow to the dorsal duct. The short ventral duct of pancreas divisum must be distinguished from "pseudo-divisum" related to stone, stricture,

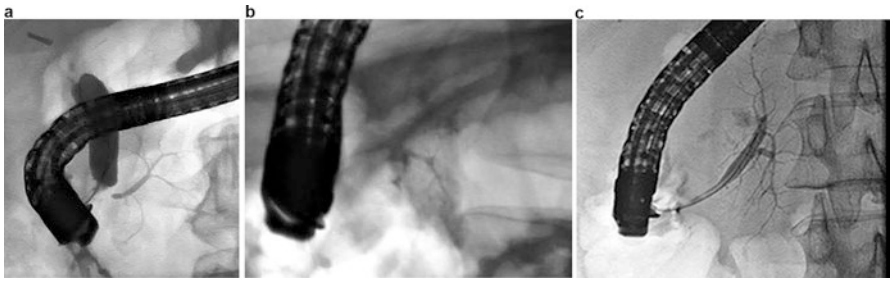

Fig. 28.2 Ventral duct pancreatography from major papilla: (**a**) dilated bile duct and generous ventral pancreatic duct in pancreas divisum, (**b**) diminutive ventral duct with surrounding blur of pancreatic acinarization from over injection, (**c**) ventral ducts in pancreas divisum versus pseudo-divisum related to obstructing stone in head (blush neighboring apex of ventral duct)

or tumor-related obstruction of the main duct near the genu (Fig 28.2c). Due to the inherent challenges with endoscopic identification, cannulation, and endotherapy of the minor papilla as well as potentially high rate of adverse events, the decision to proceed with minor papilla sphincterotomy should not be taken lightly.

Diagnosis and Therapy for Ductal Pathology When Access Through the Major Papilla Fails

Deep access to the ventral and dorsal pancreatic duct from the major papilla may fail even in the absence of anomalous anatomy, due to challenging normal or pathologic conformation of the papilla, the genu, or other segments of the duct. In this setting the region of concern may be accessible for pancreatography or therapy via the minor papilla. This route may prove necessary for any pancreatic ductal imaging, sampling, or therapy. Common situations include ventral duct obstruction by stones or strictures from chronic pancreatitis, requiring minor papilla access to decompress the dorsal duct. On occasion, "rendezvous" access with a wire passed through the major papilla and the ventral duct, then out to the duodenum through the accessory duct and the minor papilla, can facilitate subsequent access through the minor papilla to the dorsal duct [11] (Fig. 28.3a–d). Similarly rendezvous passage of a guidewire into the minor papilla and out the major papilla may enable therapy in the ventral duct or at the major pancreatic sphincter. A third form of rendezvous employs EUS-guided transmucosal puncture of the dorsal pancreatic duct from the stomach followed by passage of a guidewire downstream to the minor or the major papilla [12–14].

Contraindications

The primary contraindications for pursuit of pancreatography and/or therapy at the minor papilla relate to insufficient outcome data for benefit in some clinical syndromes and insufficient experience, skill set, or equipment for safe performance. The strongest data supporting intervention in the setting of pancreas divisum relate to recurrent acute pancreatitis with associated anatomic (duct dilation) or physiologic (secretin-stimulated MRCP) evidence for outflow obstruction. Evidence for benefit in recurrent pain (meal stimulated or random) and for mild chronic pancreatitis is lacking or weak. Cannulation and sphincterotomy of the minor papilla should only be performed in the setting of medical necessity, due to the inherent challenges of the procedure and the potential for severe acute and chronic adverse events, as discussed below.

Indications

- Diagnose and treat pancreas divisum or other anomalous ductal anatomy in patients with acute recurrent pancreatitis or isolated dorsal duct chronic pancreatitis.
- Diagnosis and therapy of Santorinicele in patients with acute recurrent or isolated dorsal duct chronic pancreatitis.
- Characterization and therapy of adenoma of the minor papilla.
- Diagnosis and potential therapy for any ductal pathology suspected of causing clinical symptoms or of contributing to abnormal/pathological clinical imaging, when access through the major papilla is hindered or prevented by failed cannulation, pancreas divisum, ventral duct stricture, or stones.
- Guidewire rendezvous from the minor papilla to the major papilla after failed cannulation of the major papilla, due to stricture, ampullary stenosis, or other non-divisum pancreatic ductal disorders.

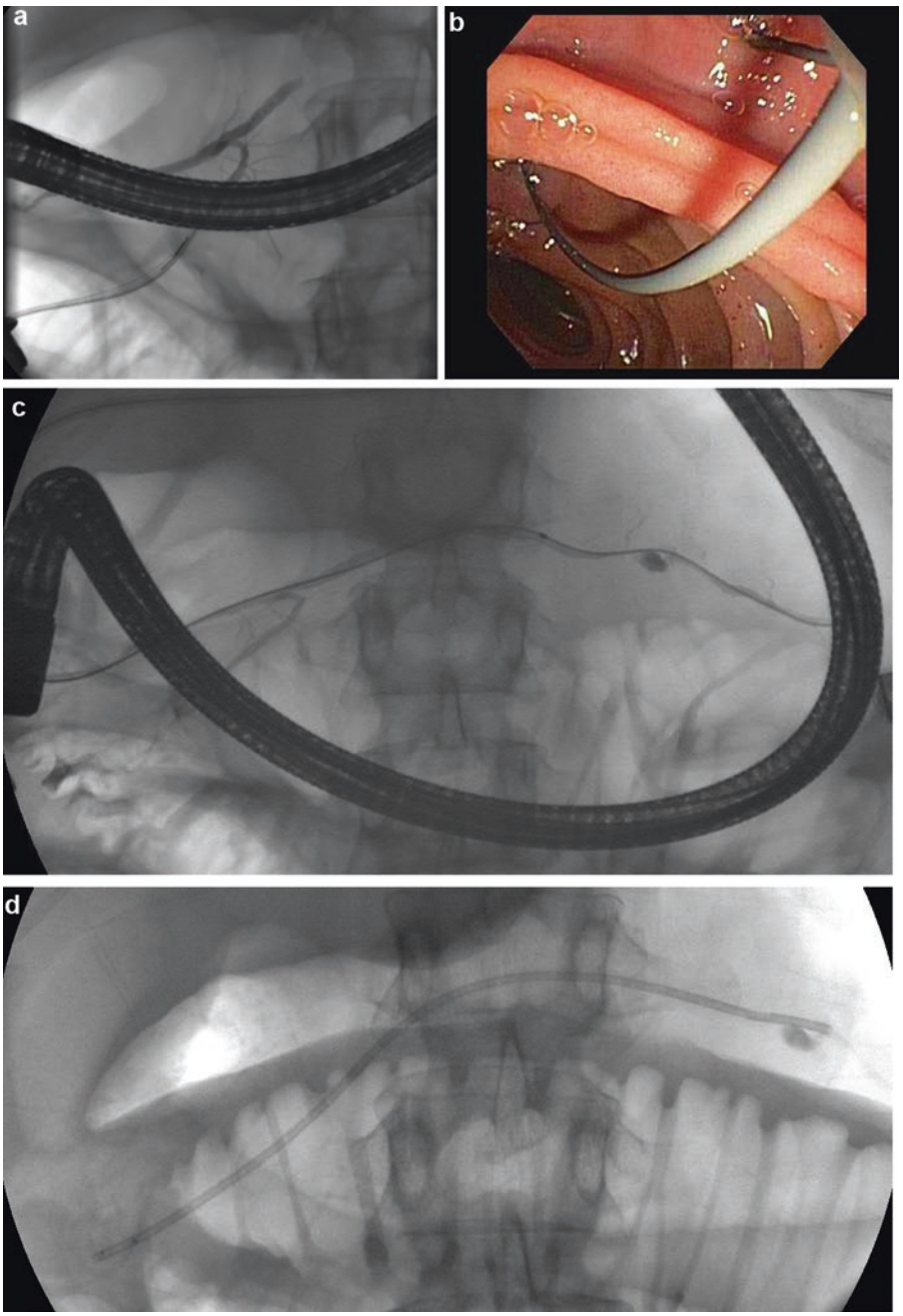

Fig. 28.3 (**a**) Pancreatography via major papilla with angulation at genu preventing upstream filling or access, (**b**) rendezvous wire passed into ventral duct at major papilla and out accessory duct at minor papilla, (**c**) dorsal pancreatography via minor papilla demonstrating leak and stricture in tail, (**d**) stenting via minor papilla for upstream leak and stricture

Contraindications

- Asymptomatic pancreas divisum with normal dorsal duct caliber on cross-sectional imaging
- As treatment for chronic nonspecific abdominal pain or pancreatitis in patients with incidentally identified pancreas divisum
- Endoscopist with lack of appropriate experience in minor ductal cannulation or resources for management of potential complications
- Inadequate endoscopic view of the minor papilla such as the case of adjacent duodenal diverticulum
- Therapeutic or pathological coagulopathy should preclude performance of minor papilla sphincterotomy, but not of cannulation, pancreatography, or stenting

Practical Considerations

- A 0.025″ angled hydrophilic guidewire through a standard flexible sphincterotome is sufficient for access, diagnosis, and therapy in most patients with anomalous drainage and sphincter stenosis.
- The 0.025″ guidewire is often the preferred choice due to the combination of small caliber, adequate rigidity, and radiographic visualization – compared to 0.018″ and 0.035″ guidewires.
- A "standard" 0.035″ wire and sphincterotome suffice for accessing upstream pathology in many patients, allowing transition from the major to minor papilla without additional equipment.
- To minimize equipment selections, availability of the 0.018″ and 0.025″ guidewires and 5-French caliber prophylactic stents will suffice for virtually all patients.
- Tapered-tip catheters are rarely needed, as tapered sphincterotomes offer greater tip control plus therapeutic options.
- The Cramer needle-tip catheter often provides mild dilation of the minor papilla os while confirming its location, thus enabling subsequent deep wire access.

Instruments and Medications

Medications:

- Standard deep sedation or general anesthesia
- Indomethacin suppositories (50 mg × 2), for prophylaxis against post-ERCP pancreatitis
- Glucagon injection for duodenal peristalsis
- Methylene blue or indigo carmine mucosal contrast for localization of the minor papilla
- Secretin injection for stimulation of pancreatic secretion
- Antibiotic administration as for any other route to pancreatography, primarily for likely filling into cystic spaces or through duct leaks to walled-off necrosis

Catheters:

- ERCP-1 Cramer blunt needle-tip catheter (Cook Medical)
- Tapered tip 3–5 French

Dilators:

- Tapered 4–7 French
- 4 mm balloon

Guidewires:

- Hydrophilic guidewires from 0.018″ to 0.035″ French with straight and angled tips

Sphincterotomes:

- 4 and 5 French pull-type short-tip sphincterotomes with 20–25 mm cutting wire
- Needle knife with 4 mm cutting wire, preferably with channels for guidewire passage and contrast injection

Cautery unit:

- Preferably with "purecut" mode

Pancreatic stents:

- Prophylactic 3–5 French stents ranging from 2 to 8 cm long, with external (duodenal) flanges or pigtail
- Therapeutic 7 French stents ranging from 3 to 15 cm long with proximal and distal flanges

Instruments and Medications

Medications

Optimal sedation, preferably with monitored anesthesia care using propofol or with general anesthesia, is required for endoscopic minor papilla cannulation and sphincterotomy. The procedure is typically more difficult and longer in duration than most pancreatic procedures performed at the major papilla, and the frequent need for use of a long duodenoscope position can diminish patient tolerance when performed with conscious sedation alone.

Visualization and access to the minor papilla is often enhanced by the administration of antispasmodic agents (e.g., intravenous glucagon in increments of 0.25 mg every 10–15 min, following passage of the duodenoscope to the second portion of the duodenum). In the event of difficult identification of the minor papilla, as is the case in up to a

third of patients, topical spraying of methylene blue or indigo carmine on the suspected area of the duodenum proximal and slightly anterior to the major papilla can facilitate visualization [15, 16]. After application of dilute methylene blue or undiluted indigo carmine 0.4%, the minor papilla orifice may appear as a punctate spot within a region of mucosal clearing of dye resulting from the flow of clear pancreatic juice from the duct.

To further augment the visualization of the minor papilla after administration of topical dye, intravenous administration of secretin at 0.2 mcg/kg over 1 min results in stimulation of pancreatic secretion, typically within 3 min of administration. Injection of secretin also results in transient pancreatic ductal dilation for approximately 15 min, which can also facilitate eventual cannulation.

Prophylactic administration of two 50 mg indomethacin suppositories (100 mg total) shortly before [17] or after [18, 19] ERCP has been shown to reduce the incidence of post-ERCP pancreatitis (PEP). Indirect data suggest this benefit is superior to that from prophylactic stent insertion [20] and the potential additive benefit from the use of both modalities is currently under study. Nevertheless, temporary prophylactic stenting is usually employed after minor papilla sphincterotomy.

Instruments

Due to the small size and variation in minor papilla anatomy, an array of catheters, sphincterotomes, and guidewires should be available. Most minor papilla interventions require the use of smaller caliber devices than are usually employed at the major papilla. Hydrophilic angled or straight 0.025, 0.021, or 0.018″ diameter wires are commonly used. The larger caliber wires are more easily visualized and manipulated. When fine-tipped catheters or sphincterotomes are too large for accessing the suspected minor papilla os, the blunt Cramer needle-tip catheter (Cook Medical) is often effective for initial pancreatography, but it does not allow passage of a guidewire for subsequent intervention. Minor papilla sphincterotomy is generally employed to treat symptomatic stenosis and to facilitate access for interventions above the level of the papilla. Both wire-guided (standard or fine-tipped) and needle-tip sphincterotomes are commonly employed.

Small caliber 3–5 Fr pancreatic stents should be available to facilitate drainage and for prophylaxis against procedural pancreatitis. Larger caliber therapeutic stents for therapy of ductal pathology are employed through the minor papilla as they would be through the major papilla.

Procedure

Minor Papilla Cannulation

Patients can be placed in the supine, lateral, or prone position, per preference of the performing endoscopist and anesthetist. After appropriate sedation, a duodenoscope is advanced to the second portion of the duodenum. The minor papilla can be found proximal (cephalad) and anterior to the major papilla along the medial wall, and rarely may be located in a diverticulum. The distance between the major and minor papilla varies, but is generally about 2–3 cm. The minor papilla is often appreciated with the long scope position during initial intubation to the deeper second portion of the duodenum, in which case it is usually easy to return to. In other cases identification requires gradual withdrawal of the duodenoscope from the major papilla while torqued slightly clockwise. Careful probing displacement of duodenal folds may be necessary to identify flat or diminutive examples. Once identified, a stable en face view that does not obscure the fluoroscopic view is sought. This typically employs either a short and slightly torqued position or return to a moderately long (>80 cm of scope inserted to the incisors) position [21, 22]. The latter is often most easily accomplished by withdrawing to the stomach or bulb and repeating a partial long scope insertion maneuver.

Once identified careful inspection for the os should be performed prior to making contact with any devices. The use of glucagon or other paralytic agents to limit small bowel contractions is strongly advisable during inspection and intervention. If the orifice is obscure or multiple potential sites are apparent, application of a topical dye such as methylene blue or indigo carmine followed by intravenous secretin (as described above) is often helpful (Fig. 28.4a, b) [15, 16, 23, 24].

After the minor papilla has been confidently identified, and with the endoscope in a stable position, cannulation can be undertaken, usually beginning with a reduced caliber wire through either a partially flexed sphincterotome or a tapered-tip cannula. The former is generally preferable as tip flexion can enhance access when an ideal en face approach is not feasible and it provides immediate availability of therapy without a wire-guided exchange. Failing wire-guided access, impaction of the needle-tip Cramer catheter that is specifically designed for pancreatography via the minor papilla often suffices. While this catheter does not accept a guidewire, its use often dilates the os enough to facilitate access with the wire-guided device (Fig. 28.4c–e).

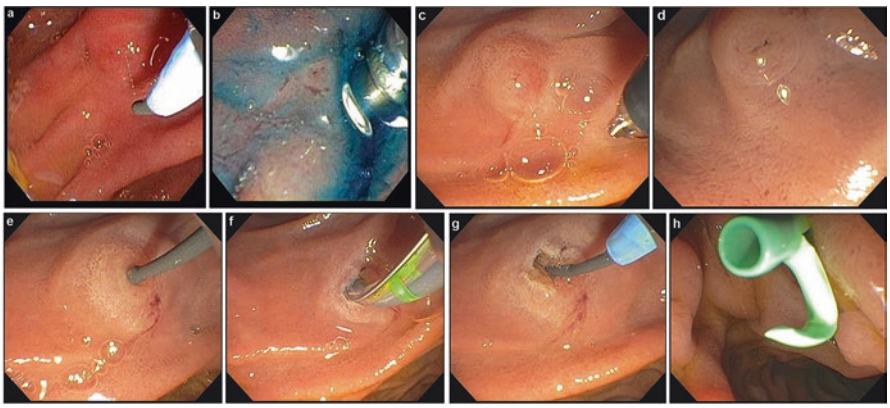

Fig. 28.4 Endoscopic views at minor papilla demonstrating (**a**) obvious papilla with uncertain os, (**b**) use of methylene *blue* demonstrating minor papilla os in the center, (**c**) Cramer catheter approaching diminutive os, (**d**) obvious papillary os after Cramer catheter pancreatogram, (**e**) wire in minor papilla to dorsal duct, (**f**) pull-type sphincterotome, (**g**) limited sphincterotomy, (**h**) 5 French stent in minor papilla after sphincterotomy

Minor Papilla Sphincterotomy

After pancreatography and deep minor papilla access, subsequent interventions require performance of a sphincterotomy (Fig. 28.4f–h). When possible, this is most easily and safely accomplished with a pull-type sphincterotome. The direction of incision is usually guided by the anatomic path of the guidewire and the most evident prominence of the sphincter. Limiting the length of wire contact with the papilla, cutting to a limited depth of 3–4 mm, and using a "pure-cut" cautery mode will minimize injury to the pancreatic duct and reduce development of late strictures after endotherapy. Successful minor papilla sphincterotomy is achieved after extending the cut to the outer rim of the minor papilla mound. At the completion of the procedure, a 3, 5, or 7 French – 3 to 8 cm long – temporary plastic stent should be inserted to prevent acute obstruction due to edema. When stents are placed only for prophylaxis against procedural pancreatitis, a smaller caliber stent (3 Fr or 5 Fr) with no internal/intraductal barbs should be used, and an abdominal X-ray should be obtained after 7–10 days to ensure it has migrated out of the duct. If still present in the head of the pancreas at that time, an EGD should be performed to remove it.

An alternative approach to minor papilla sphincterotomy after deep access employs needle-knife incision over a previously placed pancreatic stent. This presumably provides greater control of depth and radial orientation of the incision, but it has declined in use as skills and equipment have improved.

When papillary stenosis prevents deep access other than with a guidewire, consideration can be given to advanced techniques such as wire-guided needle-knife precut, rendezvous passage of a guidewire via the major papilla, rendezvous by EUS passage of a wire from the stomach into the dorsal duct (see above), or freehand needle-knife incision. These techniques should only be attempted by experienced endoscopists due to their high potential for adverse events. Precut with a needle knife alongside an existing deep guidewire is relatively controlled and should not risk loss of access or errant incision. The greatest control, at the expense of minimal length of incision, uses the needle catheter passed over the guidewire. Following partial incision, the cut can be extended with a standard wire-guided pull-type sphincterotome. Alternatively the needle can then be passed parallel to the guidewire, yielding greater mobility of the tip and slightly greater risk. Needle-knife precut without wire guidance should only be done after successful pancreatography has confirmed the location of the papillary os. Bare exploratory needle-knife incision to find the duct has been described, but EUS-guided rendezvous from the stomach through the dorsal duct is probably a safer option [14].

Practical Considerations for Cannulation and Sphincterotomy

- Most often use long duodenoscope position (>80 cm from incisors) for optimal view of the minor papilla, stability, and fluoroscopic guidance.
- Glucagon administered at 0.25 mg increments throughout the procedure to reduce motility.
- For difficult identification of the minor papilla or the os, apply topical methylene blue or indigo carmine in conjunction with secretin 0.2 mcg/kg IV to stimulate and identify flow of clear juice.

(continued)

- Needle-tip Cramer catheter is often helpful for initial pancreatography and dilation of the minor papilla.
- Deep access facilitated by gentle contrast and wire guidance.
- Reserve advanced cannulation techniques (rendezvous, needle-knife precut free hand, or over wire) for more experienced endoscopists.
- For sphincterotomy use purecut cautery mode and limit depth of incision to reduce risk of chronic strictures at orifice.
- Prophylactic pancreatic stenting should be employed after all minor papilla procedures.

Specific Technique for Minor Papilla Pancreatography and Therapy

1. If pancreatography planned or anticipated administers indomethacin suppositories before or after procedure.
2. Perform cholangiography or pancreatography at the major papilla, as indicated.
3. Briefly assess the view of the minor papilla in short scope position.
4. Usually withdraw to bulb and advance to moderately long position.
5. Administer IV glucagon for duodenal paralysis.
6. Optimize en face view of the minor papilla.
7. Inspect closely *without contact* for minor papilla os.
8. Employ already used sphincterotome with either original wire or new 0.025″ hydrophilic guidewire to start.
9. Gently advance wire into papilla up to1–3 cm if passes easily without significant tension.
10. If wire passage fails:
    - Attempt pancreatography with Cramer catheter.
    - Consider downsizing guidewire through sphincterotome.
    - If opening remains uncertain, consider topical spraying plus secretin IV.
    - If not pancreas divisum anatomy, assess feasibility of rendezvous from the major papilla.
11. Attempt pancreatography with the tip of the sphincterotome either inserted or impacted.
12. When pancreatography is accomplished, advance wire deep into the body or tail for stability during therapy.
13. For sphincterotomy, ensure ongoing gut paralysis and optimal sedation.
14. Incise preferably with pull-type sphincterotome minimally inserted using purecut current.
15. After planned duct evaluation, sampling, or therapy, leave at least a 3 or 5 Fr prophylactic stent.

Complications

Prior to consideration for minor papilla sphincterotomy, both immediate adverse events and long-term complications should be considered. Early and immediate adverse events are seen in fewer than 8% of the patients undergoing minor papilla sphincterotomy for pancreas divisum. The most common complications are post-ERCP pancreatitis (PEP), hemorrhage, and perforation. Multivariate logistic regression has identified predictors for PEP including age less than 40 years old, minor papilla sphincterotomy, female sex, previous PEP, and dorsal duct cannulation [25]. The rate of PEP after minor sphincterotomy has been inversely related to the use of prophylactic pancreatic stenting, similar to PEP in patients undergoing major papilla sphincterotomy. No studies to date have investigated the use of rectal indomethacin or have identified the ideal stent caliber (3 French versus 5 French) or length for reducing PEP in this specific setting. Hemorrhage is usually controlled with endoscopically directed epinephrine injection. While electrocautery techniques can also be employed, these methods may result in minor papilla stenosis.

The most worrisome and common late complication of minor papilla sphincterotomy is papillary or ductal stenosis, which occurs in 11.5–19% of patients [26]. While this may result from natural healing, the intractable examples are generally attributed to cautery-induced intraductal scarring. Repeat endoscopic therapy may involve extension of the sphincterotomy if a residual sphincter is evident or, more commonly, dilation with a 4 mm balloon and stenting for 6–12 weeks or more. As larger caliber dilation is required, the use of multiple small caliber stents is theoretically safer than single larger stents. Surgical intervention is rarely required, though sphincteroplasty, lateral pancreaticojejunostomy, or pancreaticoduodenectomy must sometimes be considered for endotherapy-refractory stenoses.

Common Early and Late Complications of Minor Papilla Sphincterotomy

- Early complications
  - Post-ERCP pancreatitis (6.8%)
    - Prevention: minor papilla stenting
  - Hemorrhage (0.07%)
    - Prevention: minor papilla stenting
    - Treatment: dilute epinephrine injection
  - Perforation (0.2%)
    - Prevention: limiting extension/depth of sphincterotomy
    - Treatment: if limited or no free contrast leakage – stenting if deep access available, antibiotics, nasoduodenal suction
- Late complications
  - Papillary stenosis (11–19%)
    - Prevention: use of purecut cautery setting, limiting the use of electrocautery for treatment of bleeding, avoidance of deep cautery within duct
    - Treatment: extension of sphincterotomy if feasible, dilation of orifice, increasing caliber of pancreatic stenting, surgical sphincteroplasty, or decompression of pancreatic duct

Follow-Up and Outcome

Multiple studies among patients after minor papilla endotherapy for symptomatic pancreas divisum, with follow-up of 20–43 months, have demonstrated marked clinical improvement in those with acute recurrent pancreatitis [25, 27–31]. In these studies, 69% of 143 patients identified with acute recurrent pancreatitis reported clinical improvement in symptoms as opposed to only 44% of 81 patients with chronic pancreatitis and 35% of patients with only pancreas-type pain. These data suggest that minor papilla sphincterotomy in patients with pancreas divisum should be reserved for those experiencing recurrent acute pancreatitis, as this cohort is most likely to experience clinical benefit. In our practice, minor papilla sphincterotomy is not routinely performed for patients with pancreas divisum who demonstrate clinical, EUS, and/or imaging findings consistent with chronic pancreas-type pain unless a clear dorsal distribution, with sparing of the ventral gland, is present.

Conclusion

Pancreatography and sphincterotomy at the minor pancreatic papilla of Santorini are increasingly used for diagnosis and therapy of pancreatic disease when access cannot be gained through the major papilla and when pancreas divisum warrants imaging or duct decompression via the accessory duct. As a result of the inherent difficulty of this procedure, the risk of significant complications, the high likelihood of repeat procedures, and the marginal clinical improvement for some clinical entities, minor papilla cannulation with sphincterotomy for symptomatic pancreas divisum should be reserved for patients with recurrent acute pancreatitis or clearly isolated dorsal duct chronic pancreatitis. These procedures should be performed by advanced endoscopists with appropriate training, experience, and resources necessary to address the technical challenges and complications during and after the procedure. Despite these precautions, when appropriately employed in the optimal clinical setting, minor papilla sphincterotomy can provide significant improvement in quality of life for patients with pancreatic ductal pathology.

References

1. Kin T, Shapiro AM, Lakey JR. Pancreas divisum: a study of the cadaveric donor pancreas for islet isolation. Pancreas. 2005;30(4):325–7.
2. Yu J, Turner MA, Fulcher AS, Halvorsen RA. Congenital anomalies and normal variants of the pancreaticobiliary tract and the pancreas in adults: part 2, pancreatic duct and pancreas. AJR. Am J Roentgenol. 2006;187(6):1544–53.
3. Gelrud A, Sheth S, Banerjee S, et al. Analysis of cystic fibrosis gener product (CFTR) function in patients with pancreas divisum and recurrent acute pancreatitis. Am J Gastroenterol. 2004;99(8):1557–62.
4. Garg PK, Khajuria R, Kabra M, Shastri SS. Association of SPINK1 gene mutation and CFTR gene polymorphisms in patients with pancreas divisum presenting with idiopathic pancreatitis. J Clin Gastroenterol. 2009;43(9):848–52.
5. Mosler P, Akisik F, Sandrasegaran K, et al. Accuracy of magnetic resonance cholangiopancreatography in the diagnosis of pancreas divisum. Dig Dis Sci. 2012;57(1):170–4.
6. Akisik MF, Sandrasegaran K, Aisen AA, Maglinte DD, Sherman S, Lehman GA. Dynamic secretin-enhanced MR cholangiopancreatography. Radiographics Rev Publ Radiol Soc North Am Inc. 2006;26(3):665–77.
7. Manfredi R, Pozzi MR. Secretin-enhanced MR imaging of the pancreas. Radiology. 2016;279(1):29–43.
8. Crino SF, Bernardoni L, Conti Bellocchi MC, et al. Efficacy of endoscopic minor papilla sphincterotomy for symptomatic santorinicele. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2017;15(2):303–6.
9. Lutzak GD, Gluck M, Ross AS, Kozarek RA. Endoscopic minor papilla sphincterotomy in patients with santoriniceles reduces pain and improves quality of life. Dig Dis Sci. 2013;58(7):2075–81.
10. Boninsegna E, Manfredi R, Ventriglia A, et al. Santorinicele: secretin-enhanced magnetic resonance cholangiopancreatography findings before and after minor papilla sphincterotomy. Eur Radiol. 2015;25(8):2437–44.
11. Dumonceau JM, Cremer M, Baize M, Deviere J. The transduodenal rendezvous: a new approach to deeply cannulate the main pancreatic duct. Gastrointest Endosc. 1999;50(2):274–6.
12. Will U, Meyer F, Manger T, Wanzar I. Endoscopic ultrasound-assisted rendezvous maneuver to achieve pancreatic duct drainage in obstructive chronic pancreatitis. Endoscopy. 2005;37(2):171–3.

13. Papachristou GI, Gleeson FC, Petersen BT, Levy MJ. Pancreatic endoscopic ultrasound-assisted rendezvous procedure to facilitate drainage of nondilated pancreatic ducts. Endoscopy. 2007;39(Suppl 1):E324–5.
14. Fujii LL, Topazian MD, Abu Dayyeh BK, et al. EUS-guided pancreatic duct intervention: outcomes of a single tertiary-care referral center experience. Gastrointest Endosc. 2013;78(6):854–64. e851
15. Park SH, de Bellis M, McHenry L, et al. Use of methylene blue to identify the minor papilla or its orifice in patients with pancreas divisum. Gastrointest Endosc. 2003;57(3):358–63.
16. Ohshima Y, Tsukamoto Y, Naitoh Y, et al. Function of the minor duodenal papilla in pancreas divisum as determined by duodenoscopy using indigo carmine dye and a pH sensor. Am J Gastroenterol. 1994;89(12):2188–91.
17. Luo H, Zhao L, Leung J, et al. Routine pre-procedural rectal indometacin versus selective post-procedural rectal indometacin to prevent pancreatitis in patients undergoing endoscopic retrograde cholangiopancreatography: a multicentre, single-blinded, randomised controlled trial. Lancet. 2016;387(10035):2293–301.
18. Elmunzer BJ, Scheiman JM, Lehman GA, et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. N Engl J Med. 2012;366(15):1414–22.
19. Dumonceau JM, Andriulli A, Elmunzer BJ, et al. Prophylaxis of post-ERCP pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) guideline – updated June 2014. Endoscopy. 2014;46(9):799–815.
20. Elmunzer BJ, Higgins PD, Saini SD, et al. Does rectal indomethacin eliminate the need for prophylactic pancreatic stent placement in patients undergoing high-risk ERCP? Post hoc efficacy and cost-benefit analyses using prospective clinical trial data. Am J Gastroenterol. 2013;108(3):410–5.
21. Petersen BT. Cannulation techniques: biliary and pancreatic. Tech Gastrointest Endosc. 2003;5(1):17–26.
22. Benage D, McHenry R, Hawes RH, O'Connor KW, Lehman GA. Minor papilla cannulation and dorsal ductography in pancreas divisum. Gastrointest Endosc. 1990;36(6):553–7.
23. Devereaux BM, Lehman GA, Fein S, Phillips S, Fogel EL, Sherman S. Facilitation of pancreatic duct cannulation using a new synthetic porcine secretin. Am J Gastroenterol. 2002;97(9):2279–81.
24. Devereaux BM, Fein S, Purich E, et al. A new synthetic porcine secretin for facilitation of cannulation of the dorsal pancreatic duct at ERCP in patients with pancreas divisum: a multicenter, randomized, double-blind comparative study. Gastrointest Endosc. 2003;57(6):643–7.
25. Moffatt DC, Cote GA, Avula H, et al. Risk factors for ERCP-related complications in patients with pancreas divisum: a retrospective study. Gastrointest Endosc. 2011;73(5):963–70.
26. Lehman GA, Sherman S, Nisi R, Hawes RH. Pancreas divisum: results of minor papilla sphincterotomy. Gastrointest Endosc. 1993;39(1):1–8.
27. Coleman SD, Eisen GM, Troughton AB, Cotton PB. Endoscopic treatment in pancreas divisum. Am J Gastroenterol. 1994;89(8): 1152–5.
28. Kozarek RA, Ball TJ, Patterson DJ, Brandabur JJ, Raltz SL. Endoscopic approach to pancreas divisum. Dig Dis Sci. 1995;40(9):1974–81.
29. Gerke H, Byrne MF, Stiffler HL, et al. Outcome of endoscopic minor papillotomy in patients with symptomatic pancreas divisum. JOP J Pancreas. 2004;5(3):122–31.
30. Chacko LN, Chen YK, Shah RJ. Clinical outcomes and non-endoscopic interventions after minor papilla endotherapy in patients with symptomatic pancreas divisum. Gastrointest Endosc. 2008;68(4):667–73.
31. Borak GD, Romagnuolo J, Alsolaiman M, Holt EW, Cotton PB. Long-term clinical outcomes after endoscopic minor papilla therapy in symptomatic patients with pancreas divisum. Pancreas. 2009;38(8):903–6.

Endoscopic Management of Bile Duct Stones: Small and Large

29

Hendrikus Vanderveldt and Sandeep Patel

Introduction

Gallstone disease is one of the most common diseases of the digestive system affecting patients worldwide. It is estimated that over 20 million people in the United States alone have gallbladder disease at any given time [1]. As a result, cholecystectomy has become one of the most common operations performed by US general surgeons. A majority of these procedures are now performed by laparoscopic means and have been highly successful at alleviating patient's symptoms with low complication rates.

Approximately 15% of these patients present with or subsequently develop choledocholithiasis. Although historically a surgical disease, these patients are now managed predominantly with endoscopic techniques. In this chapter, we will discuss the risk factors identified with the formation of biliary stone disease followed with the diagnosis and management of this entity.

Epidemiology

Gallstone disease affects both genders and all ages and ethnicities; however, the Native Americans have the highest prevalence of the disease with rates approaching 73% in Pima Indian females [2]. The prevalence rates in Mexican American (8.9%; 26.7%), Caucasian (8.6%; 16.6%), and African-American (5.3%; 13.9%) men and women were found in a large US epidemiologic study performed by Everhart et al. in the late 1990s.

In the United States, the incidence of gallstone disease is higher in women than men at a ratio of 2:1. Risk factors for the development of gallstone disease other than gender include age, obesity, rapid weight loss, certain medication use, pregnancy, and family history of gallstone disease. Certain chronic medical conditions such as cirrhosis, hyperlipidemia, and diabetes mellitus also render patients high risk for the formation of gallstones:

(a) *Age*: Age distribution for stone formation seems to be concentrated between the ages of 40 and 69 [3]. Children are rarely affected unless they have a hemolytic condition. Young females of child-bearing age are at increased risk over the general population.
(b) *Pregnancy*: Increased incidence of stone formation in pregnant females has been linked to physiologic changes seen in bile as a result of changes in circulating sex hormones. The cholesterol/bilirubin homeostasis shifts toward cholesterol supersaturation as a result of both estrogen-induced increase in cholesterol secretion and progesterone-induced reduction in bile secretion [4]. Stasis of this saturated bile as a result of progesterone-induced impaired gallbladder emptying further facilitates cholesterol stone formation.
(c) *Family history*: There is evidence that genetics plays a strong role in gallstone formation. A cholecystography showed that patients with affected first-degree relatives had a relative risk of 2 [5] compared to controls. Other studies have shown similar results with relative risk ranging up to 5 in patients with positive family history of gallstone disease [6].
(d) *Rapid weight loss*: This particular risk factor has become clinically relevant with the expanding popularity of weight loss surgeries. The mechanism by which rapid weight loss promotes gallstone formation is not currently well understood. Interestingly, a few studies have shown that prophylaxis with ursodeoxycholic acid in these patients reduced the risk of stone formation [7, 8].
(e) *Drugs/TPN*: Various medications have been implicated to promote the formation of gallstones: estrogen, oral contraceptives, octreotide, clofibrate, and ceftriaxone to name a few. Patients on TPN in prolonged fasting states are at increased risk for gallstone formation from gallbladder stasis due to lack of enteral CCK-induced gallbladder activity.

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Practical Considerations

- Native Americans have the highest prevalence of gallstone disease.
- Young females of child-bearing age are at increased risk for gallstone disease.
- Patients on TPN in prolonged fasting states are at increased risk for gallstone formation from gallbladder stasis. This is due to lack of enteral CCK-induced gallbladder activity.

Etiology

Patients form one of three types of gallstones: cholesterol, pigmented, or brown.

(a) *Cholesterol stones*: More than 90% of gallstones consist of predominately cholesterol and are formed within the gallbladder. Cholesterol stones form when bile contains more cholesterol than can be solubilized by mixed micelles of bile salts and phosphatidylcholine (lecithin). Additional factors such as biliary mucin and impaired gallbladder motility allow cholesterol microcrystals to be retained and to perpetuate into macroscopic gallstones. In principal, cholesterol supersaturation of gallbladder bile can result from hepatic hypersecretion of cholesterol or hyposecretion of bile salts or lecithin.

(b) *Pigmented stones*: A very small percentage of gallstones are of the black pigmented variety (2%). They consist predominantly of polymerized calcium bilirubinate, which precipitates if the ion product of calcium and unconjugated bilirubin exceeds its solubility product and polymerizes slowly into biliary sludge.

(c) *Brown stones*: Brown pigmented stones form as a result of stasis and infection within the bile duct. Bacterial b-glucuronidase converts soluble conjugated bilirubin back to the insoluble unconjugated state, leading to the precipitation of bilirubin as calcium salts of long-chain fatty acids. This stone type is associated with the presence of duodenal diverticula, biliary strictures, or parasitic infestations [9].

Practical Considerations

- Common types of gallstones are cholesterol, pigmented, or brown.
- Cholesterol stones form when bile contains increased cholesterol, increased mucin, and impaired gallbladder motility.
- Bacterial b-glucuronidase converts soluble conjugated bilirubin into insoluble unconjugated state, leading to the precipitation of bilirubin as calcium salts of long-chain fatty acids. This type of stone is associated with duodenal diverticula, biliary strictures, or parasitic infestations.

Presentation

Approximately 8–15% of patients with gallbladder disease have or develop gallstones in the biliary tract known as choledocholithiasis [10]. Most cases are due to the passage of gallstone(s) from the gallbladder into the common bile duct via the cystic duct. Formation of stones within the biliary system known as primary choledocholithiasis is less common and generally occurs in the setting of biliary stasis: patients with very large ducts in the setting of duodenal diverticula or choledochal cysts. Chronic obstruction from choledocholithiasis is a known cause of secondary biliary cirrhosis.

Patients with choledocholithiasis generally present with a constellation of symptoms and findings. Symptoms tend to include right upper quadrant pain radiating to the right subscapular area associated with nausea and vomiting induced by the ingestion of fat-rich foods. Pain is felt to be due to acute blockage of the biliary duct with resultant increased intraductal pressure and duct dilatation. Physical examination in these patients generally elicits right upper quadrant or epigastric tenderness. Patients may also have icteric sclera and jaundice. Laboratory data reveals liver test abnormalities in a cholestatic pattern (elevated total bilirubin, alkaline phosphatase, and gamma-glutamyl transpeptidase (GGT) > alanine aminotransferase (ALT) and aspartate aminotransferase (AST)). Various imaging modalities are also utilized in diagnosing choledocholithiasis such as transabdominal ultrasound, magnetic resonance cholangiopancreatography (MRCP), endoscopic cholangiopancreatography (ERCP), and endoscopic ultrasound (EUS).

Laboratory Data

Serum levels of AST and ALT generally rise early in the presentation of choledocholithiasis followed by elevation in alkaline phosphatase, total bilirubin, and GGT that exceed them. Of all the biochemical markers, a total bilirubin >3.5 mg/dL seems to have the highest individual sensitivity for bile duct stone disease at 69% with a specificity of 88% [11]. Conversely, normal liver enzyme levels have a negative predictive value of nearly 95% [12].

The one caveat to this is in our elderly population (age >75). These patients with choledocholithiasis commonly present with relatively normal liver enzyme panels. Leukocytosis (WBC > 12,000) in the appropriate clinically setting can suggest cholangitis. In the case of biliary pancreatitis, the amylase and lipase levels are usually elevated.

Imaging Studies

Transabdominal Ultrasound: Right upper quadrant transabdominal ultrasound (US) is usually the initial study of choice in patients with suspected choledocholithiasis because of its low cost and availability. US can identify cholelithiasis and common bile duct dilation with high accuracy (>90%). Common bile duct is considered dilated when CBD measures >6 mm (with gallbladder in situ) in a 40-year-old patient. Thereafter the CBD diameter is commonly noted to increase by 1 mm for every decade of life. The presence of overlying small bowel can limit the overall effectiveness of the US in detecting CBD stones with a sensitivity approaching 73% and a specificity of 91% [13]. Elderly patients with choledocholithiasis can present with no dilatation of the CBD on US.

Magnetic Resonance Cholangiopancreatography: MRCP is an effective, noninvasive tool in diagnosing choledocholithiasis with a sensitivity of 93% and a specificity of 94% [14]. Results from this study can be variable as this imaging modality requires sound technical expertise and patient cooperation.

Endoscopic Ultrasound (EUS): EUS has the distinct advantage of identifying very small stones and even sludge/microlithiasis. The sensitivity and specificity of EUS compare well to MRCP. EUS has a sensitivity of 95% (95% CI 0.91–0.97) and specificity of 97% (95% CI 0.94–0.99) [(16)].

Endoscopic Retrograde Cholangiopancreatography (ERCP) and Interoperative Cholangiogram (IOC): ERCP is no longer seen as a first-line diagnostic imaging test for common duct stones. Additionally, IOC is a surgical imaging procedure and when performed is usually performed at the time of cholecystectomy.

Practical Considerations

- Serum levels of AST and ALT generally rise early in the presentation of choledocholithiasis followed by elevation in alkaline phosphatase, total bilirubin, and GGT.
- Serum total bilirubin >3.5 mg/dL has the highest sensitivity and specificity for bile duct stone disease (69% and 88%).
- Normal liver enzyme levels have a negative predictive value of 95% for bile duct stones.
- Elderly patients with bile duct stones commonly present with relatively normal liver enzymes.

Management

The first step in appropriately managing those with bile duct stones or choledocholithiasis is to first accurately assess whether bile duct stones are present. The most straightforward way to identify those with bile duct stones is to visualize a stone in the bile duct using traditional imaging mentioned previously (transabdominal ultrasound, computerized tomography(CT), or magnetic resonance imaging/magnetic resonance cholangiopancreatography (MRCP)). It is important to realize that the traditional imaging tests do not always identify stones. Consequently, in order to properly manage a patient with suspected choledocholithiasis, it is often necessary to have risk assessment of the patient for the presence of bile duct stones. Traditionally, the presence of Charcot's triad was used as an indicator of infective biliary obstruction/bile duct stones. However, only a proportion of patients with symptomatic bile duct stones present with cholangitis. Additionally, even in the presence of cholangitis, Charcot's triad has been demonstrated to have a low sensitivity (26.4%) [15].

There are several tools available to risk-assess the patients who present without convincing evidence of bile duct stones. These include the use of alternative imaging techniques such as endoscopic ultrasound, diagnostic endoscopic retrograde cholangiopancreatography, and interoperative cholangiogram (IOC would be performed at the time of cholecystectomy) versus risk assessment tools using a combination of clinical history, laboratory parameters, and imaging, such as the one developed by the American Society of Gastroenterology (ASGE).

Given the risks of the procedure and the presence of alternative investigative tools, as mentioned, diagnostic ERCP is no longer commonly used as a method for determining the presence of common bile duct stones. Additionally, interoperative cholangiogram, which would be performed at the time of cholecystectomy, is not always appropriate for this clinical setting. Therefore, yet another tool with excellent specificity and sensitivity for the diagnosis of common bile duct stones is endoscopic ultrasound. Additionally, EUS has the additional functionality of allowing the endoscopist to remove the stones by ERCP if a bile duct stone is seen.

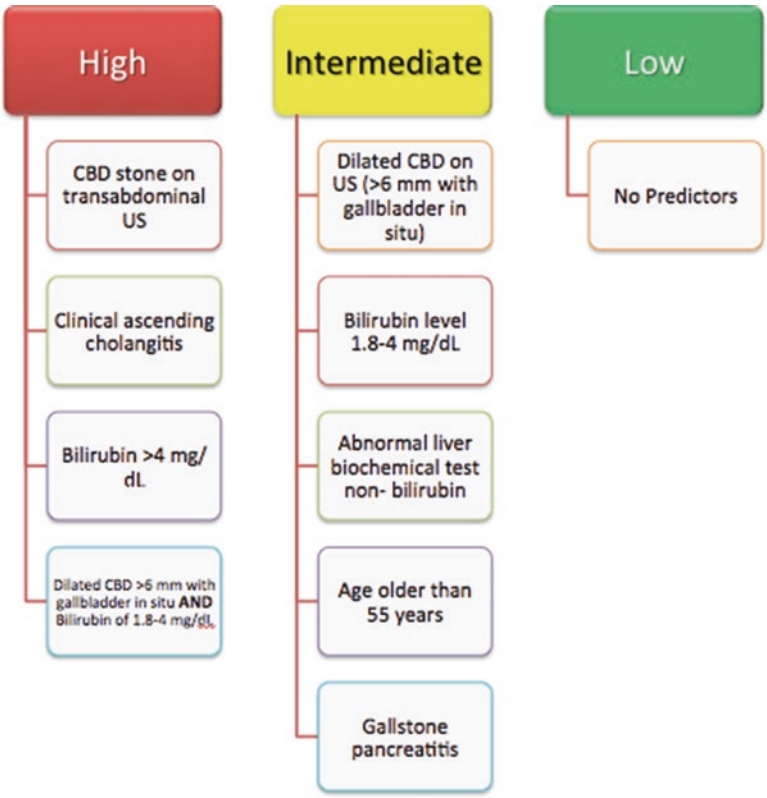

Fig. 29.1 Caption (Based on data presented in ASGE standard of practice committee [17])

Another way to risk-assess the patient for the probability of common bile duct stones is through the tools utilizing a combination of clinical features, lab results, and imaging findings. The American Society for Gastrointestinal Endoscopy released a standard of practice entitled: The Role of Endoscopy in Suspected Choledocholithiasis [17]. The society categorizes the risk of choledocholithiasis in patients with symptomatic cholelithiasis and also breaks down those at risk for bile duct stones into those at high risk, intermediate risk, and low risk. This is based on the presence or absence of clinical, laboratory, or imaging features (see Fig. 29.1).

Patients who are classified at high risk for choledocholithiasis have a greater than 50% probability of choledocholithiasis, while those with low or intermediate risk have a lower risk of choledocholithiasis. Low risk is noted to have a less than 10% probability of bile duct stones, while those at intermediate risk are noted to have between a 10% and 50% probability of choledocholithiasis. The clinical importance of this classification is that those noted to be at high risk should be considered for an endoscopic retrograde cholangiopancreatography prior to cholecystectomy without further testing, while those classified as being at intermediate to low risk should have more testing if clinically indicated. Although the paper was written to risk-assess those with symptomatic cholelithiasis for bile duct stones, it provides a framework for evaluation of patients at risk for choledocholithiasis. However, neither algorithm nor list of clinical features can replace a physician's clinical judgment regarding the risk of a patient for choledocholithiasis.

Once it has been determined that the patient has evidence of a bile duct stone or high clinical suspicion of a stone, the next question which obviously arises is whether the stone should be removed? In those patients presenting with clinical symptoms or clinical issues (such as cholangitis) due to the presence of bile duct stones, the answer is clear that an attempt at stone removal should be undertaken.

However, what about the incidentally found asymptomatic bile duct stone or stones? The answer to this question appears to be that even asymptomatic bile duct stones should be removed. Supporting this statement is a guideline from the United Kingdom which states that the bile duct clearance should be offered to those with symptomatic or asymptomatic bile duct stones [18]. A study noted that 25.3% of patients with untreated choledocholithiasis (found during intraoperative cholangiogram) had an unfavorable outcome. Those outcomes defined as postoperative pancreatitis, cholangitis, obstruction of bile duct/jaundice, and/or need for unplanned ERCP [19]. This risk of an "unfavorable outcome" was not changed by the presence of symptoms.

The next question which appears for the clinician is the urgency for removing the bile duct stones. As mentioned above, all biliary stones have the potential to create complications. Although the timing of a future potential

complication(s) cannot be known, certain clinical scenarios require a quicker therapeutic response. Again, as with many situations in medicine, the clinician's judgment regarding the timing of a therapeutic response is the most important factor in deciding when to act. Having said that in certain situations such as cholangitis, available medical literature provides some data to guide the decision-making as to the timing. For example, in patients who present with cholangitis, one study demonstrated that ERCP performed earlier following presentation (<48 h) results in lower hospital length of stay, while delayed ERCP (performed >72 h following admission) results in poorer composite outcomes (death or persistent organ failure or ICU stay) [20].

How should the bile duct stones be removed? Prior to the advent of the endoscopic approach to the removal of bile duct stones, stones had been removed using a surgical approach. In the early 1970s, physicians such as Classen, Demling, Kawai, and others helped to develop endoscopic sphincterotomy in the management of biliary stones [21]. Currently, endoscopic retrograde cholangiopancreatography is the standard method for non-operative removal of the bile duct stones (Fig. 29.2).

Overall, the endoscopic removal of bile duct stones is based on the concept that one must make the ampullary orifice wider, the stone smaller, or both. There are many standard techniques used in accomplishing these tasks. In the next section, we will review some of the standard methods for doing this.

Practical Considerations

- Both symptomatic and asymptomatic bile duct stones should be removed.
- Patients with cholangitis and bile duct stones do better if the stones are removed within 48 h of presentation.

Endoscopic biliary stone clearance begins with bile duct access through biliary cannulation. Once this is established, the next step in stone clearance is typically to widen the ampullary orifice through sphincterotomy. There are many different types of sphincterotomes; however, the basic sphincterotome is a Teflon catheter with a guidewire channel fitted with a 2–3 cm cutting wire. Following biliary cannulation, the sphincterotome is positioned bridging the ampullary orifice. At this point the sphincterotome can be bowed so that the distal third of the cutting wire makes contact with the roof of the ampulla. An electrosurgical generator is then used to pass a cutting current (commonly blended cut/coagulation setting) through the wire. Optimally the cut is continued through the intraduodenal portion of the ampulla. Following sphincterotomy, stone extraction can be attempted through the use of balloon sweep with an extraction balloon. Although sphincterotomy is commonly performed during biliary stone extraction, sphincterotomy has risks. Freeman et al. noted that the 30-day risk of complication was 9.8% with the most common risks being pancreatitis and bleeding [23].

At times a complete or partial sphincterotomy cannot be accomplished, and/or the sphincterotomy is not large enough to accommodate stone extraction. When this occurs other techniques for removing the stone include widening the ampullary orifice through sphincteroplasty and reducing the size of the stone through stone fracturing or lithotripsy.

Sphincteroplasty can be performed with or without sphincterotomy. While sphincteroplasty alone has been preferentially used in patients with disorders of hemostasis, sphincteroplasty without sphincterotomy has been noted to be associated with an increased risk of post-ERCP pancreatitis. Therefore, many endoscopists prefer sphincterotomy and sphincteroplasty together. It is hypothesized that using sphincterotomy with sphincteroplasty will decrease the risk of pancreatitis by creating a papillary defect away from the pancreatic orifice. Consequently, the force of dilatation will be directed toward the weak point in the papilla (the papillary sphincterotomy defect) instead of creating pressure on the pancreatic septum. Additionally, the combination of sphincterotomy and sphinc-

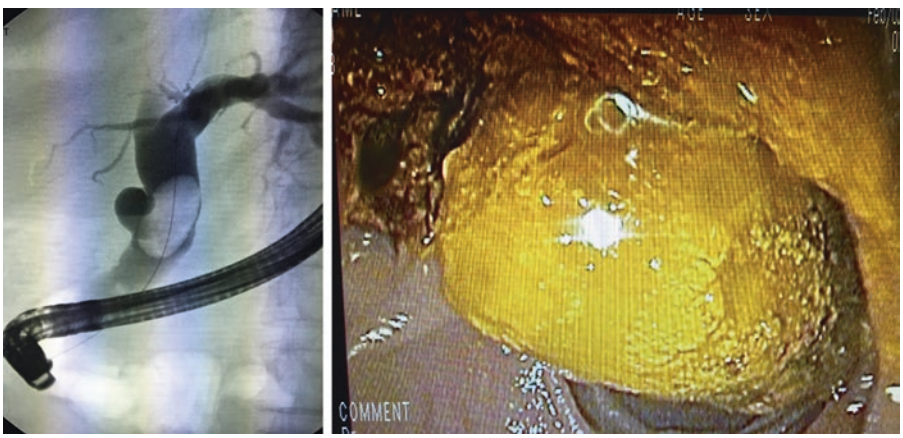

Fig. 29.2 On the *left*, a large bile duct stone seen on fluoroscopic image. The same stone (*right*) after removal from the biliary duct is seen in the lumen of the duodenum

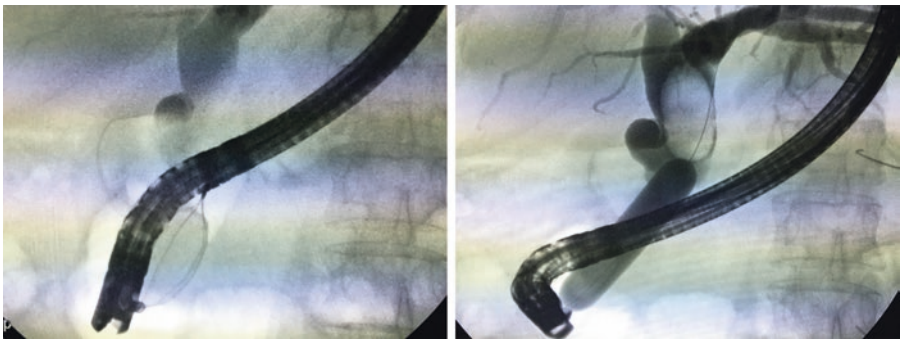

Fig. 29.3 Endoscopic picture of balloon sphincteroplasty (left) and fluoroscopic image of balloon sphincterotomy (*right*)

teroplasty often allows for the creation of a larger ampullary opening especially useful in cases where the intraduodenal segment landmarks are difficult to appreciate or when larger stones are present. Recently several notable studies have demonstrated the benefit of dual therapy sphincterotomy/sphincteroplasty for the removal of large biliary stones. Attasaranya demonstrated that large stones (>1 cm) could be removed effectively (95%) and relatively safely (5.4% procedure-related complications) with a combination of sphincterotomy and sphincteroplasty with or without mechanical lithotripsy [23] (Fig. 29.3).

The technique for combined sphincterotomy/sphincteroplasty begins with a standard sphincterotomy. Once a sphincterotomy has been performed, a sphincteroplasty or dilating balloon catheter, sized to the diameter of the distal common bile duct, is chosen. The duct size is estimated by comparing the bile duct diameter proximal to the ampullary segment to the diameter of the duodenoscope. The sphincteroplasty catheter is then passed through the scope, and the ampullary segment is bridged. The overall goal of dilatation is to visualize an ampullary narrowing/residual sphincter muscle on the balloon. Seen as a "waist," this narrowed area is then dilated with the goal of obliterating the narrowing. The optimal length of time to hold dilatation has not been established. Laio indicated that failure to remove stone of ≤15 mm was less when dilatation was held for 5 min as opposed to 1 min. Additionally, in the same study, the risk of overall complication also appeared less for dilatations held for 5 min instead of 1 min [24]. Once the diameter of the ampullary orifice has been increased and the stone still cannot be extracted, the next alternative step is to decrease the size of the stone through fragmentation. Stone fragmentation or destruction is otherwise known as lithotripsy. There are many different lithotripsy techniques (mechanical, electrohydraulic lithotripsy, and laser lithotripsy).

Practical Considerations

- Sphincteroplasty without sphincterotomy carries an increased risk of post-ERCP pancreatitis.
- Sphincterotomy followed by sphincteroplasty is preferred.

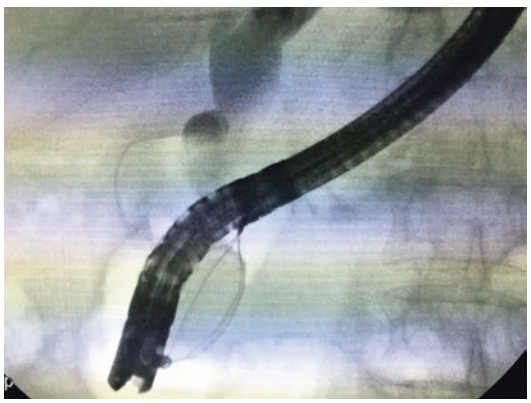

Fig. 29.4 Fluoroscopic image of large stone in a mechanical lithotripsy basket

Mechanical lithotripsy involves passing a wire basket through the working channel of the scope into the bile duct in an attempt to capture and crush a stone. Once the stone is caught inside the basket or "captured," the stone is crushed. This is performed by pulling the wires against a hardened sheath. The stone fragments can then be extracted through the ampullary opening using standard extraction techniques. Overall, the success of mechanical lithotripsy in stone extraction varies widely, but this method has a reported range of success from 84% to 99% [25] (Fig. 29.4).

Occasionally, the stone captured by the basket is too hard to be crushed, and the wires become embedded in the stone and cannot be freed from the basket. In this case, salvage or rescue lithotripsy is undertaken. Wire cutters are used to cut the handle off the lithotripser. Following this a metal sheath is advanced over the exposed wires, and the end of the wires is fixed to the rescue handle. This added apparatus often creates enough pressure to allow stone fracture or at least break the basket over the stone freeing the device. Rarely, the lithotripsy basket will become impacted on a stone and therefore cannot be freed even with the use of a rescue handle. Although these complications happen rarely, if the impacted basket cannot be freed, ultimately the patient may have to go for a surgical removal of the wire.

Other endoscopic options for stone fracture include methods that require a cholangioscopy system for delivery such as

electrohydraulic lithotripsy or methods that are delivered externally such as extracorporeal shock wave lithotripsy.

Electrohydraulic lithotripsy (EHL) involves the use of a probe that has bipolar electrodes. Using a cholangioscopy system, the EHL probe is visually placed adjacent to the stone. The bile duct is filled with a fluid medium such as normal saline. A bipolar power generator generates a charge, and the result is a shock wave that can fracture a stone. One study evaluated the efficacy of EHL on stone removal in which 99% of patients had failed previous ERCP; endoscopic stone clearance was accomplished in 90% of these patients using EHL. In this group there was an 18% overall complication rate, the majority of those complications being recurrent jaundice and/or cholangitis [26].

Laser lithotripsy uses a similar concept as EHL that being a probe is visually advanced using a cholangioscopy system to the vicinity of a stone. At that point, energy (in the form of a laser discharge) is released resulting in the creation of a cavitation bubble. This cavitation bubble consequently causes fragmentation of the stone. There are several different types of lasers used in lithotripsy. The properties of each of the lasers are based on wavelengths. For example, the holmium:yttrium aluminum garnet laser or Ho:Yag laser has a wavelength of 2140 nm. This wavelength happens to be close to the peak absorption of water. Consequently, because the scatter from a Ho:Yag laser is absorbed in water, the shock wave delivered is very accurate. Additionally, the Ho:Yag laser has a limited tissue penetration (0.5 mm) making it more safe than some of the other lasers [27] (Fig. 29.5).

Results from studies using Ho:Yag laser lithotripsy

Author	*N*	Stone clearance (%)	Complications (%)
Lee et al. [13]	10	90	10
Maydeo et al. [14]	60	100	14
Patel et al. [15]	69	97	4
Weighted average	*139*	*98*	*9*

Based on data presented in Rosenkranz et al. [21]

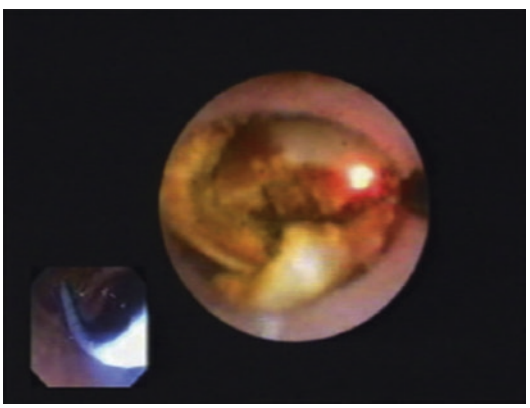

Fig. 29.5 Large stone directly visualized and targeted with laser

Other options for biliary stone fracture include extracorporeal shock wave lithotripsy (ESWL). Extracorporeal shock wave lithotripsy involves the use lithotripsy device to generate biliary stone fracturing shock wave therapy from outside the abdominal wall. It has been used successfully to treat kidney stones. In patients who undergo this therapy for biliary stones, a pre-ESWL ERCP with nasobiliary drain placement is performed (or in those without endoscopically accessible bile ducts, surgical biliary drainage placement was performed). Once this is accomplished, an ESWL machine is used to deliver the therapy using fluoroscopy or ultrasound for targeting. Following the procedure, a follow-up ERCP is generally required for final stone clearance. Studies have demonstrated a high success in stone clearance in those who have failed ERCP. In one study, authors were able to achieve a 90% clearance rate [30]. Of the 313 patients included in the study, reported complications included cholangitis (four patients) and acute cholecystitis (one patient). However, three patients required emergency surgery. Two of the three patients required surgery for complications that resulted from subsequent ERCP. One patient of the three required surgery for the development of acute cholecystitis. Additionally, while most patients in the study required only one session for stone fracture, 38% of patients in the study required multiple sessions [30].

Despite many endoscopic tools available, there are occasions where secondary to the patient's anatomy and/or the location of the stones, that traditional or standard endoscopic removal of stones would be more difficult and require other tools or different procedures. Some of these variables can be anticipated prior to procedure. Stone positions that can create trouble include intrahepatic stones, stones behind strictures, cystic duct stones, and impacted stones.

Anatomical variations relate to the patient's native anatomy (periampullary diverticulum) or postsurgical changes (patients who have undergone a Roux-en-Y gastric bypass). Each variation of anatomy or stone position will create a different decision matrix for the optimal stone removal. Patients with a Roux-en-Y gastric bypass may require a retrograde endoscopic approach up the Roux limb or a combined surgical/endoscopic approach. The tools used (such as different sphincterotomes) in each situation will need to be modified as well.

Additionally, as discussed earlier, complete stone removal is at times not possible in one endoscopic session. In those situations, a temporizing measure should often be used to maintain patent biliary drainage by the placement of a biliary stent while a definitive therapy is awaited. Stent placement when complete stone removal cannot be accomplished allows for continued biliary drainage but also secondarily allows for mechanical friction on the stone, potentially easing secondary attempts for stone removal.

Despite all of the above methods, there are rare occasions where stone removal is not amenable to endoscopic therapy. In these situations the approach to bile duct stones can be

either surgical (open, laparoscopic) or by radiological method (percutaneous).

Patients with a history of bile duct stones and intact gallbladder are at risk for cholecystitis and/or further biliary obstruction [9]. Therefore, once the stone has been removed from the bile duct in patients with an intact gallbladder, elective cholecystectomy should be recommended within 6 weeks of ERCP.

Conclusion

In conclusion, the character of bile duct stones and presentation vary widely. Appropriate modality of investigation and therapy should be chosen based on the symptoms of patients and local expertise.

References

1. Everhart JE, Khare M, Hill M, Maurer KR. Prevalence and ethnic differences in gallbladder disease in the United States. Gastroenterology. 1999;117:632.
2. Sampliner RE, Bennett PH, Comess LJ, et al. Gallbladder disease in Pima Indians. Demonstration of high prevalence and early onset by cholecystography. N Engl J Med. 1970;283:1358.
3. Barbara L, Sama C, Marselli-Labate AM, et al. A ten-year incidence of gallstone disease: the Sirmione study. J Hepatol. 1993;18(1):S43.
4. Everson GT. Pregnancy and gallstones. Hepatology. 1993;17:159.
5. Gilat T, Feldman C, Halpern Z, et al. An increased familial frequency of gallstones. Gastroenterology. 1983;84:242.
6. Sarin SK, Negi VS, Dewan R, et al. High familial prevalence of gallstones in the first-degree relatives of gallstone patients. Hepatology. 1995;22:38.
7. Broomfield PH, Chopra R, Sheinbaum RC, et al. Effects of ursodeoxycholic acid and aspirin on the formation of lithogenic bile and gallstones during weight loss. N Engl J Med. 1988;319:1567.
8. Shiffman ML, Kaplan GD, Brinkman-Kaplan V, Vickers FF. Prophylaxis against gallstone formation with ursodeoxycholic acid in patients participating in a very low calorie diet program. Ann Intern Med. 1995;122:899.
9. Lammert F, Miguel JF. Gallstones disease: from genes to evidence-based therapy. J Hepatol. 2008;48:S124.
10. Gallstones and laparoscopic cholecystectomy. NIH Consensus Statement. 1992;10:1.
11. Abboud PC, Malet PF, Berlin JA, et al. Predictors of common bile duct stones prior to cholecystectomy: a meta-analysis. Gastrointest Endosc. 1996;44:450.
12. Easler J, Sherman S. Endoscopic retrograde cholangiopancreatography for the management of common bile duct stones and gallstone pancreatitis. Gastrointest Endosc Clin N Am. 2015;25:657.
13. Gurusamy KS, Giljaca V, Takwoingi Y, et al. Ultrasound versus liver function tests for the diagnosis of common bile duct stones. Cochrane Database Syst Rev. 2015;2:CD011548.
14. Kaltenhaler E, Vergel YB, Chilcott J, et al. A systematic review and economic evaluation of magnetic resonance cholangiopancreatography compared with diagnostic endoscopic retrograde cholangiopancreatography. Health Technol Assess. 2004;8:iii. 1
15. Kiriyama S, Takada T, Strasberg SM, Solomkin JS, et al. TG13 guidelines for diagnosis and severity grading of acute cholangitis (with videos). J Hepatobiliary Pancreat Sci. 2013;20(1):24–34.
16. Giljaca V, Gurusamy KS, Takwoingi Y, et al. Endoscopic ultrasound versus magnetic resonance cholangiopancreatography for common bile duct stones. Cochrane Database Syst Rev. 2015;26(2):CD011549.
17. ASGE Standards of Practice Committee, Maple JT, Ben-Menachem T, Anderson MA, Appalaneni V, Banerjee S, Cash BD, Fisher L, Harrison ME, Fanelli RD, Fukami N, Ikenberry SO, Jain R, Khan K, Krinsky ML, Strohmeyer L, Dominitz JA. The role of endoscopy in the evaluation of suspected choledocholithiasis. Gastrointest Endosc. 2010;71(1):1–9.
18. Internal Clinical Guidelines T. National Institute for Health and Clinical Excellence: Guidance. Gallstone disease: diagnosis and management of cholelithiasis, cholecystitis and choledocholithiasis. London: National Institute for Health and Care Excellence (UK), Copyright (c) National Clinical Guideline Centre; 2014.
19. Moller M, Gustafsson U, Rasmussen F, et al. Natural course vs interventions to clear common bile duct stones: data from the Swedish registry for gallstone surgery and endoscopic retrograde cholangiopancreatography (GallRiks). JAMA Surg. 2014;149:1008–13.
20. Khashab MA, et al. Delayed and unsuccessful endoscopic retrograde cholangiopancreatography are associated with worse outcomes in patients with acute cholangitis. Clin Gastroenterol Hepatol. 2012;10(10):1157–61.
21. Rosenkranz L, Patel S. Endoscopic retrograde cholangiopancreatography for stone burden in the bile and pancreatic ducts. Gastrointest Endosc Clin N Am. 2012;22:435–50.
22. Freeman ML, Nelson DB, Sherman S, et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med. 1996;335(13):909–18.
23. Attasaranya S, et al. Large-diameter biliary orifice balloon dilation to aid in endoscopic bile duct stone removal: a multicenter series. Gastrointest Endosc. 2008;67(7):1046–52.
24. Liao WC, Lee CT, et al. Randomized trial of 1-minute versus 5-minute endoscopic balloon dilation for extraction of bile duct stones. Gastrointest Endosc. 2010;72:1154–62.
25. Buxbaum J. Modern management of common bile duct stones. Gastrointest Endosc Clin N Am. 2013;23(2):251–75.
26. Arya N, Nelles SE, Haber GB, et al. Electrohydraulic lithotripsy in 111 patients: a safe and effective therapy for difficult bile duct stones. Am J Gastroenterol. 2004;99(12):2330–4.
27. Lee TY, Cheon YK, Choe WH, et al. Direct cholangioscopy-based holmium laser lithotripsy of difficult bile duct stones by using an ultrathin upper endoscope without a separate biliary irrigating catheter. Photomed Laser Surg. 2012;30:31.
28. Maydeo A, Kwek BE, Bhandari S, et al. Single-operator cholangioscopy-guided laser lithotripsy in patients with difficult biliary and pancreatic ductal stones (with videos). Gastrointest Endosc. 2011;74:1308.
29. Patel SN, Rosenkranz L, Hooks B, et al. Holmium-YAG laser lithotripsy in the treatment of pancreatico-biliary calculi utilizing peroral single operator cholangio- scopy (SpyGlass): an update on a multi-center experience [abstract]. Gastrointest Endosc. 2010;71:AB229.
30. Sackmann M, Holl J, Sauter GH, et al. Extracorporeal shock wave lithotripsy for clearance of bile duct stones resistant to endoscopic extraction. Gastrointest Endosc. 2001;53(1):27–32.

Cholangiopancreatoscopy

30

Isaac Raijman

Introduction

Cholangioscopes have been around for the last four decades, having been introduced for the nonsurgical management of difficult bile duct stones [1–3]. It was soon recognized that direct visualization of the biliary epithelium was useful in the assessment of biliary strictures and other pathologies. It was also postulated that the same miniature endoscope could be used in the pancreatic duct. Cholangioscopy and pancreatoscopy allow for the assessment of the respective lumen and mucosa and allow for targeted therapy (mainly lithotripsy), targeted tissue acquisition, and wire guidance [4–20]. Cholangioscopy and pancreatoscopy are used not only for lithotripsy but also for assurance of ductal clearance. Biliary and pancreatic strictures can be assessed not only at the level of the stricture itself but also the mucosa around the stricture and additionally can identify synchronous lesions. Filling defects during cholangiography and pancreatography can be mistaken as stones when they actually are tumors, and this can be assessed by direct visualization.

The initial cholangioscopes (pancreatoscopes) were cumbersome, difficult to use, and fragile and associated with expensive repairs and required two operators, thus limiting their use. In addition, not all available cholangioscopes/cholangioscopic methods can be used in all patients with biliary disease and certainly not in all patients with pancreatic pathologies. In 2007, a different cholangioscope was introduced to answer those issues [10]. Since the inception of the latter cholangioscope, SpyGlass^{tm}, the use of cholangioscopy has increased dramatically, and a plethora of published papers have become available.

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The majority of current literature, ongoing research, and worldwide performance of cholangiopancreatoscopy revolves around SpyGlass^{tm}, which has gained global increasing acceptance. There are two generations of the SpyGlass^{tm}: the initial generation or "Legacy" and the second generation or SpyGlass^{tm} DS. Before we describe SpyGlass^{tm}, it is important to understand the various methods of performance of cholangiopancreatoscopy. In this chapter, I will concentrate on the use of single-operator cholangioscopy and pancreatoscopy with SpyGlass^{tm}.

Cholangioscopy

Peroral cholangioscopy is divided into two main systems: mother-daughter or dual-operator systems and catheter-based or single-operator systems. The methods are also known as direct peroral cholangioscopy (single-scope introduction from the mouth to the bile duct) and indirect peroral cholangioscopy (a scope is inserted through the duodenoscope into the bile duct). Direct peroral cholangioscopy is limited to a certain caliber extrahepatic bile duct or pancreatic duct, and thus it is not possible in all patients with biliary or pancreatic pathology.

SpyGlass^{tm} Legacy is a catheter-based single-operator fiber-optic miniature scope (Boston Scientific, Natick, MA, USA) [12–14]. It is composed of a disposable 10 French, 230 cm long catheter with four lumens: two for irrigation (0.6 mm each), one for the optical fiber (0.9 mm), and one for instrumentation. The latter has a caliber of 1.2 mm. The optical fiber is a 0.77 mm, 6000 pixel fiber-optic bundle that is introduced through the catheter allowing for visualization. The optical fiber is 231 cm long and provides a 70° field of view. This fiber is reusable. In our experience, this fiber can be used numerous times (up to 20 in some instances). However, further uses of the fiber deteriorate visualization. The catheter has a four-way tip deflection much like a regular endoscope. In addition, it allows for simultaneous instrumentation and

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irrigation due to its independent channels. The irrigation port is attached to a water pump that is actuated by a pedal; the endoscopist controls. Scope tip movement is accomplished not only by the SpyGlass[tm] itself but also by the movements of the duodenoscope and the movements of the endoscopist. The combination of these allows for literally infinite possibilities. Limitations to the system are primarily dictated by the size of the duct to be investigated, sharp and angulated strictures, and in patients with anatomic variations of any etiology that do not allow for proper duodenoscope position.

The new SpyGlass[tm] DS is a single-use, all-inclusive digital scope. It is 10.5 French in OD, 220 cm long catheter with three lumens: two for irrigation (0.6 mm each) and one for instrumentation (1.3 mm). The tip can deflect 30^0 in each direction. The DS system has also undergone major changes in the head of the scope as well as in its connecting cord to the light source, which have been greatly simplified. The tip of the DS scope has a beveled side, where the instrumentation channel is. Significant performance improvements include optical resolution, depth of light penetration, a 60% increase in field of view, steerability, and depth of reach.

Because SpyGlass[tm] (either generation) is the one more commonly used worldwide and it is increasing in popularity (especially DS), I will from now on refer to the cholangioscope/pancreatoscope as SpyGlass[tm]. I was fortunate to be the first in using the SpyGlass[tm] DS in a human in February of 2015. Since then I have exclusively used it as will be described below. The majority of the available literature is based on results of the Legacy system, but it is expected that the same or better will be achieved with the DS system. In my experience in 200 DS procedures in the last 13 months, the visualization, maneuverability, and depth of reach have been superior. The setup has been simplified to a "plug and play" (Figs. 30.1, 30.2 and 30.3).

Fig. 30.1 The SpyGlass DS[tm]. Note the beveled shape of the tip of the cholangioscope where the therapeutic channel is. The all-inclusive design allows for better maneuverability. The two irrigation channels and the two lamps are noted

Fig. 30.2 This is the new plug-and-play system

Fig. 30.3 The SpyGlass DS[tm] head now contains only the port for the therapeutic channel, facilitating handling. The irrigation and suction ports have now been moved away from the head of the scope via extension tubing. The loop that the cholangioscope creates after insertion into the duodenoscope channel is smaller, thus making it less intrusive. The head of the cholangioscope is light and adds minimal weight to the duodenoscope. Note the knobs of the SpyGlass DS[tm] being aligned to the knobs of the duodenoscope

Performance of SpyGlass[tm] Procedure in Bile Duct and Pancreatic Duct

SpyGlass[tm] is performed at the time of ERCP and can also be performed percutaneously. Because of the design improvements, SpyGlass[tm] DS is easier to perform percutaneously compared to SpyGlass[tm] Legacy. The preparation and sedation for cholangioscopy are the same as for ERCP. In our

unit, the vast majority of the procedures are performed under intravenous propofol (monitored anesthesia), the head of the fluoroscopy table is elevated approximately 30° to decrease the risk of aspiration, and all patients receive prophylactic antibiotics. In some patients, especially those with strictures or those immunocompromised, antibiotics are continued for few days after cholangioscopy. For pancreatoscopy, the preparation is the same, but we do not routinely use prophylactic antibiotics.

In the majority of patients, a biliary sphincterotomy (pancreatic sphincterotomy when indicated) is (are) either performed or is already existent. In patients with a mucinous papilla, a sphincterotomy is not performed. A standard cholangiogram or pancreatogram is performed to provide guidance to the site of the lesion or to define the stone (s), as well as to define the distal anatomy. The amount of contrast injected is dictated by the indication for the procedure. Contrast does not interfere with the visualization, especially with the newer DS system. It is recommended the sphincterotomy performed prior to the introduction of the scope is small, and then complete it after cholangiopancreatoscopy was finished. The advantage of doing that is to prevent the excess migration of duodenal air into the duct (s), which then improves visualization and minimizes the need for water flushing. A guidewire is left in place, and over it SpyGlass will be advanced. A long (410 cm) or short (260 cm) guidewire can be used. Once SpyGlass^{tm} is inside the bile duct or the pancreatic duct, the guidewire is removed to allow for better suction of contrast-debris and to advance any instruments needed. If the intent of cholangioscopy is to aid in the cannulation of a difficult stricture, the guidewire must be long, and an exchange can be made with SpyGlass^{tm}.

It is important to intermittently use fluoroscopy throughout the SpyGlass^{tm} procedure in order to more precisely determine the location of the lesion, as cholangioscopy alone is not very accurate in intraductal location. In the pancreas, it is easier, but, when assessing a stricture or tumor, fluoroscopy becomes important to more precisely recognize the site of involvement. It is also important to systematically assess the bile duct in order to avoid missing lesions and to fully assess the biliary lumen. For those endoscopists who first start performing SpyGlass^{tm}, it is frequently that too much movement is applied to the tip of the SpyGlass^{tm}: it is best to advance the SpyGlass^{tm} to the proximal duct when possible, identify the lumen, and then move the tip, usually with the SpyGlass^{tm} knobs first. Lastly, it is beneficial to avoid irrigation of the lumen when the SpyGlass^{tm} is advanced first. Aspiration of contents until the lumen collapses and then irrigation will improve visualization and minimize flushing.

How Do I Perform SpyGlass^{tm}?

First, I consent all patients undergoing ERCP for SpyGlass DS^{tm}. While it is not expected that all patients will need it, it is better to be prepared should it be necessary. You do not want to either be unable to perform SpyGlass DS^{tm} because you don't have consent or stop in the middle of the procedure to obtain it.

Second, engage your assistants and nurses in the procedure. A willing and capable team helping you makes a big difference. Tables 30.1 and 30.2 relate to the preparation and cholangioscopy.

Current Indications for Cholangioscopy

By far the two most common indications for cholangioscopy are management of difficult stones and stricture assessment (Table 30.3). In my practice, of all SpyGlass^{tm} procedures, 80% are for biliary indications. Of those, approximately 50% are for management of difficult biliary stones, 35% for assessment of indeterminate strictures, and 15% for other indications. For pancreatoscopy, the most common indication is lithotripsy followed by assessment of main-duct IPMN and indeterminate strictures.

Table 30.1 Practical considerations: preparation

Flush all the ports
Alignment of SpyGlass knobs to the duodenoscope knobs
All monitors in front of the endoscopist
Duodenoscope must be in a good position. Remember the SpyGlass^{tm} is an extension of the duodenoscope (which in turn is an extension of the endoscopists arm)
All patients must receive prophylactic antibiotics (biliary)

Table 30.2 Practical considerations performance

Start the procedure with a small sphincterotomy; complete it after SpyGlass^{tm}
Contrast injection does not affect the performance of SpyGlass^{tm}
Keep the duodenal lumen suctioned to decrease air leak into ducts
Introduce SpyGlass^{tm} by engaging at the papillary os and then bringing the duodenoscope big wheel up and pull scope upward
Proximal to distal evaluation of the duct is important
May use short or long wires
Luminal suction first, then flushing. Use the smallest amount possible of flushing
Avoid suctioning the duct wall. I recommend using a 20 cc Luer lock syringe for suctioning instead of wall suction
Intermittently confirm position of the SpyGlass^{tm} in the duct under fluoroscopy

Table 30.3 Therapeutic and diagnostic indications for cholangioscopy

Therapeutic[a]	Diagnostic
Lithotripsy	Biliary strictures
Tumor ablation	Tumor staging
Control of bleeding	Filling defects
Guidewire advancement	Ductal abnormalities
Reopening occluded metal stents	Choledochal cysts
Sealing of leaks	Tissue acquisition
Removal of migrated stents	Advanced imaging

[a]Some represent case reports

Cholangioscopy

Bile Duct Stones

Bile duct stones can affect approximately 10–20% of patient with cholelithiasis, and in 10% of the patients, the gallbladder is not involved. Most commonly bile duct stones occur in the extrahepatic biliary tree. Endoscopic removal of bile duct stones via standard methods is effective in about 90% of patients. In the other 10%, more advanced methods are needed because of stone location, size, shape, or presence of a stricture. Cholangioscopy-guided lithotripsy via holmium Nd-YAG laser or electrohydraulic lithotripsy is highly effective and can be used for both intrahepatic and extrahepatic stones. In addition, direct visualization of the stone allows for decreasing bile duct injury and for differentiation among stone fragments, blood clots, air bubbles, etc. [6, 8, 10–16, 18, 24].

Electrohydraulic lithotripsy (EHL) is performed by using a fiber that is connected to a power source (AUTOLITH, Nortech, Northgate technologies, IL, USA). The EHL fiber is 1.9 French, 375 cm long. The tip of the fiber contains an open tip with two coaxially insulated electrodes (bipolar technology). When the power source is activated, a spark is generated within the electrodes, which under water (0.9% saline) produces high-voltage hydraulic pressure waves, or a rapidly expanding cavitation bubble, which upon collapse creates a secondary pressure wave (shock wave). The difference in acoustic impedance at the stone-saline interface causes energy release with ensuing lithotripsy. It is important to be no more than 3–4 mm from the stone for the wave to hit the stone. Otherwise it may dissipate before reaching target. The energy density is obtained by combining frequencies of 1–20/s and voltage from 50 to 100. With EHL, the fluid media must contain electrolytes to conduct the hydraulic pressure waves. En face application is best to achieve better results and avoid ductal wall injury [11].

The overall experience with SpyGlass^{tm} since it's beginning stages to this date has reported a success rate of 90–100% for extrahepatic stones and around 80–85% for intrahepatic stones [6, 8, 10–16, 18, 24]. These reports have used either EHL or holmium laser lithotripsy. In a study of 32 patients with difficult bile duct stones, intrahepatic in 8, extrahepatic in 18 both in 6, and associated with biliary strictures. In 20, complete stone clearance was achieved with cholangioscopy and EHL in 81% and partial in 16%. When stone clearance is achieved with cholangioscopy, stone recurrence is low.

In a series of 94 patients with difficult bile duct stones, most of them greater than 20 mm, and using the mother-daughter system with EHL, complete stone fragmentation was achieved in 66% of the patients, and partial fragmentation was achieved in 30%. A significant number of patients, 18%, had complications, including cholangitis and jaundice as the most common. In a study of 121 patients, 41 of whom had biliary stones; ductal clearance was achieved in 37 patients after one session and in the remaining 4 patients, in 2 sessions. EHL and holmium laser were used [16].

Pulsed laser lithotripsy is performed in a similar fashion [14, 16]. The laser fibers are made of flexible quartz. We use the SlimLine SIS GI, 365 micron, 3 m long, end-fire fibers, with a maximum energy of 4.0 J, 100 W (Lumenis, Santa Clara, CA, USA). The fiber emits an aiming beam that facilitates tip recognition and target. The fiber is connected to a laser (VersaPulse P20, Lumenis, Santa Clara, CA, USA) that is actuated via a pedal. The settings of the laser console are adjusted to produce an energy density (watts) which is the end product of frequency (hertz) x energy (joules). The laser is immediately absorbed within the fluid media (bile) producing a "vapor bubble" (a high-kinetic energy collection of ions and electrons). This bubble (plasma) expands quickly producing a mechanical shock wave. The fiber has to be within <2 mm of the stone to reach target. Laser can be applied and fragment the stone even when not en face application. If the fiber touches the stone, it will initially drill the stone before it causes fragmentation, as there is no room for the vapor bubble to form.

In an international multicenter study of 66 patients with stone disease (out of a total of 297 patients), 92% had a successful procedure, and complete stone clearance during the study session was 71% and a complication rate of 6.1% [14]. SpyGlass^{tm} has also been used for removal of stones within the cystic duct. Another use of SpyGlass^{tm} is in the clearance of the bile duct, especially in patients at increased risk for residual or recurrent stones: juxtapapillary diverticula, largely dilated bile ducts, extensive pneumobilia, and extensive lithotripsy. It is also important to ensure clearance of the intrahepatic ducts especially when lithotripsy is carried out close to the confluence. Lastly, SpyGlass^{tm} can correctly identify choledocholithiasis in 8–30% of cases missed during routine ERCP. Table 30.4 shows practical considerations for the performance of biliary lithotripsy under cholangioscopic guidance (Figs. 30.4 and 30.5).

Table 30.4 Practical considerations: biliary lithotripsy

If possible, start with the most proximal stone. This facilitates visualization of distal stones
Secure the tip of the fiber with the Y-port attachment of the working channel of the SpyGlass[tm]. It is important to keep the fiber tip secured 3–4 mm out of the scope to avoid potential melting of the tip of the SpyGlass[tm]
The tip of the fiber should be <2 mm when firing laser or EHL. Avoid touching the stone with the fiber as this can decrease fiber performance and durability and will cause drilling and not stone fragmentation
Fragment to stone to the smallest pieces possible
Flush the duct frequently when performing lithotripsy in order to keep the field of view clean and to cool down the duct lumen

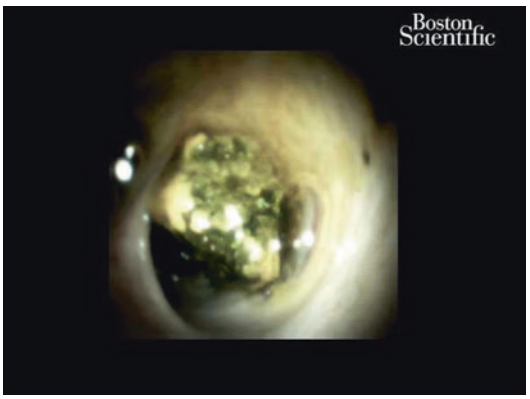

Fig. 30.4 SpyGlass DS[tm] image of intrahepatic bile duct stone

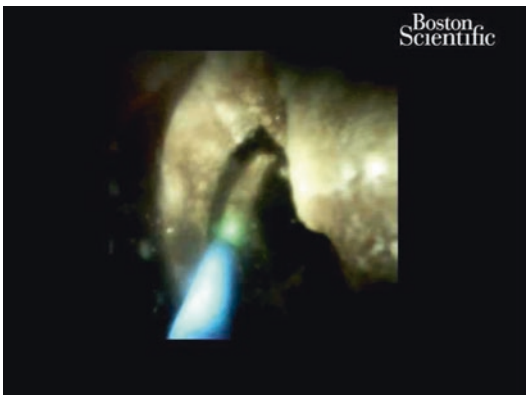

Fig. 30.5 SpyGlass DS[tm] image of holmium laser lithotripsy of cystic duct stone

Practical Considerations

Tips to Performing Biliary Lithotripsy

Bile Duct Strictures

SpyGlass[tm] can provide valuable data in the evaluation of indeterminate biliary strictures, both by providing direct assessment of the involved epithelium, the adjacent epithelium, and associated synchronous lesions and in providing direct visualization for biopsies. In various studies using the Legacy system, including multicenter studies, the diagnostic accuracy of SpyGlass[tm] cholangioscopic visualization has been in the ~90% rate, whereas the diagnostic accuracy of SpyBite[tm] cholangioscopic biopsy has been in the ~80% [6, 7, 9, 10, 16–23]. Tables 30.5 and 30.6 show the cholangioscopic characteristics of malignant and benign strictures, respectively.

Table 30.5 Characteristics of malignant biliary strictures during SpyGlass[tm]. The mnemonic is FEELN

Friability
Exophytic/nodular tissue
Elongated villi with central vessel
Luminal reduction: concentric or not concentric
Neovascularity. Tumor vessel, vascular lakes
Abnormal vascular pattern and prominent blood vessels, and lack of vascular network are the most significant indicators of malignancy

Table 30.6 Characteristics of benign biliary strictures during SpyGlass[tm]

Lack of friability
Nodular tissue may be present but seldom exophytic
Preserved vascular pattern and network. Absence of prominent vessel or vascular lakes
Scarring
Absence of neovascularity

In a multicenter study of 297 patients, SpyGlass[tm] was performed in 86 patients without biopsy and in 140 patients with biopsy [14]. Tissue acquisition was possible in most of the patients (88%). In the final analysis of 95 patients, the overall sensitivity for malignancy was 78% for visual characteristics, 49% for directed biopsies. When the analysis was done for intrinsic biliary malignancy, the sensitivity was 84% and 66%, respectively. The specificity for visualization and directed biopsy was 82% and 98%, positive predictive value was 805% and 100%, and negative predictive value was 80% and 72%, respectively.

In a study of 121 patients, 25 of whom had biliary stricture; the original diagnosis of the stricture was modified in 20, confirmed to be malignant in almost 50% of the patients and nonmalignant in 9 [16]. In a cohort of 18 patients, the overall sensitivity of cholangioscopy for detecting malignancy with or without biopsies had a sensitivity of 89%, specificity of 96%, positive predictive value of 89%, and negative predictive value of 96%.

Cholangioscopic characterization of the lesion is based on various factors: types of luminal narrowing, friability, vascularity, and mucosal changes. The presence of a tumor vessel (an irregular and tortuous vessel) by itself has a predictive value of >60% [24]. In strictures with tumor vessel present and negative biopsies, the most

common form of cancer was infiltrative type, which spreads more below the superficial epithelium and is associated with significant desmoplastic tissue. A cholangioscopic classification of nodular, papillary, and infiltrative types based on visual characteristics was offered by Seo et al. [21]. In this classification, nodular cholangiocarcinoma produces luminal narrowing, usually short strictures and intense neovascularization. Papillary cholangiocarcinoma usually has little neovascularization, spreads superficially, has papillary mucosal projections, and may have associated mucus and sludge. Infiltrative cholangiocarcinoma produces subtle mucosal elevations, luminal narrowing, and little vascularization. In more recent data and in my experience with 1500 SpyGlass^{tm} procedures, more commonly there is a combination of features, and the two more predictive of malignancy include abnormal vasculature and friability.

Primary sclerosing cholangitis can be associated with dominant strictures that cholangiography alone cannot distinguish its biologic behavior. In a study of 53 patients with PSC and dominant strictures, cholangioscopy had sensitivity in diagnosing malignancy of 92% compared to 66% of cholangiography alone, a specificity of 93% vs. 51%, a positive predictive value of 79% vs. 29%, and a negative predictive value of 97% vs. 84% [32].

A definitive diagnosis requires histological assessment. During tissue acquisition, a minimum of three biopsies is needed, and biopsies should be obtained both from the exophytic tissue and from the margins of the lesion. In our institution, we obtain a minimum of four biopsies per site of interest. The tissue is sent to pathology where a cellblock is obtained. Draganov et al. compared three tissue acquisition methods: brush cytology, fluoroscopy-guided biopsies, and SpyBite^{tm} biopsies. An adequate sample was obtained in most patients (25 of 26 of the cytology brushings (96%), 26 of 26 of the fluoroscopy-guided biopsies (100%), and 25 of 26 of the SpyBite^{tm} biopsies (96%)). They showed an accuracy of 85% for SpyBite^{tm} biopsies compared to 54% for fluoroscopy-guided biopsies and 35% for cytology brushings.

SpyGlass^{tm} can also be used in the staging of cholangiocarcinoma. It is well known that cholangiocarcinoma often shows superficial mucosal spread. In general, papillary and nodular cholangiocarcinomas offer superficial mucosal spread, whereas infiltrative-type cholangiocarcinomas are associated with wall infiltration and almost no mucosal spread. This is important in the luminal assessment of cancer as well as in tissue acquisition, where infiltrative processes are less likely to have a positive biopsy. Table 30.7 shows the various tips for the performance of cholangioscopy-guided tissue acquisition using SpyBite^{tm} (Figs. 30.6, 30.7, 30.8, and 30.9).

Table 30.7 Practical considerations: cholangioscopy in stricture assessment and tissue acquisition

Always examine the intrahepatic branches for extrahepatic strictures to ensure both extension of the disease or associated synchronous lesions
Minimize the amount of water irrigation
When obtaining biopsies, a minimum of four pieces should be obtained
Discuss with your pathologist that the biopsy sample is small
The most common site for the biopsy forceps to get stuck is at the level of the duodenoscope/cholangioscope angle. If you cannot advance the forceps past this area, then leave it in place and simply move the cholangioscope further into the bile duct, thus carrying the forceps with it. Also ensure the tip of the cholangioscope is not locked

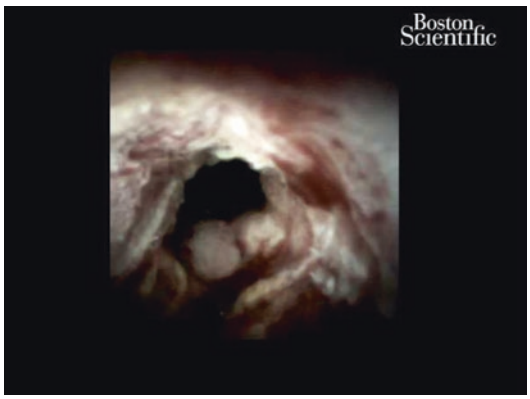

Fig. 30.6 SpyGlass DS^{tm} image of cholangiocarcinoma

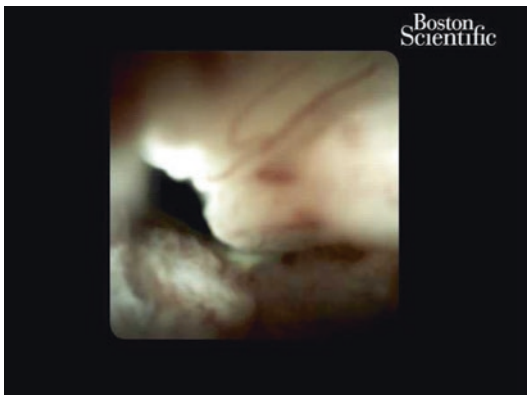

Fig. 30.7 SpyGlass DS^{tm} image of distal bile duct stricture due to pancreatic cancer

Other Indications for Cholangioscopy

Patients after liver transplantation may be complicated with biliary strictures, usually anastomotic. There are times when the stricture is related to a cast-like stone that may not be recognized with cholangiography alone [16, 25]. In addition, cholangioscopy can identify other lesions such as ischemic or infectious ulcers and distinguish blood clots from stones,

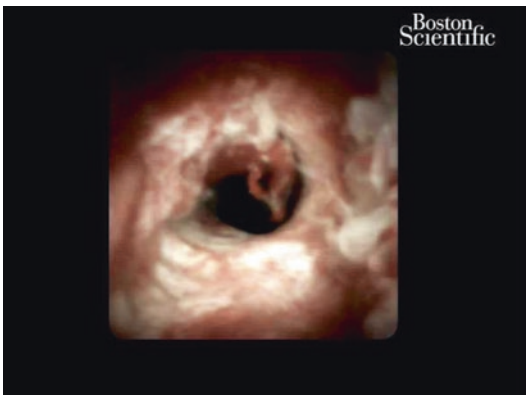

Fig. 30.8 SpyGlass DS[tm] image of cholangiocarcinoma of the hilum (Klatskin-I)

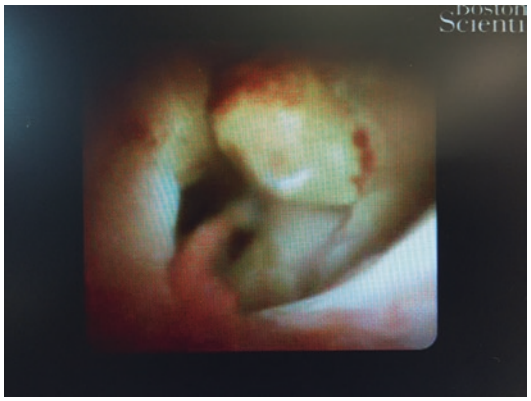

Fig. 30.10 SpyGlass DS[tm] image of hemobilia caused by cholangiocarcinoma

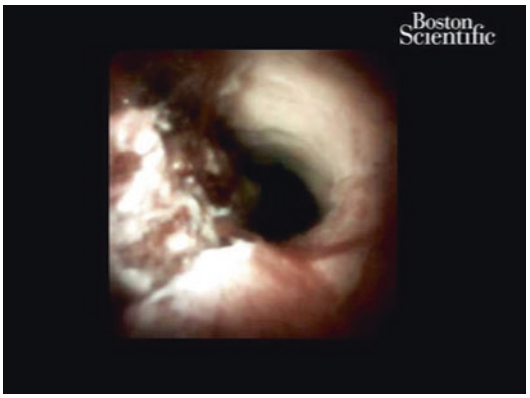

Fig. 30.9 SpyGlass DS[tm] image of distal cholangiocarcinoma

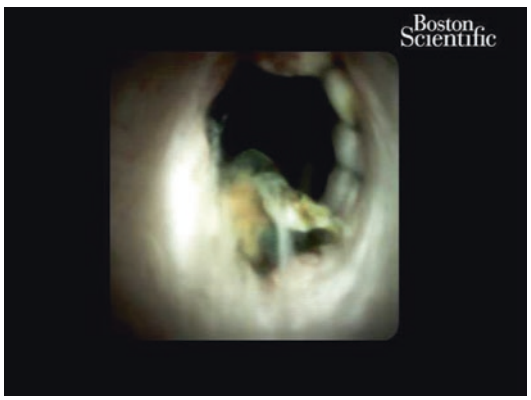

Fig. 30.11 SpyGlass DS[tm] image of an anastomosis 1 year after liver transplant

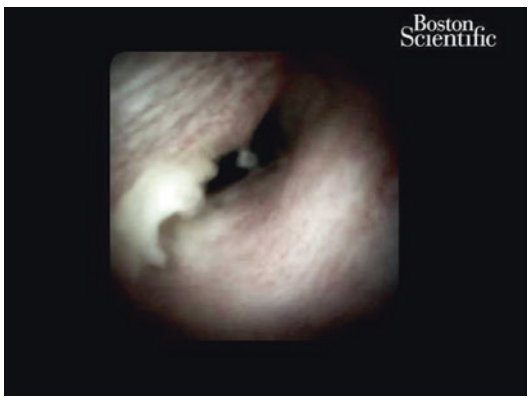

Fig. 30.12 SpyGlass DS[tm] image of autoimmune cholangiopathy

scar tissue, etc. In our experience with 60 patients, additional data was obtained with cholangioscopy in almost one third of the patients that altered management [16].

SpyGlass[tm] has been used in patients in whom a diagnosis was not possible by other means: in one case, a venous malformation was encountered in a patient with hereditary hemorrhagic telangiectasia. A case of cytomegalovirus cholangiopathy was reported. We have experience with three patients in whom metastatic breast cancer was found in one, metastatic colon cancer in one, and a pseudo-aneurysm to the left hepatic artery in one.

Local treatment with photodynamic therapy, argon plasma coagulation and brachytherapy has been reported in patients with various biliary malignancies. SpyGlass[tm] has been used to remove proximally migrated stents. It has also been used to inject sealant for refractory bile leak (Figs. 30.10, 30.11, and 30.12).

Complications of Cholangioscopy

Besides the potential complications of ERCP, the two main complications of peroral cholangioscopy include infection and perforation [26]. Diagnostic cholangioscopy is quite safe but the main risk is infection: especially in patients with strictures and immunocompromised, chronic stone disease and/or previous bile duct manipulation and patients receiving excessive intraductal flushing, etc. A contraindication for SpyGlass[tm] is

acute cholangitis. All patients should receive prophylactic antibiotics. During therapeutic cholangioscopy, the risk of bleeding or perforation increases mainly due to the use of lithotripsy, especially EHL. Direct contact of the bile duct wall during lithotripsy can cause bleeding, and excess or prolonged contact can potentially cause perforation. Thermal wall injury is a potential complication during prolonged lithotripsy especially if the stone is large and in contact with the wall. In general, the rate of cholangitis for cholangioscopy is approximately 1%, the rate of pancreatitis 2%, and perforation 1.0%.

Pancreatoscopy

There are several dedicated pancreatoscopes in the market, of varying small caliber and some with small-caliber therapeutic channels. There are electronic pancreatoscopes with surface enhancement capabilities [27]. These pancreatoscopes are fragile, limited in access and expensive. Like cholangioscopy, most of the current data reporting pancreatoscopy revolve around SpyGlass^{tm} and thus will concentrate in such. Table 30.8 shows the current indications for therapeutic and diagnostic pancreatoscopy.

The preparation for pancreatoscopy with SpyGlass^{tm} is the same as described above for cholangioscopy. Table 30.9 shows practical considerations for the performance of pancreatoscopy. I do not use prophylactic antibiotics for it. I routinely use rectal indomethacin prior to the ERCP in all patients undergoing pancreatoscopy. The performance of SpyGlass^{tm} pancreatoscopy is more difficult than cholangioscopy due to the side branches, duct tortuosity, and navigating around the genu. There is more need to steer the tip of the SpyGlass^{tm} to advance forward. Usually there is less need for irrigation and is easier to visualize the entire lumen. It is preferably to advance it over a guidewire to the tail and begin the examination then.

Pancreatic Duct Stones

The main problem with pancreatic duct stones is when they are impacted distally. This poses a problem for pancreatoscopy because the pancreatoscope does not have enough room in the duct to be accommodated or the angle is improper; there is often a suprapapillary stenosis associated which further makes pancreatoscope advancement difficult. Ideally, either there is enough ductal space distal to the stone to accommodate the pancreatoscope or the latter can be advanced proximal to the stone. It is anticipated that if a guidewire can be advanced proximal to the stone, then the likelihood of success is greater [16, 28, 29]. SpyGlass^{tm} has been used as a rescue therapy for pancreatic stones in patients in whom other forms of therapy such as extracorporeal shock wave lithotripsy failed. SpyGlass^{tm}-guided lithotripsy has a success ranging from 40% to 50% for complete stone clearance and 75–80% in achieving symptomatic improvement or allowing for placement of pancreatic stents [6, 16]. In our experience, the difficulty in managing these patients relates to the ability to negotiate distal strictures, passage of the wire proximal to the stone, tight ductal bends distal to the stone, and clearance of stone extension into side branches.

The performance of pancreatic stone lithotripsy follows the same principles as that of bile duct stones, as shown in Table 30.10 (Fig. 30.13).

Table 30.8 Current indications for pancreatoscopy

Therapeutic	Diagnostic
Lithotripsy	Strictures
Guidewire advancement	Tumor staging (IPMN)
	Filling defects
	Ductal abnormalities
	Tissue acquisition
	Advanced imaging

Table 30.9 Practical considerations: how do I perform pancreatoscopy with SpyGlass^{tm}?

Start with small sphincterotomy; complete after SpyGlass^{tm}. This significantly reduces air in the pancreatic duct and reduces the need for excessive flushing
Amount of contrast injected according to ERCP indication. Contrast does not affect performance of SpyGlass^{tm}
Keep duodenal lumen suctioned to decrease air leak into ducts. This is important especially when there is already an existing pancreatic sphincterotomy
Introduce SpyGlass^{tm} by engaging at the papillary os and then bringing the duodenoscope big wheel up and pull scope upward. This allows the tip of the SpyGlass^{tm} to engage the upper lip of the os and thus less forward resistance
The new SpyGlass DS^{tm} allows for more maneuverability of the tip which becomes very useful when entering either duct
The amount of flushing should be as little as possible
Prophylactic rectal indomethacin
Proximal to distal evaluation of the duct
May use short or long wires. Always advance over a guidewire
Luminal suction first, then flushing. Use the smallest amount possible of flushing to prevent potential complications
Avoid suctioning duct wall. When suctioning and the lumen collapses, then stop suction to allow for flushing. I recommend using a 20 cc Luer lock syringe for suctioning instead of wall suction. It is easier to control and much less likely to cause excessive luminal collapse
Intermittently confirm position of the SpyGlass^{tm} in the duct under fluoroscopy
There is an increased need to steer the tip of the SpyGlass^{tm} when maneuvering the pancreatic duct

Table 30.10 Practical considerations: pancreatic lithotripsy

Contrary to bile duct stones, you will most likely start with the most distal stone Often these stones are impacted and difficult to maneuver past them without performing lithotripsy
Secure the tip of the fiber with the Y-port attachment of the working channel of the SpyGlass[tm]. It is important to keep the fiber tip secured 3–4 mm out of the scope to avoid potential melting of the tip of the SpyGlass[tm]
The tip of the fiber should be <2 mm from the stone when firing laser or EHL. Avoid touching the stone with the fiber as this can decrease fiber performance and durability and will cause drilling and not stone fragmentation
Fragment to stone to the smallest pieces possible
Flush the duct frequently when performing lithotripsy in order to keep the field of view clean and to cool down the duct lumen

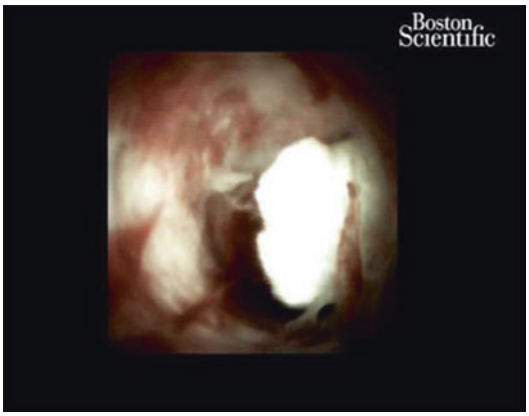

Fig. 30.13 SpyGlass DS[tm] image of main-duct pancreatic stone

Intraductal Papillary Mucinous Neoplasia

Pancreatic IPMN carries a risk of malignant transformation ranging from 15% to 60% and frequently requires surgical resection. SpyGlass[tm] is used in main-duct IPMN (Table 30.11). I have experience with mix-pattern IPMN, but navigating the lumen of the side branch even when dilated is difficult. It is somewhat easier with the new digital SpyGlass[tm] because its maneuverability is improved. In most patients with IPMN and a gaping papilla, there is no need to perform a pancreatic sphincterotomy. It is important to first sweep the duct with a balloon to remove intraductal mucus; otherwise, visualization is very limited. The mucus tends to be thick and is difficult to suction. Currently, the main use of pancreatoscopy in IPMN is in the preoperative assessment of the extent of the lesion, to rule out synchronous lesions and in identifying resection margins [30, 31]. In a study of 41 patients with IPMN, SpyGlass[tm] correctly identified 76% and 78% of the patients with main-duct IPMN and side-branched IPMN, respectively [28]. Of the 22 patients who underwent surgery, 76% had high-grade dysplasia. In that study, pancreatoscopy added diagnostic information and modified clinical decision-making in 76% of the patients. Karihara et al. [6] reported a procedural success rate of 88.2% in visualizing the target lesions. Failures included the inability to advance the SpyGlass[tm] to its target. SpyGlass[tm]-directed biopsy was diagnostic in 90.9% of the patients (Figs. 30.14 and 30.15).

Table 30.11 Practical considerations: assessment of ductal mucinous lesions

Before inserting the pancreatoscope, clear the ductal mucus out with a balloon
Always start from the tail of the pancreas and work down toward the head
Whenever an abnormality is noted with the pancreatoscope, match it with the fluoroscopic image for better location association
Biopsy all sites that show any abnormality
At the tumor site, obtain multiple biopsies, trying to cover as much of the tumor as possible. You may need to obtain eight to ten biopsies

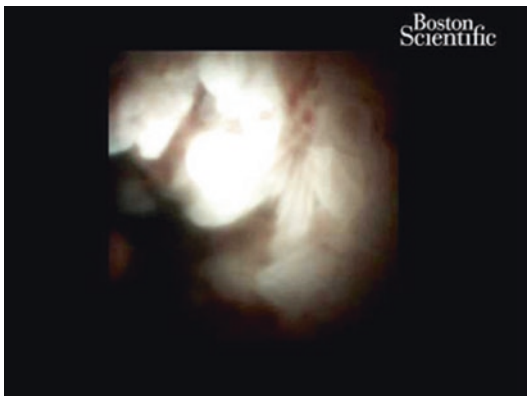

Fig. 30.14 SpyGlass DS[tm] image of main-duct IPMN

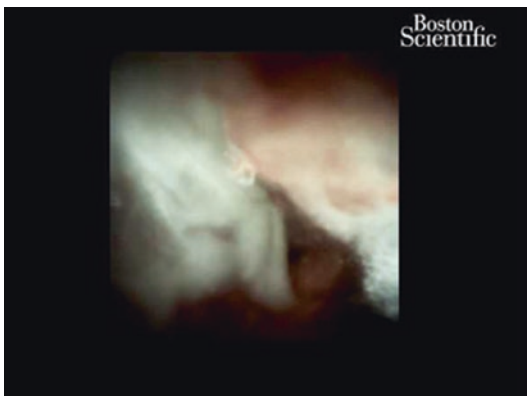

Fig. 30.15 SpyGlass DS[tm] image of main-duct IPMN

Table 30.12 Practical considerations: assessment of pancreatic strictures and lesions

Always try to advance the pancreatoscope to the tail of the pancreas
Dilate the stricture prior to pancreatoscopy if possible. Often a 4 mm balloon dilatation is sufficient
Whenever an abnormality is noted with the pancreatoscope, match it with the fluoroscopic image for better location association
Biopsy all sites that show any abnormality
At the tumor site, obtain multiple biopsies, trying to cover as much of the tumor as possible. You need to obtain at least four biopsies

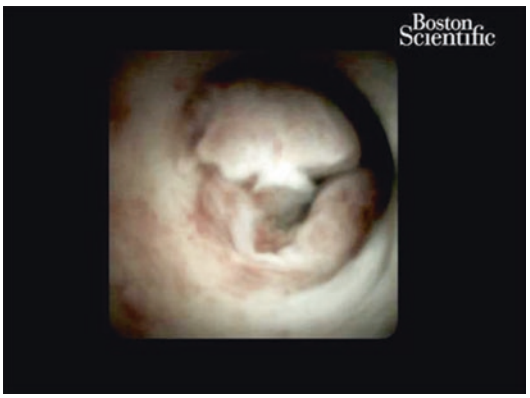

Fig. 30.16 SpyGlass DS[tm] image of main-duct stricture caused by a granuloma

Indeterminate Strictures of the Pancreatic Duct

There are patients in whom a pancreatic duct stricture is identified but there is no evidence of a mass on imaging studies, including endoscopic ultrasound. There are only a few anecdotal reports of SpyGlass[tm] in these patients. In my experience of five patients, four were identified to have scarring of the duct without visualized target lesion and in whom biopsies were nondiagnostic. One patient was found to have mucosal irregularities that showed dysplasia on biopsies. Patient underwent surgery (body-tail resection) identifying small foci of high-grade dysplasia. In these patients, the main limitation to pancreatoscopy is the caliber of the duct distal to the stricture. Table 30.12 reveals several practical considerations in this scenario (Fig. 30.16).

Conclusion

Cholangioscopes have been around for the last four decades, and although initially introduced for the nonsurgical management of difficult bile duct stones lately, cholangiopancreatoscopy allows for the assessment of the respective lumen and mucosa and allows for targeted therapy and targeted tissue acquisition. The operator should be trained and skilled to operate highly advanced technically challenging procedures.

References

1. Vennes JA, Silvis SE. Endoscopic visualization of bile and pancreatic ducts. Gastrointest Endosc. 1972;18:149.
2. Rosch W, Koch H, Demling I. Per oral cholangioscopy. Endoscopy. 1976;8:172–5.
3. Soda K, Shitou K, Yoshida Y, Yamanaka T, Kashii A, Miyata M. Per oral cholangioscopy using a new fine-caliber flexible scope for detailed examination without papillotomy. Gastrointest Endosc. 1996;43:233.
4. Fukuda Y, Tsuyuguchi T, Sakai Y, Tsuchiya S, Saisyo H. Diagnostic utility of per oral cholangioscopy for various bile-duct lesions. Gastrointest Endosc. 2005;62:374–82.
5. Siddique I, Galati J, Ankoma-Sey V, Wood RP, Ozaki C, Monsour H, Raijman I. The role of choledochoscopy in the diagnosis and management of biliary tract diseases. Gastrointest Endosc. 1999;50:67–73.
6. Kurihara T, Yasuda I, Isayama H, Tsuyuguchi T, Yamaguchi T, et al. Diagnostic and therapeutic single operator cholangiopancreatoscopy in biliopancreatic diseases: prospective multicenter study in Japan. World J Gastroenterol. 2016;22:1891–901.
7. Chen YK. Preclinical characterization of the Spyglass per oral cholangiopancreatoscopy system for direct access, visualization and biopsy. Gastrointest Endosc. 2007;65:303–11.
8. Farrell JJ, Bounds BC, Al-Shalabi S, Jacobson BC, Brugge WR, Schapiro RH, Kelsey PB. Single-operator duodenoscope-assisted cholangioscopy is an effective alternative in the management of choledocholithiasis not removed by conventional methods, including mechanical lithotripsy. Endoscopy. 2005;37(6):542–7.
9. Draganov PV, Chauhan S, Wagh MS, et al. Diagnostic accuracy of conventional and cholangioscopy-guided sampling of indeterminate biliary lesions at the time of ERCP: a prospective, long-term follow up study. Gastrointest Endosc. 2012;75:347–53.
10. Chen YK, Pleskow DK. Spyglass single-operator per oral cholangiopancreatoscopy system for the diagnosis and therapy of bile duct disorders: a clinical feasibility study. Gastrointest Endosc. 2007;65:832–8410.
11. Raijman I, Escalante Glorsky S. Electrohydraulic lithotripsy in the treatment of bile and pancreatic duct stones. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com
12. Piraka C, Shah RJ, Awadallah NS, Langer DA, Chen YK. Transpapillary cholangioscopy-directed lithotripsy in patients with difficult bile duct stones. Clin Gastroenterol Hepatol. 2007;5:333–8.
13. Patel S, Rosenkranz L, Tarnasky P, Raijman I, Fishman D, Yeaton P, Sauer B, Kahaleh M. Holmium-YAG laser lithotripsy in the treatment of difficult biliary stones utilizing peroral single operator cholangioscopy (SpyGlass): a multi-center experience. Gastrointest Endosc. 2009;69(5):AB142.
14. Chen YK, Parsi MA, Binmoeller KF, Hawes RH, Pleskow DK, Slivka A, Haluszka O, Peterson BT, Sherman S, Deviere J, Meisner S, Stevens PD, Costamagna G, Ponchon T, Peetermans JA, Neuhaus H. Single-operator cholangioscopy in patients requiring evaluation of bile duct disease or therapy of biliary stones. Gastrointest Endosc. 2011;74:805–14.
15. Seelhoff A, Schumacher B, Neuhaus H. Review single operator cholangioscopic guided therapy of bile duct stones. J Hepatobiliary Pancreat Sci. 2011;18:346–9.
16. Fishman DS, Tarnasky PR, Patel SN, Raijman I. Management of pancreatobiliary disease using a new intra-ductal endoscope: the Texas experience. World J Gastroenterol. 2009;15:1353–8.
17. Hartman DJ, Slivka A, Giusto DA, et al. Tissue yield and diagnostic efficacy of fluoroscopic and cholangioscopic techniques to assess indeterminate biliary strictures. Clin Gastroenterol Hepatol. 2012;10:1042–6.
18. Kalaitzakis E, Webster GJ, Oppong KW, Kallis Y, Vlavianos P, Huggett M, Dawwas MF, Lekharaju V, Hatfield A, Westaby D, et al.

Diagnostic and therapeutic utility of single-operator peroral cholangioscopy for indeterminate biliary lesions and bile duct stones. Eur J Gastroenterol Hepatol. 2012;24:656–64;Manta R, Frazzoni M, Conigliaro R et al. SpyGlass single-operator peroral cholangioscopy in the evaluation of indeterminate biliary lesions; a single center. Prospective, cohort study. Surg Endosc 2012; 27:1569–1572.

19. Siddiqui AA, Mehendiratta V, Jackson W, Loren DE, Kowalski TE, Eloubeidi MA. Identification of cholangiocarcinoma by using the Spyglass Spyscope system for peroral cholangioscopy and biopsy collection. Clin Gastroenterol Hepatol. 2012;10:466–71.
20. Ramchandani M, Reddy DN, Gupta R, et al. Role of single-operator peroral cholangioscopy in the diagnosis of indeterminate biliary lesions; a single center, prospective study. Gastrointest Endosc. 2011; 74:511–9.
21. Seo DW, Lee SK, Yoo KS, Kang GH, Kim MH, Suh DJ, Min YI. Cholangioscopic findings in bile duct tumors. Gastrointest Endosc. 2000;52:630–4.
22. Nimura Y. Staging cholangiocarcinoma by cholangioscopy. HPB. 2008;10:113–5.
23. Maydeo A, Kwek BE, Bhandari S, Bapat M, Dhir V. Single-operator cholangioscopy-guided laser lithotripsy in patients with difficult biliary and pancreatic ductal stones (with videos). Gastrointest Endosc. 2011;74:1308–14; Vicot DW, Sherman S, Karakan T, Khashab MA. Current endoscopic approach to indeterminate biliary strictures. World J Gastroenterol 2012; 18:6197–6205.
24. Parsi MA. Peroral cholangioscopy in the new millennium. World J Gastroenterol. 2011;17:1–6; Kim HJ, Kim MH, Lee SK, Yoo KS, Seo DW, Min YI. Tumor vessel: a valuable cholangioscopic clue of malignant biliary stricture. Gastrointest Endosc 2000; 52:635–63.
25. Parsi MA, Guardino J, Vargo JJ. Per oral cholangioscopy-guided stricture therapy in living donor liver transplantation. Liver Transpl. 2009;15:263–9.
26. Hammerle CW, Haider S, Chung M, Pandey A, Smith I, Kahaleh M, Sauer BG. Endoscopic retrograde cholangiopancreatography complications in the era of cholangioscopy: is there an increased risk? Dig Liver Dis. 2012;44:754–8.
27. Coté GA, Smith J, Sherman S, et al. Technologies for imaging the normal and diseased pancreas. Gastroenterology. 2013;144(6):1262–71.
28. Ito K, Igarashi Y, Okano N, et al. Efficacy of combined endoscopic lithotomy and extracorporeal shock wave lithotripsy, and additional electrohydraulic lithotripsy using the SpyGlass direct visualization system or X-ray guided EHL as needed, for pancreatic lithiasis. Biomed Res Int. 2014;2014:732781.
29. Attwell AR, Brauer BC, Chen YK, et al. Endoscopic retrograde cholangiopancreatography with per oral pancreatoscopy for calcific chronic pancreatitis using endoscope and catheter-based pancreatoscopes: a 10-year single center experience. Pancreas. 2014;43: 268–74.
30. Arnelo U, Siiki A, Swahn F, et al. Single operator pancreatoscopy is helpful in the evaluation of suspected intraductal papillary mucinous neoplasia (IPMN). Pancreatology. 2014;14:510–4.
31. Nagayoshi Y, Aso T, Ohtsuka T, et al. Peroral pancreatoscopy using the Spyglass system for the assessment of intraductal papillary mucinous neoplasm of the pancreas. J Hepatobiliary Pancreat Sci. 2014;21(6):410–7.
32. Tanaka M, Fernández-del Castillo C, Adsay V, et al. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatology. 2012;12(3):183–97.

ERCP in Surgically Altered Anatomy Patients

31

Yen-I Chen and Patrick Okolo III

Background

Endoscopic retrograde cholangiopancreatography (ERCP) in patients with surgically altered anatomy is a challenging clinical situation. In order to successfully perform such procedures, the clinician must first understand the indications for ERCP, the surgical anatomy involved which can often be complex, the equipment needed including endoscopes and accessories, and finally the different alternative approaches if failure occurs. In addition, with the advent of bariatric bypass surgery, altered anatomy ERCP has not only grown in complexity but also in volume given that both rapid weight loss and bariatric surgery are associated with increased biliary lithogenicity and its complications [1–5]. The development of novel endoscopes and assist devices such as the single-balloon enteroscope (SBE), double-balloon enteroscope (DBE), and spiral enteroscope (SE) as well as accessories such as the transparent cap has facilitated and increased the capabilities of the endoscopic approach in the management of biliary pathologies in altered anatomy. However, the expanding technology can also be often confusing to the clinician, and proper selection of the appropriate endoscope, assist devices, and accessories requires a deep understanding of both the patient's anatomy and subtle nuances in the different endoscopic tools. Despite these challenges, the current success rate of altered anatomy ERCP is quite respectable ranging from 60% to 91% depending on the anatomy involved [6–8]. In addition, in the event of failure with the traditional endoscopic route, several novel techniques have been developed including the laparoscopic-assisted ERCP (LA-ERCP), the ERCP via the gastrostomy tract (GT), the percutaneous-assisted transprosthetic endoscopic therapy (PATENT), and the interventional radiology (IR) or endoscopic ultrasound (EUS)-assisted ERCP [9–13].

With this intricate backdrop in mind, it is our goal to clarify the understanding of altered anatomy ERCP in hopes of improving the performance of this complex procedure. The following will first explain the anatomy and terminologies used in altered anatomy ERCP followed by a description of the indications for ERCP, available endoscopes and accessories, the most optimal technical approach and equipment choices based on the surgical anatomy involved, possible complications associated with this minimally invasive treatment modality, and alternative methods following failure.

Terminology in Altered Anatomy ERCP

Understanding the terminologies in altered anatomy ERCP is of upmost importance in both the performance and description of the procedure. The different small bowel limbs and surgical anastomosis need to be uniform in their terminology in order to allow proper communication between clinicians. To start with, the afferent limb or biliopancreatic limb refers to the segment of small bowel that is draining its contents, which include the biliary and often the pancreatic secretions, caudally toward the gastrojejunostomy in the case of a Billroth II or the jejunojejunostomy in the case of a Roux-en-Y. The efferent limb refers to the small bowel segment that is draining away from the gastrojejunostomy in a Billroth II configuration. The Roux limb or the alimentary limb refers to the jejunal segment that is separated from the proximal small bowel (most often just distal to the ligament of Treitz) and pulled up and connected with the stomach. The common channel is similar to the efferent limb and refers to the small bowel portion that is draining contents away from the jejunojejunostomy.

In terms of the different types of surgical anatomy, it is best to divide them into altered anatomy with intact papilla

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Table 31.1 Commonly encountered surgical configurations during altered anatomy ERCP modified from [53]

Anatomy	Common indications	Distance from the mouth to biliary orifice	Biliary drainage
Billroth I	Complications of peptic ulcer disease	Short limb <100 cm	Native papilla
Billroth II	Complications of peptic ulcer disease	Short limb <100 cm	Native papilla
Roux-en-Y gastric bypass	Weight management	Long limb >150 cm	Native papilla
Whipple resection	Pancreatic head cancer Periampullary tumors	Short limb <150 cm	Bilioenteric anastomosis
Roux-en-Y hepatico- or choledochojejunostomy	Bile duct injury Cholangiocarcinoma Liver transplant	Variable	Bilioenteric anastomosis

vs. altered anatomy with a pancreaticobiliary surgical anastomosis. The second important differentiation is the distance from the mouth to the pancreaticobiliary orifice, which can be divided into long >150 cm or short <150 cm. In general, a long limb anatomy requires deep enteroscopy with balloon or spiral assistance or the use of transabdominal ERCP, while a short limb anatomy can be performed with an adult/pediatric colonoscope or sometimes even with a standard side-viewing duodenoscope. A practical approach is to divide surgical anatomies into four categories (Table 31.1):

1. Intact papilla with short limb anatomy (Billroth I and II or short Roux-en-Y)
2. Intact papilla with long limb anatomy (Roux-en-Y gastric bypass (RYGB))
3. Surgical pancreaticobiliary anastomosis with short limb anatomy (Whipple surgery)
4. Surgical pancreaticobiliary anastomosis with long limb anatomy (Roux-en-Y hepaticojejunostomy (length of the limb can be variable))

Indications and Contraindications

In general, the indications for ERCP are similar in altered anatomy as in native pancreaticobiliary configuration [14]. However, as mentioned, gastric bypass surgery is associated with increased lithogenicity and its complications such as choledocholithiasis and cholangitis [1–5]. Moreover, pancreaticobiliary surgery can lead to complications such as biliary or pancreatic anastomotic strictures, bile leak, bile duct obstruction, recurrent pancreatitis, and pancreatic leak [15–17]. It is also important to note that making a prompt diagnosis of pancreatobiliary conditions in patients with altered anatomy may require a heightened index of suspicion and a nuanced approach to the interpretation of axial imaging. Biliary sepsis in patients with altered anatomy, for example, may not always present with all the elements of fever, jaundice, and biochemical dysfunction.

Also, as with native anatomy, ERCP is generally not indicated in the evaluation of abdominal pain of obscure origin, prior to cholecystectomy without evidence of biliary obstruction, and evaluation of suspected gallbladder disease without evidence of bile duct disease [14]. Absolute contraindications include pharyngeal or esophageal obstruction, severe uncorrected coagulopathy, inadequate indication, known or suspected viscous perforation, unobtainable consent (except in emergent cases), and in situations where the risk of the procedure outweighs the potential benefits [18]. In addition, altered anatomy ERCP is contraindicated if required expertise or equipment is not available.

Endoscopes and Accessories

Endoscopes used in altered anatomy ERCP include the traditional side-viewing duodenoscope, pediatric colonoscope, adult colonoscope, and device-assisted enteroscopy ERCP (DAE-ERCP) such as the single-balloon enteroscope (SBE), double-balloon enteroscope (DBE), and spiral enteroscope (SE) (Table 31.2). Choosing the appropriate instrument largely depends on the anatomy, the endoscopist's preference, and local availability. These endoscopes vary in terms of their lengths, working channel diameters, and the presence or absence of an elevator. Due to their shorter lengths, the duodenoscope, pediatric colonoscope, and adult colonoscope are able to accommodate most ERCP accessories. However, both the pediatric and adult colonoscopes are limited by the lack of an elevator making pancreaticobiliary cannulation more difficult. Also, given the smaller-caliber working channel of 3.7 mm with the adult colonoscope and 3.2 mm with the pediatric colonoscope, plastic stent sizes are limited to10 Fr and 7 Fr, respectively. In addition, these three endoscopes are too short to reach to pancreaticobiliary orifice in long limb anatomy (>150 cm). An enteroscope with an assist device such as the SBE, DBE, or SE is necessary when tackling these cases. Although the advent of these assist devices has allowed successful ERCPs in anatomical

Table 31.2 Endoscope options and specific attributes

Endoscope	Length (cm)	Working channel diameter (mm)	Elevator	Use of ERCP accessories	Facilitate afferent limb intubation	7 Fr plastic stents	10 Fr plastic stents
Duodenoscope	124	4.2	X	X		X	X
Adult colonoscope	168	3.7		X		X	X
Pediatric colonoscope	168	3.2		X	X	X	
Single-balloon enteroscope	200	2.8			X	X	
Double-balloon enteroscope	200/220	2.8			X	X	

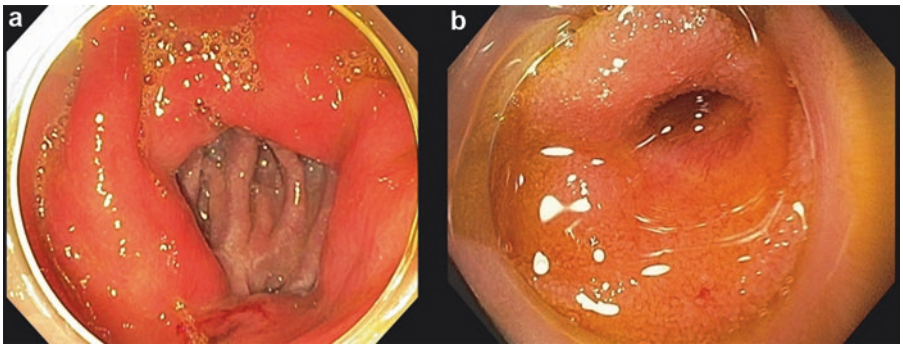

Fig. 31.1 (**a**, **b**) ERCP post-Whipple surgery with pediatric colonoscope and clear cap assistance. (**a**) Gastrojejunostomy and (**b**) hepaticojejunostomy with clear cap allowing for en face position facilitating cannulation

configurations that were once deemed out of reach of the endoscope, they are limited by a small working channel of 2.9 mm in diameter and long endoscope length meaning that stent insertion sizes are limited to 7 Fr in addition to the fact that most traditional ERCP accessories are too short to be used in this setting. Long wires and enteroscope-specific accessories are available; however, this is not ubiquitous at all centers. A shorter single-balloon enteroscope measuring 152 cm in length and allowing use of most ERCP accessories has also been developed and made commercially available but is also limited in its availability.

As discussed, except for the duodenoscope, none of the other endoscopes or enteroscopes have an elevator to facilitate cannulation. This can prove to be extremely challenging especially in cases of long limb anatomy with a native papilla such as those found in RYGB. Without an elevator, the papilla is approached from a tangential view instead of an en face view, making it onerous to obtain proper alignment for cannulation of the bile duct [19]. In order to circumvent this issue, some experts have adopted the use of a transparent plastic cap on the tip of the endoscope. The use of this accessory may improve visualization of the papilla, flatten small bowel folds, and improve the cannulation angle while optimizing stability by anchoring the plastic cap around the papilla (Fig. 31.1a, b). In the largest series of Cap-SBE-ERCP, excellent diagnostic and procedural success rates of 72.7% and 65.9% were achieved, respectively, even in the most difficult anatomy such as the Roux-en-Y with a native papilla [20]. As such, the use of a transparent cap should be strongly considered in all ERCPs performed with a forward-viewing endoscope especially if it involves a native papilla or a stenosed biliary or pancreatic anastomosis.

Technical Approaches According to Surgical Anatomy

Intact Papilla

Short Limb Anatomy

Most common surgeries resulting in a short limb anatomy with an intact papilla include the Billroth I and II reconstruction postgastrectomy. A Billroth I surgery entails the performance of an antrectomy followed by a direct anastomosis between the remnant stomach and duodenum, while a Billroth II involves an antrectomy followed by an end-to-side anastomosis between the remnant stomach and jejunum. Billroth I surgeries were commonly performed prior to the advent of acid-suppressive therapy and the discovery of *H. pylori* as a major etiology of peptic ulcer disease by Marshal and Warren [21]. Billroth II is still commonly performed for gastric tumor resection.

Billroth I

The anatomy post Billroth I is very similar to the one found in native anatomy. The major difference is that the papilla is located closer to the insertion point with loss of the superior

duodenal angle. As such, a side-viewing duodenoscope is the preferred endoscope facilitating an en face view of the papilla while allowing the use of an elevator for cannulation. The major challenge with the Billroth I anatomy is the loss of the duodenal angle and pylorus resulting in the tendency for the endoscope to slip back into the stomach. However, using a long position for cannulation can usually easily circumvent this problem. Once at the level of the papilla, cannulation can be achieved with the usual ERCP accessories and techniques. The success rate for ERCP in Billroth I is generally excellent with one series showing a success rate of 100% in 42 patients using the side-viewing duodenoscope [22].

Billroth II

ERCP in Billroth II (Fig. 31.2) is more challenging given the longer distance of the biliary orifice away from the stomach, the sharp angulation to access the afferent loop at the anastomosis, and looping at the ligament of Treitz [23]. Both the side-viewing duodenoscope and forward-viewing endoscopes (gastroscope or colonoscope) can be used in this surgical configuration. When intubating the afferent loop, it is important to remember that the afferent limb is often joined in an acute angle to the lesser curvature of the stomach, while the efferent limb is relative straight in its alignment with the stomach lumen. Though not infallible, the direction of the *valvulae conniventes* provides a more reliable guide than the presence of bile, which is frequently found in both limbs. Fluoroscopy with contrast injection can also direct the endoscopist toward the correct limb. If looping occurs at the ligament of Treitz, abdominal counterpressure may aid in the advancement of the endoscope to the biliary orifice [8]. Some experts also favor starting the procedure with the patient in the left lateral decubitus position to facilitate afferent limb intubation and then turning the patient supine once in a stable position is achieved within that limb [24].

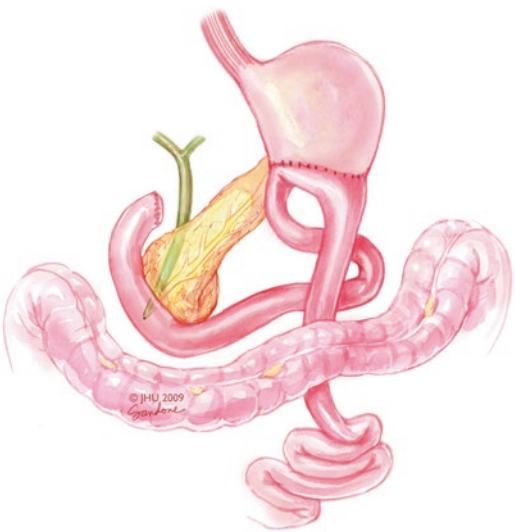

Fig. 31.2 Billroth II anatomy

The side-viewing duodenoscope may allow for easier cannulation with the availability of the elevator; however, this may be offset by a more difficult afferent loop intubation. Nevertheless, successful afferent loop intubation with the side-viewing endoscope in Billroth II has been reported to be as high as 86.4–94.7% with a biliary cannulation rate of 88.2–100% [6, 23, 25, 26]. In a recent, large series from Italy involving 713 patients with a Billroth II anatomy, the afferent loop intubation and biliary cannulation rates were 86.7% and 93.8%, respectively [24]. Excellent results can also be achieved with a forward-viewing endoscope (gastroscope or colonoscope), which can facilitate afferent loop intubation, but the lack of an elevator may make biliary cannulation more challenging. Despite this difficulty, in a recent retrospective series involving 164 patients, biliary cannulation was achieved in 87.3% of the cases with the forward-viewing endoscope [27]. An older RCT comparing the forward-viewing endoscope vs. the duodenoscope in performing an ERCP in Billroth II anatomy also suggested that the use of a forward-viewing endoscope might be safer than its side-viewing counterpart with lower risk of perforation at the level of the anastomosis and small bowel [28]; however, more recent series demonstrate very low rates of viscous perforation with the use of a side-viewing endoscope that is comparable to examinations performed with the forward-viewing endoscope [6, 24]. Therefore, the decision to proceed with a forward-viewing endoscope vs. a side-viewing duodenoscope to perform an ERCP in Billroth II largely depends on the experience and comfort of the operator; however, if a forward-viewing instrument is chosen, then one should strongly consider the use of clear plastic cap to facilitate biliary cannulation.

Occasionally, the afferent loop in a Billroth II may be long and the papilla out of reach of the regular duodenoscope, gastroscope, and colonoscope. In such situations, assist devices such as SBE and DBE may be used to reach the biliary orifice. A systematic review showed that balloon-assisted ERCP may be successful in Billroth II in 90% of the cases [29]. To our knowledge, there are currently no data on the use of spiral-assisted ERCP in Billroth II anatomy; however, one can extrapolate its comparable results with SBE- and DBE-assisted ERCP in Roux-en-Y anatomy [30]. Therefore, when facing a long afferent loop Billroth II, ERCP can be performed with SBE, DBE, or SE depending on local expertise and availability.

Biliary Cannulation in Billroth II

Biliary cannulation and sphincterotomy in the setting of a Billroth II surgery are often in the caudal rather than cephalad direction; in this instance, use of a commercially available Billroth II sphincterotome can be quite helpful. In the author's experience, a rotatable sphincterotome, i.e., the Autotome

(Boston Scientific, Natick, MA), provides more precise orientation for performing sphincterotomy in the setting of a Billroth II ampulla. This option is only possible when a colonoscope or other shorter endoscopes are used. The single- and double-balloon enteroscope platforms are too long to permit use of standard length sphincterotomes. Biliary cannulation with a side-viewing duodenoscope in Billroth II has been reported to be as high as 88.2–100% [6, 23, 25, 26]. Although biliary cannulation with a forward-viewing endoscope may be more challenging, the addition of a clear plastic cap may allow for better en face positioning and compensate for the lack of an elevator. In fact, in a recent retrospective series involving 164 patients, biliary cannulation was achieved in 87.3% of the cases with the forward-viewing endoscope fitted with a clear plastic cap [27]. In terms of sphincterotomy, it is important to reiterate the caudal direction of the bile duct in Billroth II. As such, sphincterotomies should generally be performed toward the six o'clock direction rather than the traditional 11–12 o'clock position when viewing the papilla en face. The simplest and safest approach is to place a stent in the bile or pancreatic duct to act as a guide [26, 31]. Sphincterotomy is then performed using a needle knife over the stent, which ensures proper orientation of the cut. Another relatively straightforward technique which may mitigate some perforation risk is to perform a partial or "small" sphincterotomy in the cephalad direction followed by balloon sphincteroplasty.

Practical Considerations

- Billroth I:
  - Performed with standard side-viewing duodenoscope and ERCP technique
  - Long position may help with stability
- Billroth II:
  - Performed with standard side-viewing duodenoscope, gastroscope, or colonoscope depending on operator's preference.
  - Clear plastic cap assistance to facilitate cannulation (if forward endoscope is used).
  - Afferent limb intubation: usually in an acute angle, the direction of vavulae conniventes may aid in identifying the correct limb along with fluoroscopic guidance. Abdominal counterpressure and change in patient position may aid in intubation.
  - Rotatable sphincterotome given a six o'clock direction of the bile duct in Billroth II.
  - Sphincterotomy over a stent or a small sphincterotomy followed by sphincteroplasty may be the safest approach.

Long Limb Anatomy

Roux-en-Y Gastric Bypass

RYGB is the most commonly performed bariatric surgery in North America [32]. RYGB entails creating a small proximal gastric pouch (less than 30 ml in volume) by separating it from the distal stomach with an anastomosis to a Roux limb. This anastomosis is usually narrow measuring 10–12 cm (Fig. 31.3). The Roux limb is comprised of the jejunum divided a few centimeters distal to the ligament of Treitz. The native biliopancreatic limb is then anastomosed to the jejunum 75–150 cm distal to the gastrojejunostomy forming the common channel distal to the jejunal-jejunostomy.

Intubating the Biliopancreatic Limb in RYGB

ERCP in Roux-en-Y gastric bypass (RYGB) is a challenging procedure given the long Roux limb and native papilla. Assist devices such as the SBE, DBE, or SE are almost always necessary to reach the papilla. Recent systematic reviews demonstrated an ERCP success rate ranging between 61.7% and 70% in RYGB [7, 29]. Moreover, when comparing between the three assist devices, there seems to be no significant differences in procedure success [30, 33]. Navigation of the small bowel when using the SBE is best accomplished with low CO_2 insufflation and sequential

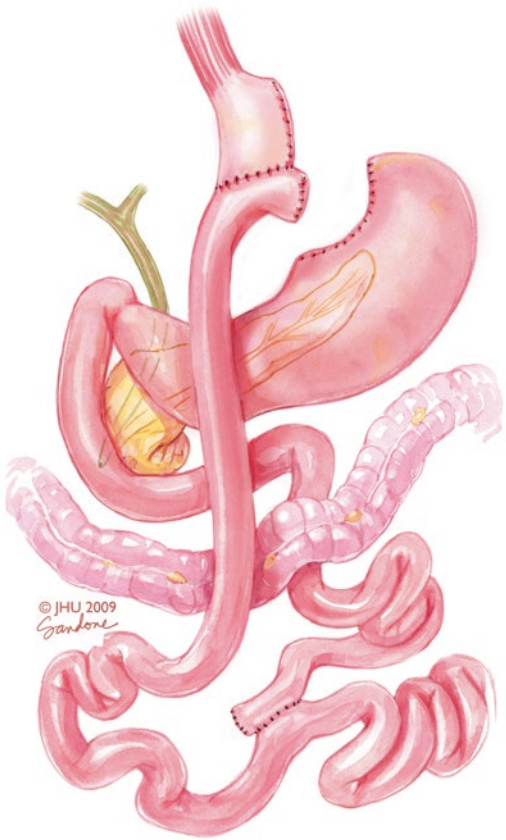

Fig. 31.3 Roux-en-Y gastric bypass

inflation/deflation of the overtube balloon accompanied by aggressive pleating of the small bowel. Once at the jejunojejunal anastomosis, it is often difficult to identify the biliopancreatic limb. Two lumens are usually visualized at the anastomosis. An additional blind-end lumen may be present if the anastomoses have been created in an end-to-side fashion. Once again, the direction of the *valvulae conniventes* provides a more reliable guide than the presence of bile, which is frequently found in both limbs. When intubating the biliopancreatic limb, it is suggested that the bare enteroscope enters the limb first followed by the overtube. Only once the position in the limb is well established, pleating of the small bowel with the balloon should be initiated. Often, the biliopancreatic limb is situated at an obtuse angle and requires abdominal counterpressure and/or a change in the patient's position along with careful endoscopic navigation. Fluoroscopy may also help in identifying the biliopancreatic limb such that inadvertent entry into the common channel is often followed by the appearance of multiple intestinal loops in the pelvis. An enterogram obtained by injecting contrast via the accessory scope channel can often delineate the likely positions of the biliopancreatic and the common limb. When the common limb is unintentionally intubated, the enteroscope should be withdrawn slowly to the level of the jejunojejunostomy. A submucosal tattoo placed at the entry point of the common limb is very helpful to minimize repeated inadvertent entry to the common limb. Passage of a colon length dilating or special length stone extraction balloon into the biliopancreatic limb can sometimes simplify entry into this limb by stiffening the enteroscope and providing countertraction.

Biliary Cannulation and Sphincterotomy in RYGB

Success rates of DAE-ERCP are lower in cases with an intact papilla (50–61.7%) vs. bilioenteric anastomoses (80–90%) [7, 30, 33–35]. From the authors' personal experience, manipulating the ampulla to a near six o'clock position whenever possible is often helpful. An intact ampulla mandates the use of special length ERCP accessories to cannulate the duct of intention. A special length stone extraction balloon, sphincterotome, and extra-long guide wire are commercially available and well suited for use via the 2.8 mm accessory channel of the enteroscope. The absence of an elevator and the forward-viewing approach make cannulation of the ducts of intention onerous. Once again, the use of a clear plastic cap is recommended. It may be also helpful to approach the papilla using the closest en face position possible since the special length sphincterotomes do not provide much of an arc. This position, therefore, is often necessary for precise sphincterotome insertion using torque of the endoscope shaft with or without abdominal counterpressure. As with the Billroth II configuration, the safest approach for sphincterotomy is performed over a biliary or pancreatic stent [26, 31] or to start with a small sphincterotomy followed by balloon sphincteroplasty.

Practical Considerations in RYGB

- Performed with SBE, DBE, or SE.
- Navigating the small bowel should be done with minimal CO_2 insufflation.
- Direction of vavulae conniventes most reliable in identifying the biliopancreatic limb, which can be complemented with fluoroscopy guidance.
- Clear plastic cap strongly suggested to facilitate identification of the papilla and improving cannulation position.
- Special length balloon catheters, sphincterotomes, and wires required.
- Cannulation best performed with the papilla en face using the plastic cap to flatten the small bowel folds and placing the orifice at the six o'clock position.

Surgical Anastomosis

Whipple Surgery

The most common indications for the Whipple procedure are malignant or premalignant tumors involving the pancreatic head or periampullary structures [36]. Whipple surgery entails resection of the pancreatic head, duodenum, the first 15 cm of the jejunum, common bile duct, and gallbladder with or without an antrectomy depending on whether it is a pylorus-preserving resection or a conventional pancreaticoduodenectomy. Reconstruction for this vital region is then performed through several anastomosis including a hepaticojejunostomy, pancreaticojejunostomy, and gastrojejunostomy (Fig. 31.4).

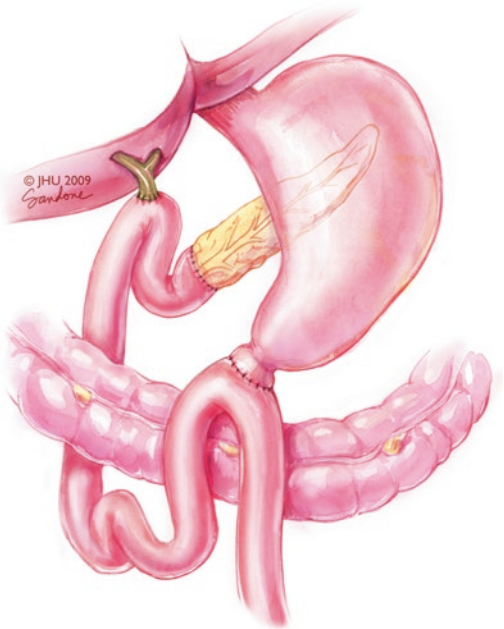

Fig. 31.4 Pyloric-sparring Whipple

As with the Billroth II reconstruction, a single anastomosis is seen at the level of the gastric or duodenal anastomosis with two visible lumens. The technique for biliopancreatic limb intubation has been previously described. The biliopancreatic limb is usually relatively short, and the hepaticojejunostomy and pancreaticojejunostomy are most often within the reach of a pediatric colonoscope and even a side-viewing duodenoscope. In fact, in a retrospective series involving 44 patients with post-Whipple anatomy needing biliary intervention, successful ERCPs were performed in 84% of the patients by starting with a side-viewing duodenoscope, which was replaced by a pediatric colonoscope if the procedure failed with the former. However, significant amount of procedure failure occurred (15%) with the duodenoscope in this series due to failure to intubate the biliopancreatic limb or to reach the biliary anastomosis [37]. Therefore, a pediatric colonoscope may be the more suitable initial instrument for ERCP in Whipple anatomy. Promising data are also emerging on the use of DAE-ERCP in this patient population. In a single-center series using SBE (conventional or short enteroscope) for ERCP in 28 Whipple patients, the success rate of reaching the hepaticojejunostomy was 93%, while biliary intervention was achievable in 95% [38]. Our approach to Whipple anatomy ERCP is to start with a pediatric colonoscope, which in general allows us to reach the hepaticojejunostomy. In the event of failure, we would then recommend the use of DAE-ERCP.

In terms of biliary cannulation, the choledochojejunostomy is typically located 5–10 cm downstream from the pancreaticojejunostomy, which is found near the end of the afferent limb. The anastomosis is often variable in its location, and a number of findings may denote its position – the presence of surgical material such as sutures/staples and a frequently bland appearance of the mucosa surrounding the perimeter of the anastomosis. In some instances, high-volume contrast enterography once the endoscope is situated in the periphery of the anastomosis may help identify its (anastomosis) position. Biliary cannulation using the forward-viewing endoscope has been described above. Once again, the use of a clear plastic cap is suggested. Maneuvers to rotate the biliary anastomosis to six o'clock while keeping the biliary orifice close to the endoscope usually allow for more stable and precise cannulation. It is important to remember that except in cases of severe anastomotic strictures, cannulation of bilioenteric anastomosis is generally more successful than native papilla in altered anatomy ERCP [38].

Unlike biliary cannulation, access to the pancreaticojejunostomy has historically been very difficult in Whipple anatomy. Challenges include reaching and locating the small (<3 mm) pancreaticoenteric anastomosis in addition to a difficult cannulation with a pancreaticojejunostomy that is often very narrow and strictured. In fact, successful ERP in Whipple anatomy has been reported to be as low as 8% in experienced hands [37]. EUS-guided pancreatic duct drainage (PDD) is a technique that may be emerging as the more optimal access to the main pancreatic duct post-Whipple surgery. Overall, the success of EUS-guided PDD has been shown to be between 72% and 92% [39, 40]. A detailed technical description of EUS-guided pancreatic drainage is beyond the scope of this review; however, with accumulating evidence, it may become the modality of choice.

Roux-en-Y Hepaticojejunostomy

A Roux-en-Y hepaticojejunostomy is most commonly performed for benign biliary stricture, iatrogenic biliary stricture, or repair of bile duct injury. The jejunum is divided a few centimeters beyond the ligament of Treitz and anastomosed to the common hepatic duct forming the hepaticojejunostomy. A jejunal-jejunostomy is then constructed downstream. The approach to biliopancreatic limb intubation is similar to RYGB and described above. However, it is important to remember that the pancreatic duct is kept intact with the native papilla and therefore can be reached with conventional side-viewing duodenoscope and ERP technique. The hepaticojejunostomy, on the other hand, is usually located a few centimeters distal to the end of the afferent limb. Given that the stomach is intact, significant looping can occur; therefore, longer endoscopes such as the colonoscope or device-assisted enteroscopes are preferred in this surgical configuration. In a systematic review, the pooled ERCP success rate of using a SBE in Whipple or Roux-en-Y hepaticojejunostomy configuration was noted to be as high as 71% [29]. Moreover, according to a large single-center US series involving 199 ERCPs performed in patients with Roux-en-Y hepaticojejunostomy post-liver transplant, SBE may be superior to a pediatric colonoscope in achieving biliary intervention (75.9% vs. 58.5%) [41]. In addition, the majority of patients who failed ERCP with a colonoscope may be salvaged with a repeat exam with SBE. Therefore, we suggest using DAE-ERCP whenever possible when approaching a Roux-en-Y hepaticojejunostomy; however, if the expertise is not available, a pediatric or adult colonoscope may also be fairly successful.

Practical Considerations in Whipple and Roux-en-Y Hepaticojejunostomy

- Whipple
  - Can usually be performed with forward-viewing colonoscope
  - SBE or DBE if failure to reach the biliary anastomosis with colonoscope
  - Biliary anastomosis usually located 5–10 cm proximal to the end of the afferent limb
  - Pancreaticoenteric anastomosis most often located near the end of the afferent limb
- Roux-en-Y hepaticojejunostomy
  - Limb length is variable but best approached with device-assisted enteroscopy ERCP.
  - Similar technique as RYGB.
  - Note that the pancreatic duct remains intact with the duodenum and can be reached with a standard side-viewing duodenoscope.

Transabdominal Approach to ERCP

When ERCP is not successful using one of the previously described endoscopic techniques, a transabdominal approach via a mature gastrostomy tract or 15 mm trocar at laparoscopy may be required. The advantage to using this approach for ERCP is that a duodenoscope and all other standard ERCP accessories can be used. The gastrostomy tract can be created either percutaneously (by interventional radiology or gastroenterology via DAE), laparoscopically, or via open surgery. ERCP through a gastrostomy in a Roux-en-Y anatomy was first reported by Baron et al. in 1998 [11]. An open Stamm gastrostomy of the bypassed stomach was created with the placement of a 24 Fr Malecot tube. The gastrostomy tract was allowed to mature, then the tube was removed, and wire-guided dilation of the tract was performed, permitting insertion of the duodenoscope to perform the ERCP. Since then, several versions of the same method have been reported with good success rates [42–47]. A retrospective study compared 28 DBE-ERCP with 44 ERCP through a gastrostomy in RYGB patients [48]. Indications for ERCP, procedure length, success, and complications all significantly differed between the two groups. SOD was the most common reason for ERCP through a gastrostomy, while choledocholithiasis and malignant strictures were the most common indications in the DBE-ERCP group. Gastrostomy ERCP was significantly shorter at mean 46 min compared to 101 min for DBE-ERCP. Completely, successful ERCP was accomplished in 100% of the gastrostomy ERCPs while only 56% of the DBE-ERCPs. Complications were more common with gastrostomies (15%) versus 3% with DBE; however, this was attributable to gastrostomy-related issues. It is important to note that maturation of the gastrostomy tract for safe passage of the duodenoscope requires approximately 4 weeks to occur; therefore, a significant amount of time is required for patients to receive the appropriate treatment for their biliary pathology, which can be inconvenient and sometimes not feasible in more acute pathologies such as cholangitis. Therefore, a modification on the original technique, which allows for single-session ERCP through a gastrostomy, has been developed for RYGB patients. The percutaneous-assisted transprosthetic endoscopic therapy (PATENT) is performed by first reaching the excluded stomach with a DAE followed by placement of three T-tags around the intended gastrostomy site to appose the stomach and abdominal wall. Following creation of the gastrostomy, a fully covered esophageal stent is deployed, dilated, and held in place, while ERCP is performed through it. Finally, a 26 Fr gastrostomy tube is left in place followed by removal of the stent after it is cut longitudinally [10, 49]. In a case series of five patients with RYGB who underwent the PATENT technique, biliary cannulation was achieved in 100% of the patients with only one mild adverse event where a prophylactic fully covered biliary stent was inserted for a possible perforation during sphincterotomy (the patient recovered uneventfully). Overall, gastrostomy ERCP is an appealing modality for difficult altered anatomy ERCP such as the RYGB; however, it requires waiting nearly a month for the tract to mature. Single-session ERCP with gastrostomy creation, on the hand, appears promising; however, further studies with larger sample sizes are required in order to truly delineate its efficacy and safety.

Novel Techniques in Altered Anatomy ERCP

Laparoscopic-assisted ERCP is a well-established method of performing ERCP in Roux-en-Y patients. This method involves close coordination between the surgeon and endoscopist. The surgeon creates a laparoscopic access into the gastric remnant or small bowel in addition to a trocar that measures up to 15 mm for introduction of the duodenoscope. The endoscopist then advances a sterile standard duodenoscope through the trocar into the laparoscopic access point created. This method has been reported in several case series with high success rates (90–100%) and low rates of complications, mostly mild pancreatitis [43–47]. One study compared laparoscopic-assisted ERCP to DAE-ERCP [47]. This study included 24 patients who had laparoscopic-assisted ERCP and 32 patients who underwent DAE-ERCP. Laparoscopic-assisted ERCP was superior for papilla identification (100 versus 72%, $p = 0.005$), cannulation rate (100 versus 59%, $p < 0.001$), and therapeutic success (100 versus 59%, $p < 0.001$). In addition, there were no significant differences in adverse events. Length of the Roux combined with biliopancreatic limb greater than 150 cm was associated with poor therapeutic success during DAE-ERCP [47]. Thus, in patients with limb length greater than 150 cm, laparoscopic-assisted ERCP may be considered the first approach if the expertise is available.

A novel single-session EUS-assisted guided ERCP in RYGB has also been recently described by Kedia et al. [50]. The EUS-directed transgastric ERCP (EDGE) entails the sonographically guided creation of a gastric-gastric fistula with a fully covered lumen-apposing metal stent (Axios; Xlumena, Mountain View, CA) between the gastric pouch and the excluded stomach in RYGB anatomy. This tract is then dilated allowing the passage of a side-viewing duodenoscopy from the gastric pouch through the stent and into the excluded stomach thereby bypassing the Roux-en-Y limb and reaching the native papilla with a short endoscope where traditional ERCP techniques and accessories can be used. The stent is then removed after the completion of the biliary or pancreatic intervention and the fistula closed with endoscopic suturing. The main advantage of this procedure is the one-stage approach using a single team while remaining

intraluminal without the need for an external gastrostomy [51]. However, there are concerns regarding the safety of this procedure mainly whether a gastric pouch and remnant stomach fistula can truly be closed with endoscopic suturing [52]. Failure to closure such defects can lead to weight gain and loss of the bypass benefit of the RYGB. Although promising, the EDGE modality should remain an experimental procedure until more robust data can support its use and safety.

Complications

The most feared complication in altered anatomy ERCP is the risk of perforation especially at the site of surgical anastomosis. Initial small retrospective studies involving Billroth II patients showed a peritoneal perforation rate of up to 18% with the side-viewing duodenoscopy [28]; however, larger and more recent series suggest a much more modest risk for perforation of 2.7% [24]. Although excellent and safe results can be attained with a side-viewing duodenoscope in Billroth II, endoscopists who choose this modality should be experienced and skilled in using this endoscope in this anatomy. Operators who are less seasoned may achieve safer results with a forward-viewing endoscope. In terms of safety with DAE-ERCP, one systematic review involving 945 altered anatomy ERCPs using SBE, DBE, or SE in Billroth II, RYGB, Roux-en-Y hepaticojejunostomy, or Whipple anatomy showed excellent results with an overall complication rate of 3.4% [29]. These included cholangitis (n = 1), pancreatitis (n = 11), bleeding (n = 3), perforation (n = 13), and death (n = 1), which were due to an embolic stroke during the procedure. Similar results were also seen in another systematic review, which included 489 patients with Whipple anatomy, RYGB, or Roux-en-Y hepaticojejunostomy reconstruction who underwent ERCP with SBE and showed a major complication rate of 3.6% (pancreatitis n = 11, bleeding n = 2, perforation n = 4, and death from embolic stroke n = 1). These results are encouraging and demonstrate strongly the safety of performing altered anatomy ERCP.

Conclusion

Overall, technical strategy and equipment used in altered anatomy ERCP should be based on the surgical configuration involved. Cap assistance should be employed whenever a forward-viewing endoscope is used especially when dealing with a native papilla. A short limb anatomy with a native papilla such as Billroth I should be performed with the traditional side-viewing duodenoscope, while a Billroth II can be performed with either the side-viewing or forward-viewing endoscope with great success (Fig. 31.5). It is important to keep in mind the caudal direction of the bile duct in the Billroth II with both cannulation and sphincterotomy generally performed toward the six o'clock location while in the en face position with the papilla. A long limb anatomy with

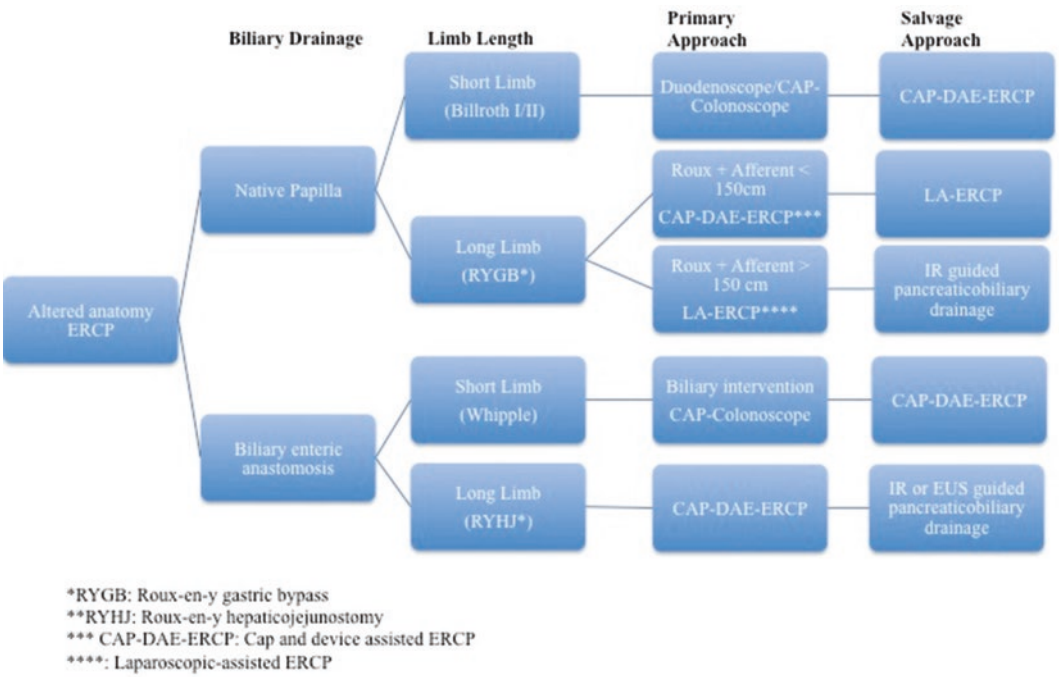

Fig. 31.5 Algorithmic approach to altered anatomy ERCP

a native papilla on the other hand such as the RYGB is best addressed with DAE-ERCP. This configuration is challenging, and failure with DAE may be salvaged with the transabdominal approach with either an ERCP performed through a mature gastrostomy tract or a LA-ERCP. In fact, very long limb RYGB with the combination length of the Roux and biliopancreatic limb greater than 150 cm may be best approached with LA-ERCP as the starting modality. Novel techniques such as PATENT and EDGE are promising and enable pancreaticobiliary interventions in a single session by a single team in RYGB; however, more data are needed to validate the safety and efficacy of these methods. Short limb anatomy with surgical biliary anastomosis such as the Whipple anatomy is generally best approached with a colonoscope with DAE-ERCP reserved as the salvage method. Lastly, long limb anatomy with a surgical biliary anastomosis such as the RY hepaticojejunostomy should be first tackled with DAE-ERCP. Although challenging, current data suggest that technical and therapeutic success can be achieved in the majority of altered anatomy ERCPs with minimal risks for adverse events. Therefore, altered anatomy ERCP, a medical dilemma that was once deemed outside the reach of the gastroenterologist, is now primarily managed endoscopically. With the growth of bariatric surgery, these techniques will continue to be relied on for pancreatic and biliary interventions, while novel endoscopic approaches will continue to grow and hopefully improve and facilitate these interventions.

References

1. Amaral JF, Thompson WR. Gallbladder disease in the morbidly obese. Am J Surg. 1985;149(4):551–7
2. Deitel M, Petrov I. Incidence of symptomatic gallstones after bariatric operations. Surg Gynecol Obstet. 1987;164(6):549–52
3. Shiffman ML, Sugerman HJ, Kellum JM, Moore EW. Changes in gallbladder bile composition following gallstone formation and weight reduction. Gastroenterology. 1992;103(1):214–21
4. Yang H, Petersen GM, Roth MP, Schoenfield LJ, Marks JW. Risk factors for gallstone formation during rapid loss of weight. Dig Dis Sci. 1992;37(6):912–8
5. Zapata R, Severin C, Manriquez M, Valdivieso V. Gallbladder motility and lithogenesis in obese patients during diet-induced weight loss. Dig Dis Sci. 2000;45(2):421–8
6. Cicek B, Parlak E, Disibeyaz S, Koksal AS, Sahin B. Endoscopic retrograde cholangiopancreatography in patients with Billroth II gastroenterostomy. J Gastroenterol Hepatol. 2007;22(8):1210–3
7. Inamdar S, Slattery E, Sejpal DV, Miller LS, Pleskow DK, Berzin TM, et al. Systematic review and meta-analysis of single-balloon enteroscopy-assisted ERCP in patients with surgically altered GI anatomy. Gastrointest Endosc. 2015;82(1):9–19
8. Lin LF, Siauw CP, Ho KS, Tung JC. ERCP in post-Billroth II gastrectomy patients: emphasis on technique. Am J Gastroenterol. 1999;94(1):144–8
9. Attam R, Leslie D, Freeman M, Ikramuddin S, Andrade R. EUS-assisted, fluoroscopically guided gastrostomy tube placement in patients with Roux-en-Y gastric bypass: a novel technique for access to the gastric remnant. Gastrointest Endosc. 2011;74(3):677–82
10. Baron TH, Song LM. Percutaneous assisted transprosthetic endoscopic therapy (PATENT): expanding gut access to infinity and beyond! (with video). Gastrointest Endosc. 2012;76(3):641–4
11. Baron TH, Vickers SM. Surgical gastrostomy placement as access for diagnostic and therapeutic ERCP. Gastrointest Endosc. 1998;48(6):640–1
12. Goitein D, Gagne DJ, Papasavas PK, McLean G, Foster RG, Beasley HS, et al. Percutaneous computed tomography-guided gastric remnant access after laparoscopic Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2006;2(6):651–5
13. Tekola B, Wang AY, Ramanath M, Burnette B, Ellen K, Schirmer BD, et al. Percutaneous gastrostomy tube placement to perform transgastrostomy endoscopic retrograde cholangiopancreaticography in patients with Roux-en-Y anatomy. Dig Dis Sci. 2011;56(11):3364–9
14. Committee ASoP, Chathadi KV, Chandrasekhara V, Acosta RD, Decker GA, Early DS, et al. The role of ERCP in benign diseases of the biliary tract. Gastrointest Endosc. 2015;81(4):795–803
15. Gastaca M. Biliary complications after orthotopic liver transplantation: a review of incidence and risk factors. Transplant Proc. 2012;44(6):1545–9
16. Takano S, Ito Y, Oishi H, Kono S, Yokoyama T, Kubota N, et al. A retrospective analysis of 88 patients with pancreaticogastrostomy after pancreaticoduodenectomy. Hepato-Gastroenterology. 2000;47(35):1454–7
17. Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg. 1997;226(3):248–57. discussion 57–60
18. Cohen S, Bacon BR, Berlin JA, Fleischer D, Hecht GA, Loehrer PJ Sr, et al. National Institutes of Health State-of-the-Science Conference Statement: ERCP for diagnosis and therapy, January 14–16, 2002. Gastrointest Endosc. 2002;56(6):803–9
19. Saleem A, Baron TH, Gostout CJ, Topazian MD, Levy MJ, Petersen BT, et al. Endoscopic retrograde cholangiopancreatography using a single-balloon enteroscope in patients with altered Roux-en-Y anatomy. Endoscopy. 2010;42(8):656–60
20. Trindade AJ, Mella JM, Slattery E, Cohen J, Dickstein J, Garud SS, et al. Use of a cap in single-balloon enteroscopy-assisted endoscopic retrograde cholangiography. Endoscopy. 2015;47(5):453–6
21. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet. 1984;1(8390):1311–5
22. Wu WG, Mei JW, Zhao MN, Zhang WJ, Gu J, Tao YJ, et al. Use of the conventional side-viewing duodenoscope for successful endoscopic retrograde cholangiopancreatography in postgastrectomy patients. J Clin Gastroenterol. 2015;50(3):244–51
23. Osnes M, Rosseland AR, Aabakken L. Endoscopic retrograde cholangiography and endoscopic papillotomy in patients with a previous Billroth-II resection. Gut. 1986;27(10):1193–8
24. Bove V, Tringali A, Familiari P, Gigante G, Boskoski I, Perri V, et al. ERCP in patients with prior Billroth II gastrectomy: report of 30 years' experience. Endoscopy. 2015;47(7):611–6
25. Costamagna G, Mutignani M, Perri V, Gabrielli A, Locicero P, Crucitti F. Diagnostic and therapeutic ERCP in patients with Billroth II gastrectomy. Acta Gastroenterol Belg. 1994;57(2):155–62
26. Hintze RE, Veltzke W, Adler A, Abou-Rebyeh H. Endoscopic sphincterotomy using an S-shaped sphincterotome in patients with a Billroth II or Roux-en-Y gastrojejunostomy. Endoscopy. 1997;29(2):74–8
27. Park TY, Kang JS, Song TJ, Lee SS, Lee H, Choi JS, et al. Outcomes of ERCP in Billroth II gastrectomy patients. Gastrointest Endosc. 2015;83(6):1193–201

28. Kim MH, Lee SK, Lee MH, Myung SJ, Yoo BM, Seo DW, et al. Endoscopic retrograde cholangiopancreatography and needle-knife sphincterotomy in patients with Billroth II gastrectomy: a comparative study of the forward-viewing endoscope and the side-viewing duodenoscope. Endoscopy. 1997;29(2):82–5
29. Skinner M, Popa D, Neumann H, Wilcox CM, Monkemuller K. ERCP with the overtube-assisted enteroscopy technique: a systematic review. Endoscopy. 2014;46(7):560–72
30. Lennon AM, Kapoor S, Khashab M, Corless E, Amateau S, Dunbar K, et al. Spiral assisted ERCP is equivalent to single balloon assisted ERCP in patients with Roux-en-Y anatomy. Dig Dis Sci. 2012;57(5):1391–8
31. van Buuren HR, Boender J, Nix GA, van Blankenstein M. Needle-knife sphincterotomy guided by a biliary endoprosthesis in Billroth II gastrectomy patients. Endoscopy. 1995;27(3):229–32
32. Santry HP, Gillen DL, Lauderdale DS. Trends in bariatric surgical procedures. JAMA. 2005;294(15):1909–17
33. Shah RJ, Smolkin M, Yen R, Ross A, Kozarek RA, Howell DA, et al. A multicenter, U.S. experience of single-balloon, double-balloon, and rotational overtube-assisted enteroscopy ERCP in patients with surgically altered pancreaticobiliary anatomy (with video). Gastrointest Endosc. 2013;77(4):593–600
34. Emmett DS, Mallat DB. Double-balloon ERCP in patients who have undergone Roux-en-Y surgery: a case series. Gastrointest Endosc. 2007;66(5):1038–41
35. Itoi T, Ishii K, Sofuni A, Itokawa F, Tsuchiya T, Kurihara T, et al. Long- and short-type double-balloon enteroscopy-assisted therapeutic ERCP for intact papilla in patients with a Roux-en-Y anastomosis. Surg Endosc. 2011;25(3):713–21
36. Cameron JL, He J. Two thousand consecutive pancreaticoduodenectomies. J Am Coll Surg. 2015;220(4):530–6
37. Chahal P, Baron TH, Topazian MD, Petersen BT, Levy MJ, Gostout CJ. Endoscopic retrograde cholangiopancreatography in post-Whipple patients. Endoscopy. 2006;38(12):1241–5
38. Itokawa F, Itoi T, Ishii K, Sofuni A, Moriyasu F. Single- and double-balloon enteroscopy-assisted endoscopic retrograde cholangiopancreatography in patients with Roux-en-Y plus hepaticojejunostomy anastomosis and Whipple resection. Dig Endosc. 2014;26(Suppl 2):136–43
39. Fujii-Lau LL, Levy MJ. Endoscopic ultrasound-guided pancreatic duct drainage. J Hepatobiliary Pancreat Sci. 2015;22(1):51–7
40. Itoi T, Kasuya K, Sofuni A, Itokawa F, Kurihara T, Yasuda I, et al. Endoscopic ultrasonography-guided pancreatic duct access: techniques and literature review of pancreatography, transmural drainage and rendezvous techniques. Dig Endosc. 2013;25(3):241–52
41. Azeem N, Tabibian JH, Baron TH, Orhurhu V, Rosen CB, Petersen BT, et al. Use of a single-balloon enteroscope compared with variable-stiffness colonoscopes for endoscopic retrograde cholangiography in liver transplant patients with Roux-en-Y biliary anastomosis. Gastrointest Endosc. 2013;77(4):568–77
42. Baron TH, Chahal P, Ferreira LE. ERCP via mature feeding jejunostomy tube tract in a patient with Roux-en-Y anatomy (with video). Gastrointest Endosc. 2008;68(1):189–91
43. Gutierrez JM, Lederer H, Krook JC, Kinney TP, Freeman ML, Jensen EH. Surgical gastrostomy for pancreatobiliary and duodenal access following Roux en Y gastric bypass. J Gastrointest Surg. 2009;13(12):2170–5
44. Lopes TL, Clements RH, Wilcox CM. Laparoscopy-assisted ERCP: experience of a high-volume bariatric surgery center (with video). Gastrointest Endosc. 2009;70(6):1254–9
45. Lopes TL, Clements RH, Wilcox CM. Laparoscopy-assisted transjejunal ERCP in a patient with Roux-en-Y reconstruction following partial gastrectomy. J Laparoendosc Adv Surg Tech A. 2010;20(1):55–8
46. Pimentel RR, Mehran A, Szomstein S, Rosenthal R. Laparoscopy-assisted transgastrostomy ERCP after bariatric surgery: case report of a novel approach. Gastrointest Endosc. 2004;59(2):325–8
47. Schreiner MA, Chang L, Gluck M, Irani S, Gan SI, Brandabur JJ, et al. Laparoscopy-assisted versus balloon enteroscopy-assisted ERCP in bariatric post-Roux-en-Y gastric bypass patients. Gastrointest Endosc. 2012;75(4):748–56
48. Choi EK, Chiorean MV, Cote GA, El H II, Ballard D, Fogel EL, et al. ERCP via gastrostomy vs. double balloon enteroscopy in patients with prior bariatric Roux-en-Y gastric bypass surgery. Surg Endosc. 2013;27(8):2894–9
49. Law R, Wong Kee Song LM, Petersen BT, Baron TH. Single-session ERCP in patients with previous Roux-en-Y gastric bypass using percutaneous-assisted transprosthetic endoscopic therapy: a case series. Endoscopy. 2013;45(8):671–5
50. Kedia P, Kumta NA, Sharaiha R, Kahaleh M. Bypassing the bypass: EUS-directed transgastric ERCP for Roux-en-Y anatomy. Gastrointest Endosc. 2015;81(1):223–4
51. Kedia P, Sharaiha RZ, Kumta NA, Kahaleh M. Internal EUS-directed transgastric ERCP (EDGE): game over. Gastroenterology. 2014;147(3):566–8
52. Abu Dayyeh BK, Thompson CC, Gostout C. Endoscopic retrograde cholangiopancreatography after Roux-en-Y gastric bypass: challenges and cautions. Gastroenterology. 2015;148(4):858–9
53. Badamas J, Okolo PI 3rd. In: Lee LS, editor. ERCP in post-surgical patients: ERCP and EUS, Springer; 2015. p. 277–90. isbn:978-1-4939-2320-5

Endoscopic Management of Necrotizing Pancreatitis

32

Dongwook Oh and Dong-Wan Seo

Introduction

Acute pancreatitis is a common and potentially life-threatening disease with a wide spectrum of severity, representing acute inflammation of the pancreas, which is clinically characterized by abdominal pain and elevated blood pancreatic enzyme levels [1]. Acute pancreatitis may be triggered by various etiologies; in Western countries, it mainly occurs as a result of gallstones (40–50%) and alcohol abuse (10–40%). Other causes (20–30%) include medication, endoscopic retrograde cholangiopancreatography (ERCP), hypertriglyceridemia, hypercalcemia, and surgery. Approximately 10% of its etiology remains unknown [2].

According to the Atlanta classification, acute pancreatitis can be divided into two categories: interstitial edematous pancreatitis and necrotizing pancreatitis [3]. Interstitial edematous pancreatitis is defined by a lack of pancreatic or peripancreatic necrosis on contrast-enhanced computed tomography (CE-CT). Necrotizing pancreatitis is defined as necrosis of the pancreatic parenchyma with or without necrosis of peripancreatic tissues. It most commonly manifests as necrosis involving pancreas and peripancreatic tissues, less commonly as that of only peripancreatic tissues and rarely as that of only pancreatic parenchyma. In approximately 80% of acute pancreatitis cases, the clinical course is mild, and the disease spontaneously resolves within several days to weeks [4]. Approximately 20% of patients develop necrotizing pancreatitis [2]. Figure 32.1 demonstrates representative CT images of the two acute pancreatitis types.

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Pancreatic necrosis, defined as a diffuse or focal area of nonviable pancreatic tissues, develops within the first 4 days after symptom onset to the maximum extent. Approximately 5–10% of patients develop necrosis of the pancreatic parenchyma and/or the peripancreatic tissues [3]. Pancreatic necrosis is subdivided into three categories: parenchymal necrosis, peripancreatic necrosis, or combined necrosis. Parenchymal necrosis occurs in isolation in ≤5% of necrotizing pancreatitis [5]; peripancreatic necrosis involves peripancreatic fats; and isolated peripancreatic necrosis occurs in ≤20% of cases. Patients with isolated peripancreatic necrosis have a better prognosis than do those with parenchymal necrosis [6, 7]. Combined necrosis is the most common morphological subtype, occurring in approximately 75–80% of necrotizing pancreatitis cases [7, 8]. Most patients with severe early organ dysfunction show pancreatic necrosis on CE-CT [9, 10]. The necrosis is initially sterile, and if it remains sterile, mortality is approximately 12%. Distinguishing necrotic collections from other types of pancreatitis-associated fluid collections is important, because their management substantially differs. The vast majority of sterile collections can be conservatively managed. Infected necrosis develops in 40–70% of cases and generally requires an intervention during the disease course [11]; furthermore, it is responsible for the late deterioration of organ dysfunction in the second to third week after admission with mortality increasing to 30% [9]. Despite advances in supportive care, infected pancreatic necrosis remains the major cause of sepsis-related multi-organ failure and the main life-threatening complication of severe acute pancreatitis after the first week of acute pancreatitis onset [12, 13]. Recent developments in the overall medical management of necrotizing pancreatitis and the application of new endoscopic, interventional, and surgical techniques have led to improved outcomes [14]. This article aimed to provide updated review of the endoscopic management of necrotizing pancreatitis.

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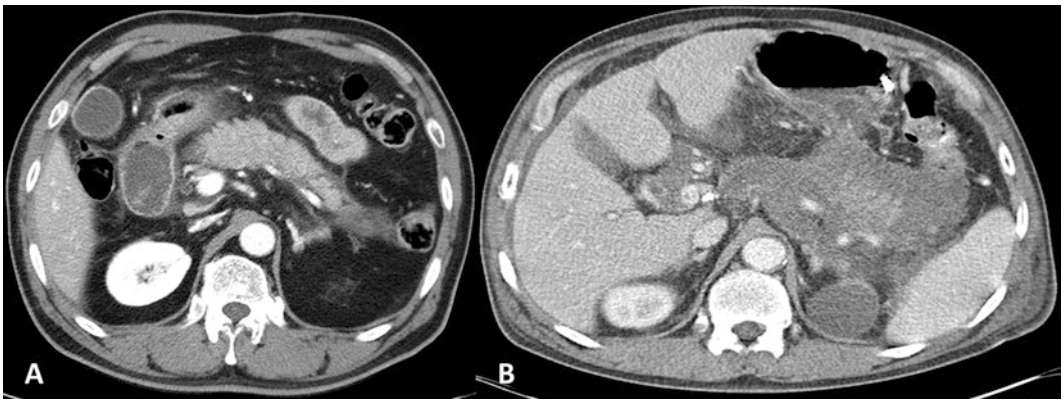

Fig. 32.1 Representative examples of acute pancreatitis as defined by the revised Atlanta classification. (**a**) Acute interstitial pancreatitis. (**b**) Acute necrotizing pancreatitis

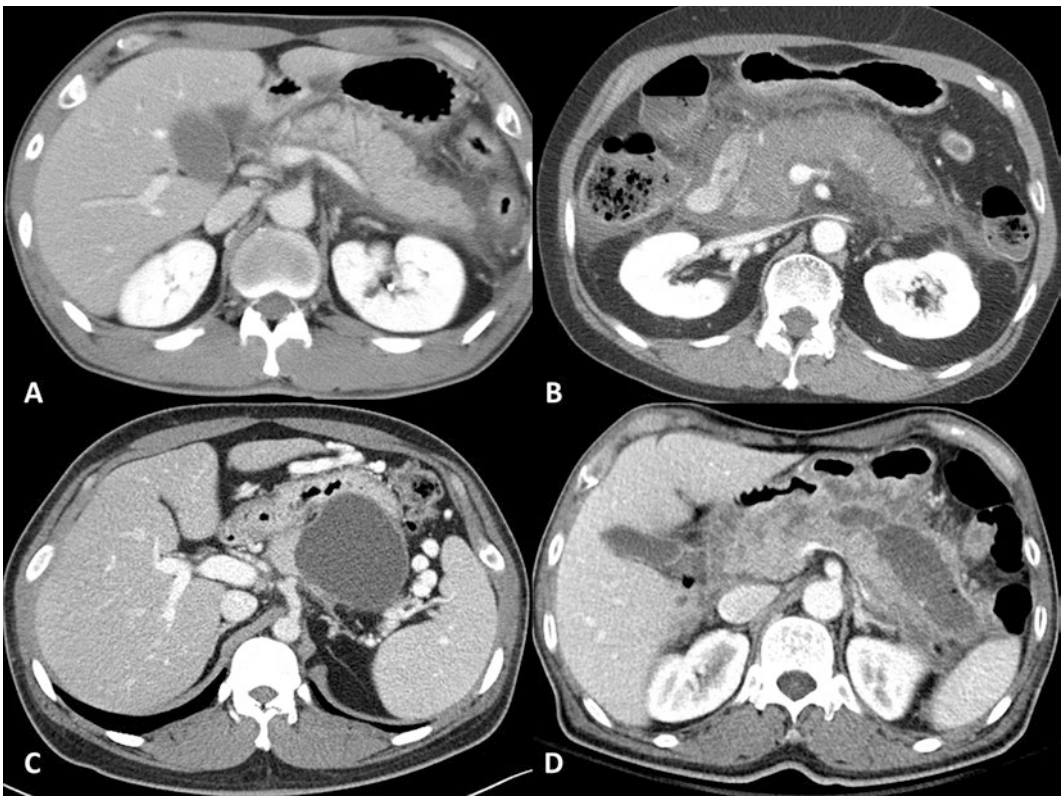

Fig. 32.2 Representative examples of peripancreatic fluid collections as defined by the revised Atlanta classification. (**a**) Acute pancreatic fluid collection. (**b**) Acute necrotic collection. (**c**) Pancreatic pseudocysts. (**d**) Walled-off necrosis

Classification of Acute Pancreatitis-Associated Pancreatic Collections

The recently updated Atlanta classification classifies acute pancreatitis-associated pancreatic collections into acute peripancreatic fluid collection (APFC), acute necrotic collection (ANC), pancreatic pseudocyst, and walled-off necrosis (WON). This classification is based on content (i.e., purely liquid or accompanied by associate necrosis) and evolution time (i.e., ≥4 weeks) [3]. Figure 32.2 demonstrates representative CT images of the four types of PFCs.

APFC usually develops in the early phases of acute pancreatitis. It contains purely homogenous liquid collections without definite walls and is confined by normal fascial planes in the retroperitoneum and may be multiple [15]. Most APFCs spontaneously resolve in the first week follow-

ing acute pancreatitis. APFCs that resolve or remain asymptomatic do not require treatment and themselves do not constitute severe acute pancreatitis [3].

Pancreatic pseudocysts develop when acute pancreatic fluid collection persists more than 4 weeks. It is surrounded by a well-defined wall and essentially contains no solid material. It can occur as a consequence of obstruction or duct leak. If aspiration of cyst content is performed, a markedly increased amylase activity is usually observed. Pancreatic pseudocyst development is more frequent in the setting of chronic pancreatitis than in that of acute pancreatitis in healthy pancreas.

ANC develops during the first 4 weeks of acute pancreatitis evolution and contains variable amounts of fluid and necrotic tissues. ANC may be associated with disruption or obstruction of the pancreatic duct within the zone of parenchymal necrosis and can become infected. Distinguishing ANC from APFC within the first week of acute pancreatitis may be difficult; however, the distinction becomes clearer after the first week.

WON is characterized by a distinct rim around areas of tissue necrosis and adjacent pancreatic parenchyma. It comprises variable numbers of necrotic tissues, which are encapsulated within a reactive tissue wall. A well-defined wall around the collection is observed in imaging studies. The complete formation of WON typically occurs ≥4 weeks after necrotizing pancreatitis onset and has a similar appearance to pseudocysts. CE-CT accuracy in the differential diagnosis between WON and pseudocysts is approximately 79–84% [16]. Correct diagnosis is crucial because it influences management of the pancreatic collection. Magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) provide better definitions of solid components inside necrotic collections [3].

Management of Necrotizing Pancreatitis

Diagnosis of Infected Necrosis

The diagnosis of infected necrosis can be suspected when the patient's clinical course is suspected, when there is extraluminal gas in pancreatic and/or peripancreatic tissues on CE-CT, or when percutaneous, image-guided, fine-needle aspiration (FNA) is positive for bacteria and/or fungi on Gram stain and culture [3, 17].

Although percutaneous FNA allows direct necrotic tissue sampling and subsequent microscopy and bacteriology will confirm the presence of infecting organisms, routine percutaneous FNA of peripancreatic collections to detect bacteria is not indicated, because clinical signs (i.e., pyrexia, hypotension, continuing tachycardia, and increasing inflammatory markers) and imaging signs (i.e., gas in peripancreatic collections) are accurate predictors of infected necrosis in most patients. Although FNA can confirm an infection, it presents a risk of false-negative results [18, 19]. FNA is indicated in patients without clinical improvement for several weeks after necrotizing pancreatitis onset in the absence of clear clinical and imaging signs of infected necrotizing pancreatitis [20]. Gas in peripancreatic collections occasionally indicates fistula formation between the intestinal lumen and necrotic cavity. Therefore, careful review of cross-sectional images is required before diagnosing infected necrosis.

Surgical Management

Patients with necrotizing pancreatitis are best managed through the cooperation of gastroenterologists, interventional radiologists, and surgeons. Management depends on several factors, including disease severity, disease phase, and presence of complications. Intervention is generally required for infected pancreatic necrosis and less commonly for symptomatic patients with sterile necrosis. Open necrosectomy has been the traditional treatment for the complete removal of infected necrosis [21, 22], because it provides wide access to the infected necrosis. However, open necrosectomy is associated with significantly high morbidity (34–95%) and mortality (6–56%), depending on the disease severity at the time of surgery [23–25]. Potential immediate postoperative adverse events include organ failure, bowel perforation, hemorrhage, and wound infection, possibly requiring reoperation. Long-term complications include pancreatic and intestinal fistula, pancreatic

Practical Considerations

- Pancreatic necrosis is defined as a diffuse or focal area of nonviable pancreatic tissues which usually develops within the first 4 days after symptom onset.
- APFC usually develops in the early phases of acute pancreatitis and spontaneously resolves in the first week following the episode of acute pancreatitis and therefore does not require treatment.
- ANC develops during the first 4 weeks of acute pancreatitis and contains variable amounts of fluid and necrotic tissues and can become infected.
- WON has a distinct rim around areas of tissue necrosis and adjacent pancreatic parenchyma, typically occurs ≥4 weeks after the onset of necrotizing pancreatitis, and may have similar appearance to pseudocysts.

insufficiency, and abdominal wall hernia [26]. Necrotizing pancreatitis treatment has considerably changed over the years. During the last decade, minimally invasive interventions have essentially replaced traditional open necrosectomy to reduce the morbidity and mortality associated with open necrosectomy. Numerous reports have recently described percutaneous drainage, minimally invasive surgery, endoscopic transluminal drainage, and necrosectomy as alternatives to open surgery. These procedures may enable to postpone surgery to optimize the timing of necrosectomy or even avoid it.

Practical Considerations

- A routine percutaneous FNA of peripancreatic collections to detect bacteria is not indicated.
- Clinical signs and imaging findings more accurately predict infected necrosis.
- FNA is indicated in patients without clinical improvement for several weeks after the onset of necrotizing pancreatitis in the absence of clear clinical or imaging signs of infected necrotizing pancreatitis.
- Necrotizing pancreatitis patients are best managed jointly by gastroenterologists, interventional radiologists, and surgeons.

Timing of Intervention

Proper timing is critical for successful endoscopic treatment of necrotizing pancreatitis. Intervention within the first few weeks of necrotizing pancreatitis generally leads to poor outcomes. It is currently believed that intervention should be delayed to approximately 3–4 weeks after disease onset [11, 18]. The general guiding principle is delaying intervention until the collection is encapsulated and liquefied as much as possible. Encapsulation does not usually occur until at least 4 weeks after initial injury. Mier et al. compared early (within 72 h of symptom onset) and late (≥12 days after onset) intervention in patients with severe pancreatitis and suggested that delaying surgical intervention beyond the first 12 days reduces mortality (56% vs. 27%) [25]. Although the difference was not statistically significant, the trial was terminated because of concerns regarding very high mortality associated with early surgery. In a recent retrospective study, delaying necrosectomy until 30 days after initial admission was associated with decreased mortality compared with interventions in the first 2 weeks or from 2 weeks to 4 weeks [27].

Table 32.1 Indications for intervention of necrotizing pancreatitis

Sterile necrosis
1. Ongoing gastric outlet, intestinal, or biliary obstruction due to mass effect of walled-off necrosis
2. Persistent symptoms (i.e., intractable pain, "persistent unwellness") in patients with walled-off necrosis without signs of infection
3. Disconnected duct syndrome (i.e., full transection of the pancreatic duct in the presence of pancreatic necrosis) with persisting symptomatic (i.e., pain, obstruction) collections with necrosis without signs of infections
Infected necrosis
1. Clinical suspicion of, or documented, infected necrotizing pancreatitis with clinical deterioration, preferably when the necrosis has become walled-off
2. In the absence of documented infected necrotizing pancreatitis, ongoing organ failure for several weeks after the onset of acute pancreatitis, preferably when the necrosis has become walled-off
3. Abdominal compartment syndrome
4. Bowel ischemia
5. Ongoing gastric outlet, intestinal, or biliary obstruction due to mass effect from large walled-off necrosis

Adapted from Working Group IAP/APA Acute Pancreatitis Guidelines: IAP/APA evidence-based guidelines for the management of acute pancreatitis [20]

Indication for the Intervention of Pancreatic Necrotic Collection

Indications for intervention of necrotic collections are summarized in Table 32.1. A sterile necrotic collection almost ever requires intervention in the early disease course. Asymptomatic pancreatic and extrapancreatic necrosis do not require intervention regardless of size, location, or extension because they are likely to spontaneously resolve, even if infected [28]. Intervention for sterile necrotic collections is only indicated in symptomatic patients as follows: (1) ongoing gastric outlet, intestinal, or biliary obstruction because of mass effect of WON (i.e., arbitrarily >4–8 weeks after acute pancreatitis onset), (2) persistent symptoms (i.e., intractable pain and persistent unwellness) in patients with WON without infection signs (i.e., arbitrarily >8 weeks after acute pancreatitis onset), and (3) disconnected duct syndrome (i.e., full transection of the pancreatic duct in the presence of pancreatic necrosis) with persisting symptomatic (i.e., pain and obstruction) collections with necrosis but without infection signs (i.e., arbitrarily >8 weeks after acute pancreatitis onset) [20, 29].

Infected necrosis is virtually always an indication for intervention. Indications for infected necrosis are as follows: (1) clinical suspicion of or documented, infected necrotizing pancreatitis with clinical deterioration, preferably when necrosis has become walled-off; (2) in the absence of documented infected necrotizing pancreatitis, ongoing organ failure for several weeks after acute pancreatitis onset, preferably

when necrosis has become walled-off; (3) abdominal compartment syndrome; (4) bowel ischemia; and (5) ongoing gastric outlet, intestinal, or biliary obstruction because of mass effect from large WON (arbitrarily >4–8 weeks after pancreatitis onset) [20].

Endoscopic drainage is not recommended for immature collections or collections with vascular pseudoaneurysm, which should be treated by interventional radiology before endoscopic drainage. The presence of neovascularization by portal hypertension is considered a relative contraindication [30]. However, several reports have described safe transmural drainage in the setting of portal hypertension under EUS guidance [31, 32]. Despite EUS guidance, physicians should be cautious when attempting endoscopic drainage in the presence of portal hypertension.

Patient Preparation

Because of the potential risk for adverse events, before endoscopic intervention, patients should undergo blood testing for blood type and screening, prothrombin time/international normalized ratio, and platelet count. They should temporarily discontinue anticoagulants and antiplatelet agents before the procedure because of the risk for acute or delayed bleeding. If severe bleeding, which cannot be treated endoscopically, occurs during the endoscopic procedure, immediate help of an interventional radiologist should be requested. Patients are given prophylactic antibiotics to reduce the risk of infection [30]. Patients should fast after midnight till the morning of the procedure because of the risk for regurgitation and pulmonary aspiration, which can have very serious consequences.

Instruments and accessories
19-gauge fine-needle aspiration needle
0.025- or 0.035-inch guidewire
Tapered dilating catheter
Soehendra screw-type stent retriever
Wire-guided needle knife
Cautery dilation device (cystotome)
Hydrostatic balloon
Covered metal or plastic stent

The Procedure

Initial EUS-Guided Transmural Drainage

The techniques used are similar to those used for pancreatic pseudocyst drainage. Patients are treated under conscious sedation with either midazolam or propofol with meperidine, although conducting the procedure under general anesthesia may be helpful. A therapeutic linear-array EUS scope with working channels of 3.7 or 3.8 mm is preferred for visualizing the extent of necrosis, assessing the wall maturity, measuring the distance between the collection and luminal wall, and determining optimal puncture sites [33, 34]. Initial drainage has been tried using a therapeutic, side-viewing duodenoscope or gastroscope, although this endoscope-guided drainage is rarely used nowadays. If side-viewing duodenoscope or gastroscope is used for a blind puncture, puncture should be performed at the site of maximum bulging on the gastric or duodenal wall. In the absence of EUS, puncture should not be attempted if there is no endoscopically discernable visible bulge. In our experience, EUS-guided drainage increases the technical success rate and decreases complications [35, 36]. Fluoroscopy is generally necessary for a safe procedure. There is currently no standard method for EUS-guided transmural drainage; however, there are several methods for performing EUS-guided PFC drainage. The choice of technique is largely based on personal preference and experience. If possible, CO^2 insufflation is used to minimize the risk for air embolism, although the routine use of CO^2 has not been proven to prevent this complication [37]:

1. Localization of the best access site within the gastric or duodenal lumen: under EUS guidance, physicians can safely localize the optimal access point, even in non-bulging collection cases, in collections in the tail, or in patients with varices [36]. Although a distance of 1 cm from the intestinal lumen to the collection has been previously considered the maximum safe distance, EUS enables maximum distances of 2 cm to be safely traversed in some cases [38].
2. Puncture of optimal drainage site: the best site for transmural drainage can be identified under EUS guidance (Fig. 32.3a), with use of color flow to avoid intervening vessels at the time of wall puncture. We usually use a

Practical Considerations

- Intervention within the first few weeks of necrotizing pancreatitis generally leads to poor outcomes and therefore best delayed to 3–4 weeks after the disease onset.
- Infected necrosis is a definite indication for intervention.
- Endoscopic drainage is not recommended for immature collections or collections with vascular pseudoaneurysm and therefore best managed by interventional radiology before endoscopic drainage.

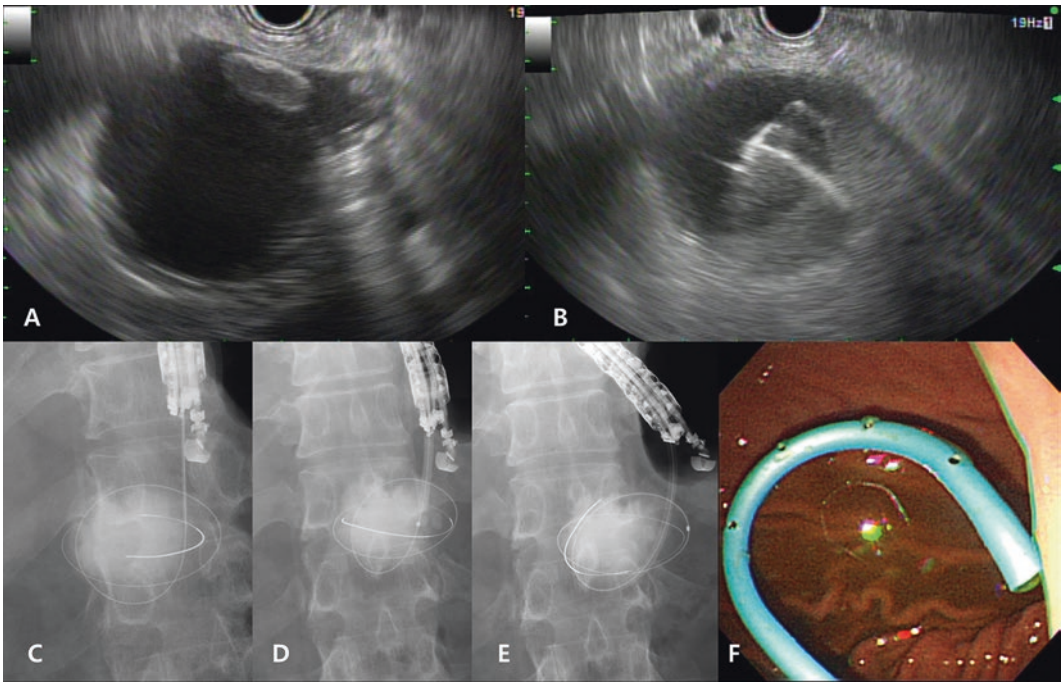

Fig. 32.3 Endoscopic ultrasound-guided transmural drainage of pancreatic fluid collections. (**a**) Localization of best access point. (**b**) Puncture of optimal drainage site. (**c**) Fistula tract creation: a 0.035-inch guidewire is inserted and coiled within the collection. (**d**) Fistula tract dilation using a 4 mm balloon. (**e**) Placement of a double-pigtail plastic stent. (**f**) Endoscopic view of the proximal end of double-pigtail stent after placement in gastric lumen

19-gauge FNA needle for puncture (Fig. 32.3b). After the puncture, aspiration of the fluid contents and injection of contrast medium are performed to confirm the cavity and fluid collection for fluid analysis (including microbial culture) under fluoroscopic guidance.

3. Fistula tract creation: after confirming the cavity, a 0.025- or 0.035-inch guidewire is inserted through the needle lumen into the fluid collection and coiled within the collection using fluoroscopic guidance. The needle is then removed, leaving the guidewire in place (Fig. 32.3c). A fistula is created between the intestinal lumen and collections. Various accessories can be used for fistula dilation including a tapered dilating catheter, Soehendra screw-type stent retriever, wire-guided needle knife, or cautery dilation devices such as cystotome.
4. Further dilation of fistula tract: the fistula tract can be dilated to at least 8 mm in size using hydrostatic balloons (Fig. 32.3d). If there are no contraindications (e.g., bleeding diathesis, disrupted cystenterostomy tract, or patient instability), the tract can be dilated up to 15–20 mm to insert the endoscope during endoscopic necrosectomy at first endoscopic drainage.
5. Placement of stent for drainage: there is currently no consensus regarding which stents (covered metal vs. multiple plastic stents) are optimal for drainage. The choice of initial drainage (nasocystic catheter, gastro- or duodenocystic stent, or combination of both) depends on the patient's condition and collection contents. In patients suspected with infected collection and/or in those with collections containing purulent or necrotic materials, a nasocystic catheter can be initially inserted to enable cystic content flushing and to avoid early stent obstruction. In some cases, both a nasocystic catheter and stent are inserted for continuous saline solution perfusion [39]. For gastro- or duodenocystic stent placement, minimum two double-pigtail stents are used for drainage because single stent placement is prone to occlusion resulting in treatment failure. After fistula tract dilation, a 7–10F double-pigtail stent is placed over the guidewire under endoscopic and fluoroscopic guidance (Fig. 32.3e, f). The guidewire is reinserted into the same opening using an echoendoscope, followed by delivery of the second 10F double-pigtail stent. When multiple stents need to be placed, some physicians prefer using a double-guidewire approach, wherein two guidewires are simultaneously inserted after the first puncture [40]. According to the physician's preference, fully covered self-expandable metal stents (FCSEMSs) may also be used for drainage. If FCSEMSs are deemed insufficiently expanded,

balloon dilation can be performed immediately after stent deployment (Fig. 32.3).

Exact steps for EUS-guided transmural drainage
1. Localization of the best access site within the gastric or duodenal lumen
2. Puncture of optimal drainage site
3. Creation of fistula tract
4. Further dilation of fistula tract
5. Placement of stent for drainage

Endoscopic Transluminal Necrosectomy

Endoscopic transluminal necrosectomy (ETN) aims to remove as much of the devitalized necrotic tissues as possible without disrupting a major vessel or cavity wall. After removing a previously inserted stent, the fistula tract can be dilated up to 20 mm using a large hydrostatic balloon to permit forward-viewing endoscope introduction. The forward-viewing endoscope is advanced within the cavity, and necrotic tissues can be evacuated via forceful irrigation and suction, as well as removal by a stone removal basket, net, forceps, polypectomy snare, or other endoscopic devices at the discretion of the endoscopist (Fig. 32.4).

In our center, we prefer water-jet endoscope for forceful irrigation of necrotic cavity. ETN is repeatedly performed at 2–3 days intervals until all debris and necrotic materials have been removed and the walls of the collections can be visualized as vital structures. Session duration is mainly determined by patient tolerance of sedation or general anesthesia. ETN procedures generally take between 60 and 120 min. This procedure is repeated until most of necrotic materials are removed. At the end of each procedure, multiple double-pigtail plastic stents (including nasocystic catheters for supplementary post-procedure naso-cavity irrigation) or FCSEMSs are inserted to keep the fistula tract open. Several types of stents can be used, as per endoscopist's preference.

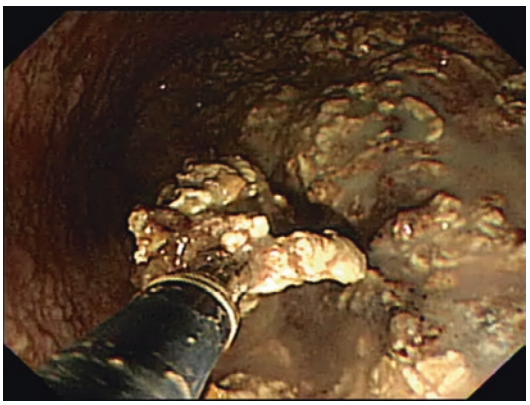

Fig. 32.4 Endoscopic transmural necrosectomy of walled-off necrosis. After forceful water irrigation, a rat-tooth forceps is used to remove necrotic debris

Practical Considerations

- If the side-viewing duodenoscope or gastroscope is chosen, a blind puncture should be performed at the site of maximum bulging on the gastric or duodenal wall.
- During the procedure, CO^2 insufflation should be used to minimize the risk for air embolism.
- Currently there is no consensus on the use of the type of stent (covered metal or multiple plastic stents) for optimal drainage

Role of ERCP for Managing Necrotizing Pancreatitis

To date, there has been no comparative or randomized study comparing transpapillary drainage and transmural drainage of pancreatic fluid collections. There have been few reports of transpapillary drainage of pancreatic fluid collections. Transpapillary drainage is preferred for initially treating fluid collections that communicate with the main pancreatic duct in the head or body of the pancreas [41]. Compared with transmural drainage, transpapillary drainage provides similar long-term success and is associated with fewer complications [42]. However, the pancreatic duct diameter is small, limiting the number of endoprostheses available for drainage. Therefore, transpapillary drainage is not indicated in patients with large pseudocysts (>6 cm) or PFCs with solid debris, because for the high risk of secondary infection consequent to inadequate drainage [43].

Furthermore, acute necrotizing pancreatitis often results in disrupting the main pancreatic duct with a considerable amount of viable pancreatic parenchyma upstream to the disruption leading to disconnected pancreatic duct syndrome (DPDS) [44]. Pancreatic ductal disruption occurs in 37–58% of severe acute pancreatitis cases [44, 45]. Healing is possible when a short (<2-cm) pancreatic duct segment is involved [46]. Endoscopic stent placement through the pancreatic duct into the cavity or across the disruption may resolve the disconnection [47]. Bakker et al. compared endoscopic transpapillary stent placement and conservative treatment in patients with pancreatic fistula associated with necrotizing pancreatitis [48]. Results showed that fistula closure was similar in both treatments (84% vs. 75%, respectively), but the median time to fistula closure was

shorter (71 vs. 120 days, respectively) in patients undergoing endoscopic transpapillary stent placement. However, ERCP is associated with significant complications including post-ERCP pancreatitis and infection. ERCP may specifically convert sterile necrosis into infected necrosis by introducing bacterial contamination during the procedure. Because of the possibility of contaminating sterile necrosis, ERCP should not be performed early in the course of severe acute pancreatitis (<2 weeks), except in rare instances wherein the information may alter the patient's treatment plan (i.e., severe gallstone pancreatitis) [49].

Disconnected Pancreatic Duct Syndrome

As previously mentioned, DPDS occurs in up to one-third or more patients with necrotizing pancreatitis [47]. A disconnected duct will serve as a feeding source for the collection, resulting in pancreatic fluid collections [50]. Endoscopic transpapillary stent placement is effective for pancreatic duct disruption. However, recurrence of pancreatic collections is relatively common after transpapillary stent placement for disconnected ducts [51]. Transmural drainage can be helpful in making an enteric fistula that facilitates drainage of disconnected segments into the intestinal lumen. Transmural stents are generally removed within 6–8 weeks after resolving fluid collection; this is confirmed by CT. However, transmural stent removal may be associated with PFC recurrence. Thus, transmural stents are permanently placed, in DPDS cases, even if PFCs are resolved, to ensure that stents maintain internal fistula patency and divert pancreatic secretions back into gastrointestinal lumens. Permanent transmural stent placement prevents PFC recurrence [52]. Moreover, permanent indwelling transmural stents appear to decrease the rate of PFC recurrence in patients with DPDS [53]. Long-term indwelling transmural stents in patients with DPDS appear to be safe and decrease the risk for PFC recurrence [54]. However, the optimal duration of stent placement is unknown and warrants further study.

Identifying Optimal Stents for EUS-Transmural Drainage?

Determining the type, size, and number of stents used for EUS-guided transmural drainage is currently of concern. To date, there is no clear evidence to suggest that metal stents are more efficient than plastic stents or that one type of plastic stent is better than the other, although the double-pigtail design is generally preferred. Plastic stents have been traditionally used for drainage. The fistula tract is maintained via plastic stent placement to prevent migration. Furthermore, concerns have been raised regarding the use of plastic stents because their small caliber may induce occlusion, resulting in unresolved or PFC recurrence. Therefore, placement of multiple plastic stents or large-caliber plastic stents is required for maintaining large fistula to ensure sufficient and effective drainage. Conversely, small-caliber plastic stents are required for multiple attempts or for accessing the cavity. These procedures may lead to the loss of guidewires (failure of multiple stent placement) or proximal migration of the first stent into the cavity, requiring additional time and involving a more cumbersome procedure. In contrast, advancing and deploying large-caliber stents through the channel of the EUS scope can be challenging [55].

Practical Considerations

- ETN should be repeated at 2–3-day intervals until all debris and necrotic materials have been removed and the walls of the collections can be visualized as vital structures.
- Water-jet endoscopes for forceful irrigation of necrotic cavity are typically used.
- Transpapillary drainage is not indicated in patients with large pseudocysts (>6 cm) or PFCs with solid debris, because of the high risk of secondary infection.
- ERCP should not be performed early in the course of severe acute pancreatitis (<2 weeks), except in severe gallstone pancreatitis.

SEMS are an available alternative to multiple plastic stents for PFC drainage. Although they are more expensive than plastic stents, they provide larger calibers than plastic stents, possibly enhancing debris drainage, reducing time to resolution. SEMS also reduces the risk of perforation, leakage, and bleeding because of minimal dilation and sealing of fistula tract including tamponade effects [55].

Novel lumen-apposing FCSEMS have been recently developed for PFCs, demonstrating effectiveness in various studies. The AXIOS® stent (Xlumena Inc., Mountain View, CA, USA), NAGI stent (Taewoong Medical Co., Ltd., Seoul, Korea), and SPAXUS stent (Taewoong Medical Co., Ltd., Seoul, Korea) are currently available for PFC drainage. These stents have a dumbbell-shaped configuration that foreshortens deployment, thereby minimizing the possibility of leakage or perforation [56]. These stents also provide stability, minimize the risk of migration because of their anchoring effect, and maintain lumen of larger SEMS lumen to allow passage, enabling endoscopic necrosectomy in repeated sessions without requiring stent replacement [57].

Sharaiha et al. compared FCSEMSs and double-pigtail plastic stents in 230 patients who underwent pancreatic pseudocyst drainage [58]. In the study, EUS-guided transmural drainage was performed in 118 patients using double-pigtail plastic stents and in 112 using FCSEMSs. At 12-month follow-up, complete pseudocyst resolution was higher using FCSEMSs than using double-pigtail plastic stents (89% vs. 98%, respectively; $P = 0.01$), with lower rates of adverse events (31% vs. 16%, respectively; $P = 0.006$). These results may be applicable to WON cases because plastic stents are prone to stent occlusion, resulting in treatment failure and increased recurrence. A recent systematic review of 17 studies examining transmural drainage of PCFs revealed no significant difference in overall treatment success (70%; 95% CI, 62–76 vs. 78%; 95% CI, 50–93), complications (16%; 95% CI, 14–39 vs. 23%; 95% CI, 16–33), or recurrence (10%; 95% CI, 8–13 vs. 9%; 95% CI, 4–19%) between patients treated for WON with plastic vs. metal stents [59]. A larger prospective randomized study should be conducted to compare FCSEMSs and plastic stents for transmural drainage of PFCs.

Outcomes of Endoscopic Treatment of Necrotizing Pancreatitis

The known efficacy of endoscopic treatment of necrotizing pancreatitis is limited because of the small number of case studies reported. However, endoscopic treatment outcomes are promising. In a recent systematic review of 14 studies reporting endoscopic necrosectomy, overall morbidity and mortality was 36% and 6%, respectively. In 81% of patients, complete resolution of necrotic collection was achieved, although it is important to note that patient characteristics differed across studies [60].

The Dutch Acute Pancreatitis Study Group recently reported the PENGUIN trial: a prospective, randomized trial of 22 patients hospitalized with infected pancreatic necrosis [61]. In the only randomized comparative trial, this group compared direct endoscopic necrosectomy ($n = 10$) and surgical necrosectomy ($n = 10$) comprising video-assisted retroperitoneal debridement (VARD) or, if not feasible, open necrosectomy. Patients underwent percutaneous catheter drainage using a step-up approach; if they failed to respond to simple catheter drainage, they were randomized to endoscopic transgastric or surgical necrosectomy. Endoscopic necrosectomy significantly reduced the post-procedural pro-inflammatory response (as measured by serum interleukin-6 levels) by avoiding laparotomy and general anesthesia. General anesthesia induces or prolongs systemic inflammation in critically ill patients [62]. Improved clinical outcomes were also observed in the endoscopic group, with a significant reduction in major complications. New-onset multi-organ failure did not occur in the endoscopic group, and fewer patients developed external pancreatic fistulas (Fig. 32.5).

Practical Considerations

- Novel lumen-apposing FCSEMSs are recently developed for effective drainage of PFCs.

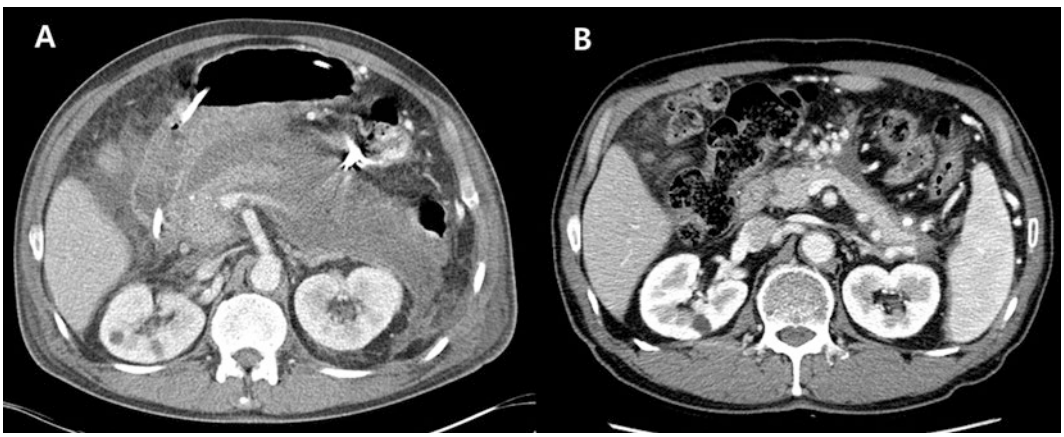

Fig. 32.5 Representative examples of outcomes of endoscopic necrosectomy. (**a**) Before endoscopic necrosectomy, the patient had high fever, abdominal pain, and persistent infection. A CT showed extensive peripancreatic necrosis. (**b**) After repeated endoscopic necrosectomy and antibiotic therapy, the patient's high fever, abdominal pain, and infection were resolved. A CT scan revealed improved peripancreatic necrosis

Complications

Endoscopic treatment of pancreatic necrotic collections presents a potential risk for complications. Endoscopists are required to understand potential complications and to appropriately manage them. In previous reports, complications were more common in patients with underlying pancreatic necrosis compared with those involving pseudocysts or abscesses [63, 64]. Most frequent complications include bleeding, perforation, and post-procedure infection. When using EUS-guided transmural drainage, rates of complication range from 1% to 52% [32, 39, 64–66]. In a recently published systematic review of endoscopic transmural necrosectomy, complications occurred in 36% (163/455) of patients [60, 67]. The most common complication was bleeding, occurring in 18% (76/420) of patients. Bleeding usually occurs during access to the collection, particularly if vessels are punctured during dilation of the transmural tract, and during actual debridement of necrotic materials [68]. Bleeding was endoscopically treated by coagulation, epinephrine injections, or clips in most patients (97%). Angiography with coiling or surgery was required in 7% of patients [60].

Perforation may develop when the necrotic collection wall is poorly maturated or is located >1 cm from the intestinal lumen [34]. Perforations usually developed during the dilation of the initial puncture site for drainage, resulting in the leakage of fluid collection contents and/or pneumoperitoneum [67]. If perforation occurs because of fistula tract disruption, it can be conservatively managed with antibiotics or nasogastric tube suction [69]. However, if the wall of the collection is disrupted during debridement, operative management may be necessary. The risk of perforation can be reduced by following key principles, including only draining collections with mature walls, performing stepwise balloon dilation in cystogastrostomy, avoiding over-insufflations of the cavity with air, and performing gentle debridement [66].

Post-procedure infection is a possible complications following endoscopic drainage and occurs because of contamination of an incompletely drained WON or pseudocyst resulting from premature stent occlusion [34, 70]. Varadarajulu et al. reported that infection occurred in four (2.7%) patients after endoscopic drainage [71]. This was resolved by new endoscopic drainage in two patients and by surgery in the other two. Proper drainage is very important. Broad-spectrum antibiotics are generally periprocedurally administered, although their efficacy is uncertain [47].

Stent migration is a potential complication of endoscopic transmural drainage of pancreatic collections. External stent migration increases the risk of pancreatic fluid collection and may require repeated procedures [43, 54]. There are few reports of intestinal obstruction because of migrated stents [53]. Based on the increasing use of covered metal stents, the internal migration of stents represents a serious complication and therapeutic challenge [72].

Finally, air embolism represents a potentially serious endoscopic complication; although very rare, it may be severe and fatal [73]. Air embolism has been described in various multicenter studies and results from air entry into the venous system [69, 74, 75]. Using CO2 rather than air has been advised because the former is better absorbed and decreases the risk of air embolism [73–75]. If cardiovascular and/or respiratory symptoms abruptly develop during the procedure without another explanation, considering air embolism is important because they allow the provision of potentially life-saving therapy [73]. Gas in the venous portal system beforehand may contraindicate additional endoscopic necrosectomy.

Potential Complications of Endoscopic Treatment of Pancreatic Necrotic Collections
Bleeding
Perforation
Post-procedure infection
Stent migration
Air embolism

Follow-Up

After initial transmural drainage, imaging studies, including CT or EUS, are required to evaluate the status of PFCs. In cases of pancreatic pseudocyst drainage, follow-up imaging studies should be performed within 4–6 weeks. If there is complete pseudocyst resolution, the stent can be removed.

For patients who underwent endoscopic necrosectomy, serial follow-up imaging is required until WON resolution. Additional debridement may be needed if the patient is not clinically improving, if some necrotic material was not removed during necrosectomy, or if imaging suggests that fluid collection is not resolving. If PFCs recur, DPDS should be considered. In that case, other interventions such as transpapillary stent placement, permanent indwelling transmural stent placement, or percutaneous drainage may be required [38]. If the collection fails to resolve or reaccumulates, minimally invasive retroperitoneal approaches (e.g., percutaneous drainage), minimally invasive retroperitoneal necrosectomy or sinus tract endoscopy using a flexible endoscope, or VARD procedure should be considered [50].

Conclusion

As the management paradigm invariably shifts to less invasive techniques, endoscopic management will play an increasing role in managing necrotizing pancreatitis. It represents a safe and effective treatment option in selected patients with necrotizing pancreatitis. It may be associated with lower morbidity and mortality than surgical necrosec-

tomy. EUS-guided transmural drainage will increase the success rate and safety of the approach. Furthermore, delayed intervention (at least 3–4 weeks after disease onset) is superior to early intervention in terms of morbidity and mortality. Although endoscopic management is promising, further prospective comparative trials are required to validate its effectiveness and safety. It must be emphasized that no single approach is optimal for all patients with necrotizing pancreatitis; thus, the best treatment should be tailored for individual patients.

Summary Points
Endoscopic treatment is a safe and effective treatment for patients with necrotizing pancreatitis.
EUS-guided transmural drainage will increase success rates and safety of endoscopic treatment.
Delayed intervention (at least 3–4 weeks after disease onset) is superior to early intervention in terms of morbidity and mortality.
Necrotizing pancreatitis requires a multidisciplinary treatment approach.

References

1. Sarles H. Revised classification of pancreatitis--Marseille 1984. Dig Dis Sci. 1985;30:573–4.
2. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. Am J Gastroenterol. 2006;101:2379–400.
3. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62:102–11.
4. van Santvoort HC, Bakker OJ, Bollen TL, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology. 2011;141:1254–63.
5. Isenmann R, Buchler M, Uhl W, et al. Pancreatic necrosis: an early finding in severe acute pancreatitis. Pancreas. 1993;8:358–61.
6. Sakorafas GH, Tsiotos GG, Sarr MG. Extrapancreatic necrotizing pancreatitis with viable pancreas: a previously under-appreciated entity. J Am Coll Surg. 1999;188:643–8.
7. Shyu JY, Sainani NI, Sahni VA, et al. Necrotizing pancreatitis: diagnosis, imaging, and intervention. Radiographics Rev Publ Radiol Soc North Am Inc. 2014;34:1218–39.
8. Thoeni RF. The revised Atlanta classification of acute pancreatitis: its importance for the radiologist and its effect on treatment. Radiology. 2012;262:751–64.
9. Beger HG, Bittner R, Block S, et al. Bacterial contamination of pancreatic necrosis. A prospective clinical study. Gastroenterology. 1986;91:433–8.
10. Tenner S, Sica G, Hughes M, et al. Relationship of necrosis to organ failure in severe acute pancreatitis. Gastroenterology. 1997;113:899–903.
11. Uhl W, Warshaw A, Imrie C, et al. IAP guidelines for the surgical Management of Acute Pancreatitis. Pancreatology Off J Int Assoc Pancreatol (IAP) [et al]. 2002;2:565–73.
12. Isenmann R, Rau B, Beger HG. Bacterial infection and extent of necrosis are determinants of organ failure in patients with acute necrotizing pancreatitis. Br J Surg. 1999;86:1020–4.
13. Buchler MW, Gloor B, Muller CA, et al. Acute necrotizing pancreatitis: treatment strategy according to the status of infection. Ann Surg. 2000;232:619–26.
14. Anand N, Park JH, Wu BU. Modern management of acute pancreatitis. Gastroenterol Clin N Am. 2012;41:1–8.
15. Lenhart DK, Balthazar EJ. MDCT of acute mild (nonnecrotizing) pancreatitis: abdominal complications and fate of fluid collections. AJR Am J Roentgenol. 2008;190:643–9.
16. Takahashi N, Papachristou GI, Schmit GD, et al. CT findings of walled-off pancreatic necrosis (WOPN): differentiation from pseudocyst and prediction of outcome after endoscopic therapy. Eur Radiol. 2008;18:2522–9.
17. Banks PA, Gerzof SG, Langevin RE, et al. CT-guided aspiration of suspected pancreatic infection: bacteriology and clinical outcome. Int J Pancreatol Off J Int Assoc Pancreatol. 1995;18:265–70.
18. Fernandez-del Castillo C, Rattner DW, Makary MA, et al. Debridement and closed packing for the treatment of necrotizing pancreatitis. Ann Surg. 1998;228:676–84.
19. Rau B, Pralle U, Mayer JM, et al. Role of ultrasonographically guided fine-needle aspiration cytology in the diagnosis of infected pancreatic necrosis. Br J Surg. 1998;85:179–84.
20. Anonymous. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology Off J Int Assoc Pancreatol (IAP) [et al]. 2013;13:e1–15.
21. Traverso LW, Kozarek RA. Pancreatic necrosectomy: definitions and technique. J Gastrointest Surg Off J Soc Surgery Alimentary Tract. 2005;9:436–9.
22. Tenner S, Baillie J, DeWitt J, et al. American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol. 2013;108:1400–15. 1416.
23. Rodriguez JR, Razo AO, Targarona J, et al. Debridement and closed packing for sterile or infected necrotizing pancreatitis: insights into indications and outcomes in 167 patients. Ann Surg. 2008;247:294–9.
24. Raraty MG, Halloran CM, Dodd S, et al. Minimal access retroperitoneal pancreatic necrosectomy: improvement in morbidity and mortality with a less invasive approach. Ann Surg. 2010;251:787–93.
25. Mier J, Leon EL, Castillo A, et al. Early versus late necrosectomy in severe necrotizing pancreatitis. Am J Surg. 1997;173:71–5.
26. Bugiantella W, Rondelli F, Boni M, et al. Necrotizing pancreatitis: a review of the interventions. Int J Surg (London, England). 2015; doi:10.1016/j.ijsu.2015.12.038.
27. Besselink MG, Verwer TJ, Schoenmaeckers EJ, et al. Timing of surgical intervention in necrotizing pancreatitis. Arch Surg (Chicago, Ill 1960). 2007;142:1194–201.
28. Freeman ML, Werner J, van Santvoort HC, et al. Interventions for necrotizing pancreatitis: summary of a multidisciplinary consensus conference. Pancreas. 2012;41:1176–94.
29. Forsmark CE, Baillie J. AGA Institute technical review on acute pancreatitis. Gastroenterology. 2007;132:2022–44.
30. Ruiz-Clavijo D, de la Higuera BG, Vila JJ. Advances in the endoscopic management of pancreatic collections. World J Gastrointest Endosc. 2015;7:381–8.
31. Sriram PV, Kaffes AJ, Rao GV, et al. Endoscopic ultrasound-guided drainage of pancreatic pseudocysts complicated by portal hypertension or by intervening vessels. Endoscopy. 2005;37:231–5.
32. Antillon MR, Shah RJ, Stiegmann G, et al. Single-step EUS-guided transmural drainage of simple and complicated pancreatic pseudocysts. Gastrointest Endosc. 2006;63:797–803.
33. Voermans RP, Veldkamp MC, Rauws EA, et al. Endoscopic transmural debridement of symptomatic organized pancreatic necrosis (with videos). Gastrointest Endosc. 2007;66:909–16.
34. Vilmann AS, Menachery J, Tang SJ, et al. Endosonography guided management of pancreatic fluid collections. World J Gastroenterol WJG. 2015;21:11842–53.
35. Varadarajulu S, Christein JD, Tamhane A, et al. Prospective randomized trial comparing EUS and EGD for transmural drainage of pancreatic pseudocysts (with videos). Gastrointest Endosc. 2008;68:1102–11.

36. Park DH, Lee SS, Moon SH, et al. Endoscopic ultrasound-guided versus conventional transmural drainage for pancreatic pseudocysts: a prospective randomized trial. Endoscopy. 2009;41:842–8.
37. Gardner TB, Chahal P, Papachristou GI, et al. A comparison of direct endoscopic necrosectomy with transmural endoscopic drainage for the treatment of walled-off pancreatic necrosis. Gastrointest Endosc. 2009;69:1085–94.
38. Gardner TB. Endoscopic management of necrotizing pancreatitis. Gastrointest Endosc. 2012;76:1214–23.
39. Hookey LC, Debroux S, Delhaye M, et al. Endoscopic drainage of pancreatic-fluid collections in 116 patients: a comparison of etiologies, drainage techniques, and outcomes. Gastrointest Endosc. 2006;63:635–43.
40. Seewald S, Thonke F, Ang TL, et al. One-step, simultaneous double-wire technique facilitates pancreatic pseudocyst and abscess drainage (with videos). Gastrointest Endosc. 2006;64:805–8.
41. Baron TH. Endoscopic drainage of pancreatic pseudocysts. J Gastrointest Surg Off J Soc Surg Alimentary Tract. 2008;12:369–72.
42. Dumonceau JM, Delhaye M, Tringali A, et al. Endoscopic treatment of chronic pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy. 2012;44:784–800.
43. Varadarajulu S, Rana SS, Bhasin DK. Endoscopic therapy for pancreatic duct leaks and disruptions. Gastrointest Endosc Clin N Am. 2013;23:863–92.
44. Neoptolemos JP, London NJ, Carr-Locke DL. Assessment of main pancreatic duct integrity by endoscopic retrograde pancreatography in patients with acute pancreatitis. Br J Surg. 1993;80:94–9.
45. Lau ST, Simchuk EJ, Kozarek RA, et al. A pancreatic ductal leak should be sought to direct treatment in patients with acute pancreatitis. Am J Surg. 2001;181:411–5.
46. Howard TJ, Moore SA, Saxena R, et al. Pancreatic duct strictures are a common cause of recurrent pancreatitis after successful management of pancreatic necrosis. Surgery. 2004;136:909–16.
47. Trikudanathan G, Attam R, Arain MA, et al. Endoscopic interventions for necrotizing pancreatitis. Am J Gastroenterol. 2014;109:969–81. quiz 982
48. Bakker OJ, van Baal MC, van Santvoort HC, et al. Endoscopic transpapillary stenting or conservative treatment for pancreatic fistulas in necrotizing pancreatitis: multicenter series and literature review. Ann Surg. 2011;253:961–7.
49. Nadkarni NA, Kotwal V, Sarr MG, et al. Disconnected pancreatic duct syndrome: endoscopic stent or Surgeon's knife? Pancreas. 2015;44:16–22.
50. Fisher JM, Gardner TB. Endoscopic therapy of necrotizing pancreatitis and pseudocysts. Gastrointest Endosc Clin N Am. 2013;23:787–802.
51. Arvanitakis M, Delhaye M, Bali MA, et al. Endoscopic treatment of external pancreatic fistulas: when draining the main pancreatic duct is not enough. Am J Gastroenterol. 2007;102:516–24.
52. Arvanitakis M, Delhaye M, Bali MA, et al. Pancreatic-fluid collections: a randomized controlled trial regarding stent removal after endoscopic transmural drainage. Gastrointest Endosc. 2007;65:609–19.
53. Varadarajulu S, Wilcox CM. Endoscopic placement of permanent indwelling transmural stents in disconnected pancreatic duct syndrome: does benefit outweigh the risks? Gastrointest Endosc. 2011;74:1408–12.
54. Rana SS, Bhasin DK, Rao C, et al. Consequences of long term indwelling transmural stents in patients with walled off pancreatic necrosis & disconnected pancreatic duct syndrome. Pancreatology Off J Int Assoc Pancreatol (IAP) [et al]. 2013;13:486–90.
55. Kawakami H, Itoi T, Sakamoto N. Endoscopic ultrasound-guided transluminal drainage for peripancreatic fluid collections: where are we now? Gut Liver. 2014;8:341–55.
56. Walter D, Will U, Sanchez-Yague A, et al. A novel lumen-apposing metal stent for endoscopic ultrasound-guided drainage of pancreatic fluid collections: a prospective cohort study. Endoscopy. 2015;47:63–7.
57. Gornals JB, De la Serna-Higuera C, Sanchez-Yague A, et al. Endosonography-guided drainage of pancreatic fluid collections with a novel lumen-apposing stent. Surg Endosc. 2013;27:1428–34.
58. Sharaiha RZ, DeFilippis EM, Kedia P, et al. Metal versus plastic for pancreatic pseudocyst drainage: clinical outcomes and success. Gastrointest Endosc. 2015;82:822–7.
59. Bang JY, Hawes R, Bartolucci A, et al. Efficacy of metal and plastic stents for transmural drainage of pancreatic fluid collections: a systematic review. Dig Endosc Off J Japan Gastroenterol Endosc Soc. 2015;27:486–98.
60. van Brunschot S, Fockens P, Bakker OJ, et al. Endoscopic transluminal necrosectomy in necrotising pancreatitis: a systematic review. Surg Endosc. 2014;28:1425–38.
61. Bakker OJ, van Santvoort HC, van Brunschot S, et al. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. JAMA. 2012;307:1053–61.
62. Strom T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. Lancet. 2010;375:475–80.
63. Baron TH, Harewood GC, Morgan DE, et al. Outcome differences after endoscopic drainage of pancreatic necrosis, acute pancreatic pseudocysts, and chronic pancreatic pseudocysts. Gastrointest Endosc. 2002;56:7–17.
64. Varadarajulu S, Tamhane A, Blakely J. Graded dilation technique for EUS-guided drainage of peripancreatic fluid collections: an assessment of outcomes and complications and technical proficiency (with video). Gastrointest Endosc. 2008;68:656–66.
65. Binmoeller KF, Soehendra N. Endoscopic ultrasonography in the diagnosis and treatment of pancreatic pseudocysts. Gastrointest Endosc Clin N Am. 1995;5:805–16.
66. Fabbri C, Luigiano C, Maimone A, et al. Endoscopic ultrasound-guided drainage of pancreatic fluid collections. World J Gastrointest Endosc. 2012;4:479–88.
67. Voermans RP, Besselink MG, Fockens P. Endoscopic management of walled-off pancreatic necrosis. J Hepatobiliary Pancreat Sci. 2015;22:20–6.
68. Haghshenasskashani A, Laurence JM, Kwan V, et al. Endoscopic necrosectomy of pancreatic necrosis: a systematic review. Surg Endosc. 2011;25:3724–30.
69. Gardner TB, Coelho-Prabhu N, Gordon SR, et al. Direct endoscopic necrosectomy for the treatment of walled-off pancreatic necrosis: results from a multicenter U.S. series. Gastrointest Endosc. 2011;73:718–26.
70. Bang JY, Wilcox CM, Trevino J, et al. Factors impacting treatment outcomes in the endoscopic management of walled-off pancreatic necrosis. J Gastroenterol Hepatol. 2013;28:1725–32.
71. Varadarajulu S, Christein JD, Wilcox CM. Frequency of complications during EUS-guided drainage of pancreatic fluid collections in 148 consecutive patients. J Gastroenterol Hepatol. 2011;26:1504–8.
72. Talreja JP, Shami VM, Ku J, et al. Transenteric drainage of pancreatic-fluid collections with fully covered self-expanding metallic stents (with video). Gastrointest Endosc. 2008;68:1199–203.
73. Donepudi S, Chavalitdhamrong D, Pu L, et al. Air embolism complicating gastrointestinal endoscopy: a systematic review. World J Gastrointest Endosc. 2013;5:359–65.
74. Seifert H, Biermer M, Schmitt W, et al. Transluminal endoscopic necrosectomy after acute pancreatitis: a multicentre study with long-term follow-up (the GEPARD study). Gut. 2009;58:1260–6.
75. Yasuda I, Nakashima M, Iwai T, et al. Japanese multicenter experience of endoscopic necrosectomy for infected walled-off pancreatic necrosis: the JENIPaN study. Endoscopy. 2013;45:627–34.

Endoscopic Management of Pancreatic Fistula and Leaks

33

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Introduction

Pancreatic fistula with leakage of pancreatic fluid into adjacent or distant spaces, structures, or organs result from a disruption of the pancreatic ductal system. Pancreatic fistula involve either the main pancreatic duct or one of its side branches and may occur in the course of (recurrent) episodes of acute pancreatitis, chronic pancreatitis, pancreatic malignancy, pancreatic resection, or trauma [1–6].The clinical consequences depend on multiple factors including etiology, site and extent of the disruption, the rate of secretion of pancreatic juice, the location of the leak relative to anatomic tissue planes, and the presence of downstream obstruction of the pancreatic duct caused by strictures or calculi [3, 6]. A small leak from one of the side branches of an otherwise unobstructed pancreatic duct may resolve spontaneously, whereas a persistent leak from a major main pancreatic duct disruption may be complicated by pseudocyst formation, internal fistula formation causing ascites or pleural effusion, and external pancreatic fistulas. Leakage of pancreatic secretions can cause significant morbidity due to infection, malnutrition, and skin excoriation.

Pancreatic fistulas have iatrogenic or non-iatrogenic causes. The former include (1) pancreatic resection and operative trauma, which typically occur in the tail of the pancreas during splenic surgery, left renal/adrenal surgery, or mobilization of the splenic flexure of the colon; (2) percutaneous drainage of a pancreatic fluid collection (pseudocyst or walled-off pancreatic necrosis); (3) complications of endoscopic interventions during endoscopic retrograde cholangiopancreatography (ERCP); and (4) intraoperative core biopsy of pancreatic masses. Non-iatrogenic causes include acute and chronic pancreatitis, most frequently caused by gallstones or alcohol, and penetrating or blunt abdominal trauma.

Following pancreatic duct disruption, pancreatic juice leaks into the peripancreatic area creating a peripancreatic fluid collection which, depending on local factors, may lead to the formation of a fluid collection, internal pancreatic fistula or external pancreatic fistula (Table 33.1).

The development of an outer wall of granulation tissue over a period of 4–6 weeks may confine the peripancreatic fluid collection to the retroperitoneum, lesser sac, or mediastinum and marks the development of a pseudocyst.

Persistent leakage of pancreatic fluid can lead to the development of an internal fistula due to spontaneous erosion into a neighboring hollow viscus (colon, duodenum, stomach, or esophagus), peritoneal or pleural cavities, or mediastinum, lesser sac, retroperitoneum, or perihepatic space. If the leak occurs anteriorly into the peritoneal cavity, it results in pancreatic ascites. A posterior communication may track into the pleural cavity or mediastinum resulting in pancreaticopleural fistula. External fistulae are pathological communications that connect any part of the gastrointestinal tract with the skin. This may occur spontaneously but usually follows after a surgical or radiological intervention of a peripancreatic fluid collection, debridement of pancreatic necrosis, or after a pancreatic resection. The likelihood of developing an external fistula increases greatly if percutaneous drainage is performed in the setting of disconnected pancreatic duct syndrome.

Signs and Symptoms

The clinical manifestations of pancreatic fistulas vary based on the size, location, and site of communication (e.g., peritoneal or pleural cavity, another hollow viscus or the skin). Patients with internal pancreatic fistulas may be asymptomatic. Symptoms of an internal pancreatic fistula

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Table 33.1 Manifestations of pancreatic fistula and leaks

1. Pancreatic fluid collections (pseudocysts)
2. Internal pancreatic fistula
Pancreaticoperitoneal (pancreatic ascites)
Pancreaticopleural
Pancreaticobronchial
Pancreaticomediastinal
Pancreaticopericardial
3. External (cutaneous) pancreatic fistula

may include vague abdominal pain, nausea, vomiting, and abdominal distension. Patients may have fever, features of sepsis, and gastrointestinal bleeding with hematemesis, melena, or hematochezia. Pancreatic ascites usually develops slowly and is associated with a variable intensity of abdominal pain and distension. Ascites may be associated with weight loss, anorexia, weakness, and severe malnutrition. Symptoms of thoracopancreatic fistulas include cough, shortness of breath, chest pain, and dysphagia [7]. These patients may have unilateral or bilateral pleural effusions with dullness to percussion over the thorax and diminished breath sounds on physical examination. External pancreatic fistula is associated with drainage of pancreatic fluid from an abdominal wound. Patients may have weight loss due to malnutrition, symptoms of dehydration due to fluid and electrolyte loss, and/or fever due to an infection.

Physical examination findings include abdominal distension and flank dullness. A large pseudocyst may be palpable in the epigastric region and can cause symptoms by compressing adjacent organs.

Pancreatic fluid effluent may be visible from an external pancreatic fistula with skin excoriation around the fistula site. Pancreatic fluid is high in bicarbonate and protein, and in the case of high-output fistulas, fluid loss may lead to metabolic acidosis, malnutrition, and dehydration. A fistula is termed a high-output fistula when the output is greater than 200 mL per 24 h and low output when the output is less than 200 mL per 24 h [8]. A fistula that drains only pancreatic juice is called a pure fistula, while a fistula that drains pancreatic juice mixed with enteric contents is referred to as a mixed fistula. The output of a pure fistula contains inactive pancreatic enzymes and is relatively inert [9] . The output of a mixed fistula contains activated proteases, which can cause further complications like necrosis and hemorrhage. A pancreatic fistula can be either a side or end fistula. An end fistula results from disruption of main pancreatic duct. The two portions of pancreas are not continuous and tend to heal separately; this condition is termed "disconnected pancreatic duct syndrome." End fistulae are unlikely to heal with conservative management because of discontinuity from the gastrointestinal tract and the remaining pancreatic duct. Also, end fistulae are not amenable to transpapillary stent placement.

Conditions that May Represent an Indications for Treatment

- Pancreatic ascites and pancreaticopleural fistula
- Disconnected pancreatic duct syndrome
- Postoperative pancreatic fistula

Indications

Pancreatic Ascites and Pancreaticopleural Fistula

Pancreatic ascites and pancreaticopleural fistula are an uncommon but well-recognized complication of chronic pancreatitis that are associated with significant morbidity and mortality. Internal pancreatic fistula with pancreatic ascites and pleural effusion share a common pathophysiology. The disruption of the pancreatic duct results in the formation of internal fistula communicating with peritoneal or pleural cavities, which result in ascites or pleural effusion, respectively. Alcohol-related chronic pancreatitis is considered the main cause. Pancreatic ascites and pleural effusion may initially be misdiagnosed being a consequence of alcoholic liver disease or pleural tuberculosis. Although a pancreaticopleural fistula is relatively rare, it is an important diagnostic consideration in patients with chronic pancreatitis who present with recurrent or persistent respiratory symptoms and pleural effusions. Pleural effusion generally occurs on the left, but it is not unusual to see right-sided or bilateral effusions. Although a high amylase level in pleural fluid is a characteristic of pleural effusions associated with chronic pancreatitis, this can also be due to acute pancreatitis, esophageal perforation, para-pneumonic effusions, and pulmonary or pancreatic malignancy [7, 10–12]. However, only pancreatic pleural fistula leads to pleural fluid amylase levels greater than 50,000 IU/L [10, 12]. Traditionally these patients are treated with prolonged conservative medical therapy (see further).

Disconnected Pancreatic Duct Syndrome

Disconnected pancreatic duct syndrome refers to a condition in which rupture of the main pancreatic duct results in a portion of the pancreatic gland becoming isolated from the duct proximal to the obstruction and not in communication with the papilla. This isolated segment of the pancreas will continue to secrete pancreatic secretions that cannot reach the duodenum through the distal main pancreatic duct and will be secreted freely into the abdominal cavity resulting in the formation of external or internal fistulas and peripancreatic fluid collections. The site of disconnection in more than

80% of cases is the head or neck/body portion of the pancreas [13, 14].

The most important clinical clue is a nonhealing pancreatic fistula or peripancreatic fluid collection that does not resolve with conservative medical management [15]. On imaging investigation, evidence of an intrapancreatic fluid collection or segmental necrosis along the expected course of the main pancreatic duct with viable upstream pancreatic parenchyma suggests the diagnosis of disconnected pancreatic duct syndrome. Abrupt discontinuity of the main pancreatic duct at the level of the fluid collection is usually diagnostic of a disconnected pancreatic duct syndrome. However, a focal stenosis or mechanical compression from an acute fluid collection can mimic a disrupted main pancreatic duct [15].

Postoperative Pancreatic Fistula

An important and potentially life-threatening complication of pancreatic surgery is the occurrence of a postoperative pancreatic fistula which can originate from the pancreatic remnant after distal pancreatectomy or enucleation, as well as from an anastomosis which is usually created as a pancreaticojejunostomy or pancreaticogastrostomy following pancreatic head resections or drainage procedures [16–18]. The incidence ranges from 0% to 24% with an average fistula rate of 12.9% following pancreaticoduodenectomy [19] and 5–28% after distal pancreatectomy [20].

The risk of developing a postoperative pancreatic fistula varies according to the underlying pancreatic pathology and the consistency of the pancreatic parenchyma. A fibrotic pancreatic remnant in patients with chronic pancreatitis facilitates the creation of an uncomplicated pancreatico-enteric anastomosis, whereas soft and friable pancreatic parenchyma makes the anastomosis more difficult to perform and is associated with a higher risk of pancreatic fistulas as is the absence of duct dilation (< 4 mm). The presence of diabetes mellitus, previous laparotomy, longer operating time, and non-stapler stump closure constitute additional risk factors for the development of pancreatic fistulas [21].

The International Study Group on Pancreatic Fistula (ISGPF) [18] consensus paper defined a postoperative pancreatic fistula (POPF) as the existence of any fluid output via an intraoperatively placed or postoperatively inserted drain on or after postoperative day 3 with amylase content greater than three times the upper normal serum value [18]. Interestingly, this definition also includes clinically asymptomatic patients, and for the same reason, a grading system (grade A, B, and C) has been proposed to assess the severity of postoperative pancreatic fistula, listed in Table 33.2.

Investigations

Laboratory Tests

In patients with an external fistula, the effluent should be collected for fluid analysis. Although there is no established cutoff, a pancreatic fluid amylase level greater than three times the serum amylase is supportive of a diagnosis of a pancreatic fistula. In patients with ascites, diagnostic paracentesis should be performed. Ascitic fluid should be sent for cell count, Gram stain, culture, amylase, albumin, total protein, and cytology. The combination of a serum-albumin ascites gradient below 1.1 g/dl, a total protein level > 3 g/L, and ascitic amylase greater than serum amylase is suggestive of pancreatic ascites. Often fluid amylase levels are 4000 units/L or higher. In some cases, the white cell count may be elevated due to a concomitant infection [22].

Endoscopic ultrasound facilitates fine-needle aspiration to sample cyst fluid for amylase, CEA, and cytology which

Table 33.2 Grading of postoperative fistula (POPF) according to the International Study Group on Pancreatic Fistula (ISGPF) [18]

Grade	A	B	C
Clinical conditions	Well	Often well	Ill appearing/bad
Specific treatment Partial (peripheral) or total parenteral nutrition, antibiotics, enteral nutrition, somatostatin analogue, and/or minimal invasive drainage	No	Yes/no	Yes
US/CT (if obtained)	Negative	Negative/positive	Positive
Persistent drainage (after 3 weeks)	No	Usually yes	Yes
Reoperation	No	No	Yes
Death-related to POPF	No	No	Possibly yes
Signs of infections	No	Yes	Yes
Sepsis	No	No	Yes
Readmission	No	Yes/no	Yes/no

can help differentiate pseudocysts from cystic neoplasms. Pancreatic fluid collections and pseudocysts will typically have high amylase levels, low CEA levels, and inflammatory cells or acellularity on cytological evaluation. Thoracentesis should be performed in patients with a pleural effusion. Effusions associated with pancreaticopleural fistulas are exudative and amylase-rich with pleural fluid amylase greater than the upper limits of normal for serum amylase or a pleural fluid to serum amylase ratio greater than 1.0. Pleural effusions due to a pancreaticopleural fistula can be distinguished from a symptomatic pleural effusion that occurs following acute pancreatitis by a therapeutic thoracocentesis. Pancreaticopleural effluents have high amylase content and tend to re-accumulate after therapeutic thoracentesis, whereas sympathetic pleural effusions do not have an elevated amylase and do not recur.

Chest Radiograph

A chest x-ray should be obtained in patients with symptoms of cough, shortness of breath, and dysphagia. It can show unilateral or bilateral pleural effusion in patients with pancreaticopleural fistula.

Abdominal CT Scan

An abdominal computerized tomography (CT) primarily serves to rule out other causes of abdominal pain. In patients with a pancreatic fistula, an abdominal CT scan may demonstrate free and walled-off fluid collections in the abdominal and thoracic cavities and changes of acute or chronic pancreatitis including focal pancreatic enlargement, parenchymal atrophy, pancreatic ductal dilatation, and calcification. Contrast enhanced CT scan has been shown to be a useful technique in particular to identify the presence of (infected) pancreatic necrosis. The location of the fluid collections seen on CECT can be suggestive of the site of pancreatic duct disruption [23]. Newer computed tomography (CT) technology with thinner collimation and multirow detector CT (MDCT) with post-processing techniques, such as multiplanar reformations, has led to improved visualization of the PD [24].

Magnetic Resonance Cholangiopancreatography (MRCP)

With MRCP one can noninvasively evaluate the pancreatic parenchyma and also delineate pancreatic duct morphology. MRCP has been shown to be particularly useful for detecting pancreatic duct disruptions [25, 26]. A recent study in 31 patients with suspected PD disruptions reported MRCP could correctly diagnose an intact pancreatic duct in 8 patients (100%) and localize the site of disruption in 21 of 23 patients with ductal leak (91%) [25]. One of the limitations of MRCP is the absence of visualization of ductal filling and extravasation in real time, as seen on ERCP, thus giving rise to the possibility of missed diagnosis of pancreatic duct injury in non-dilated ducts [27]. To overcome this limitation, dynamic secretin-stimulated MRCP was studied in 17 patients with suspected pancreatic duct disruption [28]. After secretin administration, changes in the duodenal and jejunal fluid content were evaluated as well as the size or signal intensity of pancreatic fluid collection recorded. In healthy individuals with no pancreatic duct disruption, secretin administration increases the duodenal and jejunal fluid content, with less than 1 mm transient increase in pancreatic duct diameter. Any increase in fluid outside these anatomic regions is suggestive of a pancreatic duct disruption. Dynamic MRCP was able to identify pancreatic duct disruption in 10 of 17 patients (59%), and the investigators concluded that this is a safe and noninvasive technique, providing additional information about pancreatic duct integrity and anatomy, thus facilitating appropriate management. A further advantage of MRCP over ERCP is its ability to characterize the pancreatic duct upstream of the site of complete disruption, an area that is not visualized on ERCP [25]. Though often helpful in the diagnosis, a limitation of MRCP is the obvious inability to intervene therapeutically at the time of diagnosis.

Endoscopic Retrograde Cholangiopancreatography (ERCP)

Endoscopic retrograde cholangiopancreatography (ERCP) provides direct proof of a pancreatic leak or fistula and is the test of choice if therapeutic pancreatic stenting is planned. It has the highest accuracy in diagnosing a pancreatic disruption. It enables direct and dynamic visualization of the pancreatic anatomy as well as the ability to precisely identify the location (head, neck, body, or tail of pancreas) and extent of the disruption [2, 3, 29, 30]. On ERCP, pancreatic disruption is defined as extravasation of contrast medium from the ductal system and can be further defined as partial (opacification of the proximal PD upstream to the site of disruption) or complete (no visualization of the pancreatic upstream to the leak) [2, 3, 29, 30]. It can also provide information about the presence of stricture or calculi in the downstream portion of the duct. Although being the most sensitive technique to detect a PD disruption, ERCP is invasive and requires expertise, and the rates of cannulation of the pancreatic are operator dependent, with failed cannulation or inadequate pancreatography observed in up

Table 33.3 Classification of pancreatic injuries by endoscopic retrograde cholangiopancreatography [34]

Grade	Description
I	Normal main pancreatic duct on MRCP
IIa	Injury to branches of main pancreatic duct on ERCP with contrast extravasation inside the parenchyma
IIb	Injury to branches of main pancreatic duct on ERP with contrast extravasation into the retroperitoneal space
IIIa	Injury to the main pancreatic duct on ERCP at the body or tail of the pancreas
IIIb	Injury to the main pancreatic duct on ERCP at the head of the pancreas

Table 33.4 Management strategies for pancreatic fistula and leak

1. Medical management
2. Interventional therapy
Endoscopic therapy
Transmural drainage
Transpapillary drainage
EUS-guided pancreaticoduodenostomy/ pancreaticogastrostomy
Combination of above procedures
Radiological interventions
Surgical interventions

to 10% of patients [31–33]. It also carries the disadvantage of requiring sedation and is associated with risks of post-procedure pancreatitis and subsequent infection of sterile pancreatic fluid collections. Table 33.3 shows the pancreatographic classification of pancreatic duct injuries caused by blunt trauma in the pancreas [34].

Fistulography

Fistulography should be reserved to determine the site of internal communication of an external pancreatic fistula only if it is not evident on ERCP or MRCP. For pancreatic fistula occurring after pancreatic resection, fistulography is done via ERCP. In patients with operative or percutaneously placed pancreatic drainage catheters, a fistulogram can easily be performed using fluoroscopy, CT, or MRCP. It allows visualization of the fistula tract course, locating the origin from the pancreatic duct, delineation of any fluid collection that is in communication with the fistulous tract, and guiding repositioning of catheters to optimize drainage.

Management

As pancreatic duct leaks are not common, the current scientific evidence regarding clinical management of pancreatic duct leaks and disruptions is largely based on case reports, case series, and expert opinion. There are no randomized controlled trials that have compared the efficacy of medical, endoscopic, radiologic, or surgical treatment modalities. Because of their complexity, pancreatic duct leak patients are best managed by a multidisciplinary team comprised of therapeutic endoscopists, interventional radiologists, and surgeons. The management of pancreatic fistula depends on the presence and severity of symptoms, the characteristics and location of the ductal disruption (presence of a downstream pancreatic duct obstruction, presence of a confined fluid collection, and presence of pancreatic necrosis), and the presence of associated complications such as infection. Early surgical intervention should be considered whenever there is a leak in the pancreatic tail, when the site of ductal disruption cannot be bridged by a stent, or whenever a downstream stricture cannot be stented. Careful attention to an optimal maintenance of hydration, nutrition, and electrolyte balance through the management of the disease process is of prime importance for a successful clinical outcome. Table 33.4 outlines the management of pancreatic fistula and leak.

Medical Management

Patients with a pancreatic fistula are at risk for developing significant nutritional and electrolyte imbalances. Due to the diversion of pancreatic exocrine secretions, excessive loss of sodium and bicarbonate may occur. Patients often present with significant nausea, anorexia, and an inability to tolerate oral intake. In addition, depending on the relative absence of pancreatic enzymes in the duodenum, patients often have poor nutritional absorption, particularly of protein and fat [35]. In the absence of significant symptoms or coexisting infected pancreatic necrosis, initial management of pancreatic fistula consists of supportive care.

Cornerstone of medical management is the inhibition of pancreatic stimulation by maintaining patients nil by mouth (NPO). Nutrition is provided via nasojejunal feeding or by total parenteral nutrition (TPN). Enteral nutrition is associated with a lower incidence of infection, higher 30-day fistula closure rates, and shorter time to closure of postoperative pancreatic fistula as compared with TPN [36, 37]. Enteral feeding therefore should be favored whenever possible because it maintains the mucosal barrier, is relatively simple to administer, and is less costly than TPN. Theoretically, post-pyloric and even post-duodenal feeding seems desirable to minimize stimulation of secretions and maximize pancreatic rest, but there is no scientific evidence that this approach is to be favored over gastric feeding [38]. TPN should be administered to patients who are unable to receive enteral feeding but is not without risks including the occurrence of line sepsis and cholestatic injury to the liver. Somatostatin preparations

may be effective in the reduction of fistula output and help to correct electrolyte imbalances but do not improve the rate of fistula closure. In a 2012 meta-analysis of seven randomized trials that included 297 patients of which 102 had pancreatic fistula, closure rates were not significantly higher in patients treated with somatostatin analogues as compared with controls [39]. Special attention should be directed to optimal care of the external fistula opening as pancreatic juice may cause painful and difficult to treat skin excoriation.

The abovementioned treatment approach is based on the rationale that reduction of the pancreatic secretion decreases the flow of the pancreatic juice through the pancreatic duct and thus expedites healing of the pancreatic fistula. This conservative approach of prolonged pancreatic rest may be sufficient to heal the ductal disruption but occurs at the cost of prolonged hospitalization with a concomitant increase in the cost of treatment and an increased risk of hospital-acquired infections. Moreover, conservative therapy fails in a significant proportion of patients with large disruptions or ductal obstruction downstream of the disruption. Case series have reported fistula closure in approximately 80 percent of external and 50 to 65 percent of internal fistula over 4–6 weeks following supportive care [19]. Follow-up abdominal imaging with an abdominal CT scan or MRCP should be obtained after 6–8 weeks to evaluate the pancreatic fistula and presence of persistent peripancreatic fluid collections. Imaging should be repeated sooner if the patient develops abdominal pain, fever, chills, jaundice, or early satiety. In patients with clinical symptoms and signs suggestive of sepsis, or increasing white blood cell count, pancreatic fluid should be sent for Gram stain and culture to rule out an infection. Systemic antibiotics should be administered in patients with evidence of infected pancreatic fluid collections.

In patients with pancreaticopleural fistula and mediastinal fistula, prolonged conservative therapy involving fasting, parenteral nutrition, somatostatin or its analogues, and attempts to appose leaking mucosa (serosal apposition) have been recommended. The latter includes multiple paracentesis or thoracentesis or even placement of an indwelling chest tube. Usually, medical therapy is continued for 2–3 weeks before another intervention is believed to be warranted [40].

Conservative management for external pancreatic fistula often leads to a reduction in fistula output, but closure rates of external pancreatic fistula vary from 44% to 85% [41]. In patients with persistent external pancreatic fistula despite conservative treatment, endoscopic or surgical alternatives must be considered [42]. In patients with pancreatic fistula unresponsive to medical management, additional interventional treatments are warranted.

Endoscopic Management

In the last two decades, considerable advancements have been made in therapeutic pancreatic endoscopy, and over the years, endoscopic drainage has been used to treat pancreatic duct disruptions with encouraging results.

Transpapillary Drainage

Before considering endoscopic therapy, complete assessment should be done for the site and type of pancreatic duct disruption; anatomy of the pancreatic duct, especially the duct downstream of the disruption; and presence or absence of associated pancreatic fluid collections. A clinically useful investigation that demonstrates the relationship of external pancreatic fistula with the pancreatic duct is a fistulogram which can provide important information and clearly delineate the fistulous tract [23].

The Procedure

Transpapillary drainage involves insertion of an endoprosthesis through the major or minor papilla into the pancreatic duct, creating a path of lesser resistance that directs drainage of pancreatic secretions through the papillary orifice into the duodenum rather than through the pancreatic duct disruption. The sphincter of Oddi and any ductal strictures/calculi in the downstream duct are the sites of resistance impeding the flow of pancreatic juices into the duodenum. These

Practical Considerations in the Medical Management of Pancreatic fistula

- Nil by mouth (NPO)
- Nutrition via nasojejunal feeding or total parenteral nutrition
- Administration of somatostatin or its analogues, preferably its long-acting form Sandostatin LAR (Novartis) 50–200 mcg subcutaneous 4 times daily for prolonged periods of time
- Daily care of the percutaneous fistula opening to avoid and treat skin erosions

Instruments and Accessories

- Standard pull-type sphincterotome or a needle knife
- Guidewire
- Dilation balloon (4, 6, and 8 mm)
- Dilating catheters (3–10 Fr)
- 8.5 Fr Soehendra stent retriever
- Pancreatic stents in various width and sizes (with or without pigtail)
- Brush cytology catheter and biopsy forceps (to exclude malignant strictures)
- Nasopancreatic drain

obstacles can be tackled by pancreatic sphincterotomy, stricture dilation, stone removal, and stent/nasopancreatic drainage insertion.

Pancreatic sphincterotomy increases the size of the pancreatic duct orifice and removes a source of resistance to transpapillary flow of pancreatic secretions. Pancreatic sphincterotomy can be performed using a standard pull-type sphincterotome or a needle knife [43]. When using a pull-type sphincterotome, pancreatic sphincter can be cannulated either in a single step or the biliary duct is cannulated first and a biliary sphincterotomy is performed to expose the pancreaticobiliary septum. This septum covers the intramural portion of the pancreatic duct. The pancreatic orifice can be found at the 3–6 o'clock margin of the biliary sphincterotomy. After cannulation of the pancreatic duct with the pull-type sphincterotome, a pancreatic sphincterotomy is performed in the 12 o'clock position along the full length of the pancreaticobiliary septum. Needle-knife pancreatic sphincterotomy necessitates the initial placement of a pancreatic duct stent. The pancreatic duct stent serves as a guide for the direction and extent of the needle-knife incision and provides prophylaxis against the development of post-ERCP pancreatitis. The needle-knife incision should be started at the papillary orifice and extended along the intramural portion of the pancreatic duct by following the course of the stent. Occasionally, this technique cannot be used when strictures or stones in pancreatic head impede initial placement of the stent [43].

Pancreatic duct strictures or stones can impede transpapillary flow of pancreatic secretions, forcing this flow to exit the pancreatic duct through a duct leak. This ongoing extravasation perpetuates the presence of a fistula tract. Eradication of such obstructive lesions can lead to the resolution of fistulas. Endoscopic therapy of pancreatic duct strictures involves progressive dilation and stenting. Dilation balloons are available in 4-, 6-, and 8-mm diameters [43]. The diameter of the stricture and the adjacent pancreatic duct dictates the size of balloon to be used. After passing a guidewire across the stricture site, the dilation balloon is passed over the guidewire and positioned at the area of narrowing. Radiopaque markers at the distal and proximal ends of the balloon facilitate accurate positioning. The balloon is inflated to a predetermined pressure until there is obliteration of the balloon waist at the site of narrowing. Rarely, tight strictures cannot be traversed with a balloon catheter and must initially be dilated by passing graduated dilating catheters across the stricture. These catheters are passed over a guidewire and range from 3 Fr to 10 Fr in size [43]. In very tight strictures, the use of the 8.5 Fr Soehendra stent retriever may be necessary to facilitate passage of dilation balloons or stents.

Pancreatic stent placement serves several purposes. It bridges the sphincter of Oddi and eliminates any resistance to transpapillary flow caused by the sphincter. Stenting also maintains the patency of strictures that have been dilated. Ideally, the stent should bridge the site of disruption [44]. Bridging pancreatic stents helps to close the fistula rapidly by decreasing the ductal pressure and abolition of pancreatic pressure gradient, achieved by bypassing the sphincter of Oddi and stricture and by mechanically blocking the fistula lumen. The technique for placing a stent in the pancreatic duct is similar to that used for placing a biliary stent. Stents can be placed with or without pancreatic sphincterotomy. Stent diameter, which ranges from 3 Fr to 10 Fr, is determined by the diameter of the pancreatic duct. In general, the stent diameter should not exceed the upstream duct diameter. Flaps located on both ends of the stent prevent stent migration. Stent length should be chosen such that one flap is located just outside the papilla and the other flap is positioned proximal to the area of ductal disruption. In cases where attempts to advance a guidewire into the upstream portion of the duct are unsuccessful, a shorter stent can be placed that does not traverse the site of ductal disruption but only the pancreatic sphincter.

The important factors associated with successful and poor outcome of transpapillary drainage are listed in Table 33.5 [3, 29].

The current evidence suggests that transpapillary drainage alone is safe and effective for patients with communicating small pseudocysts (<6 cm) and has best results if the pancreatic duct disruption is partial and is bridged by the endoprosthesis [45, 46]. The optimal duration of stent therapy is not clear, as shorter duration is associated with a lack of resolution of pancreatic duct disruption and, thus, increased risk of recurrences, whereas longer duration of stenting is associated with stent occlusions and stent-induced ductal changes [3, 29, 47, 48]. In the majority of case series, stents were left in place for 4–6 weeks, and it has been observed that even with this small duration, noticeable ductal changes appear in patients with acute pancreatitis who otherwise have a normal pancreatic duct. Biodegradable stents or recently designed stents that cause less ductal damage may have an increasing role in these clinical situations [49, 50].

Table 33.5 Factors associated with successful and poor outcome of transpapillary drainage [3, 29]

Factors associated with successful outcome of transpapillary drainage:
1. Partially disrupted pancreatic duct
2. Disruption in the body of pancreas
3. A bridging stent
4. A longer duration of stent therapy
Factors associated with poor outcome of transpapillary drainage
1. Female gender
2. Patients with acute pancreatitis
3. Stents not bridging the disruption
4. Shorter duration of stent therapy

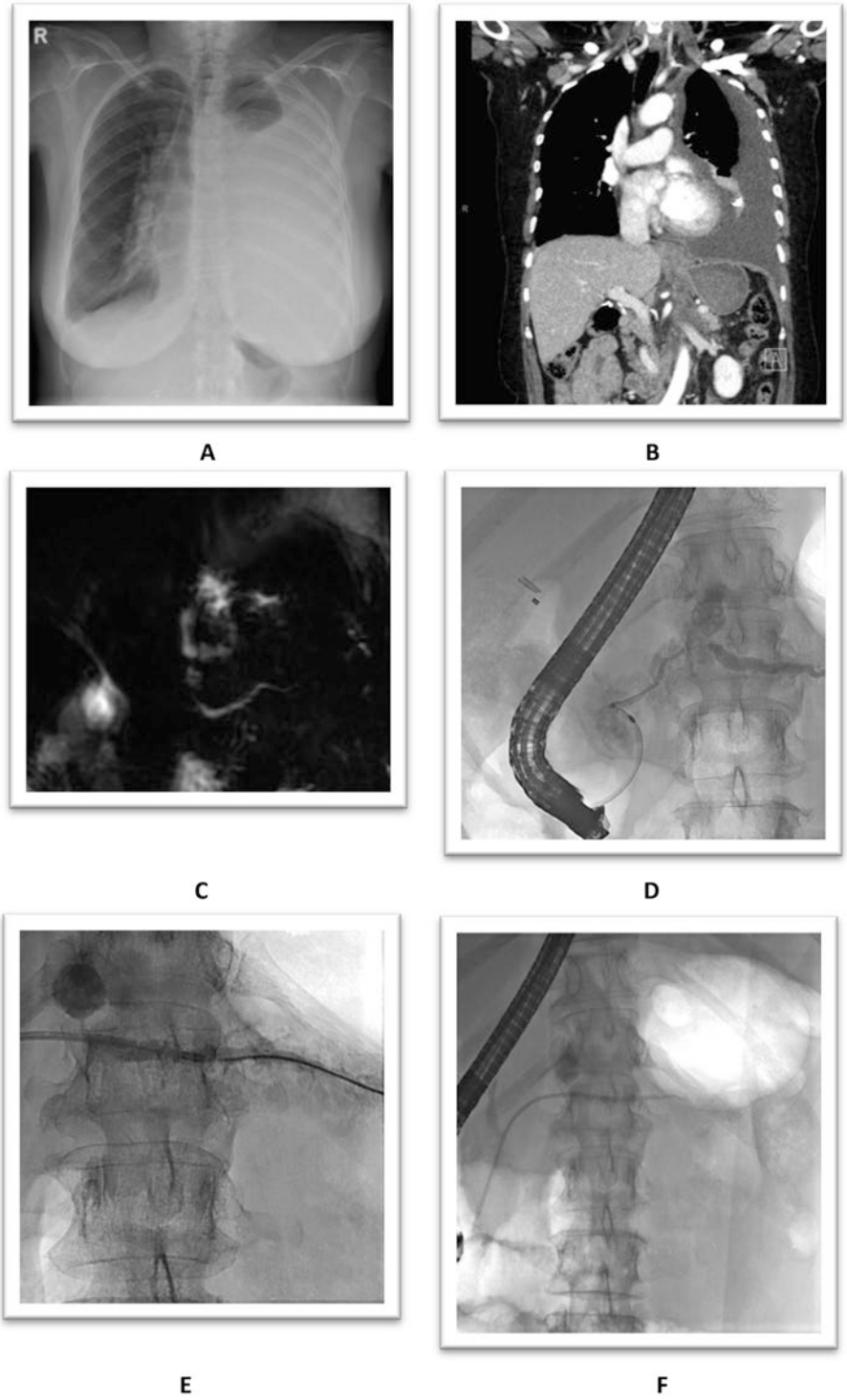

Fig. 33.1 A patient with previous history of acute severe biliary pancreatitis, presented with shortness of breath: (**a**) chest x-ray showing massive left-sided pleural effusion, (**b**) CT scan of thorax, (**c**) MRCP showing presence of peripancreatic fluid collection without any obvious leak, (**d**) ERCP showing a leakage cranial to stricture in the body of pancreas with proximal ductal dilatation, (**e**) a 6 Fr cystotome with the help of electrocautery was used to negotiate the stricture, (**f**) a 12 Fr 5 cm plastic stent placed with the proximal tip proximal of the stricture and site of leakage

Experience with transpapillary drainage for pancreatic ascites and effusions are limited to case reports and series [51–56]. Saeed and colleagues had the first report on a case of successful resolution of percutaneous pancreatic fistula after pancreatic stent placement [44]. Since then, several reports have been demonstrated the efficacy of the endoscopically placed pancreatic stents in facilitating fistula closure [57–62]. Telford and colleagues reported successful resolution of pancreatic ascites in six of seven patients (86%) after endoscopic PD stent placement with a median duration to resolution of 6 weeks [29]. Figure 33.1 below clearly demonstrates the role of pancreatic stent in the management of internal pancreatic fistula with massive left-sided pleural effusion secondary to pancreatic duct stricture and leak.

In the above-described patient, at follow-up ERCP 2 months later, no more leakage was seen, and the stricture was less pronounced. The 5 Fr stents was exchanged for a single 7 Fr stent. Brush cytology showed no signs of malignancy. Due to a poor neurological condition, the decision was made to remove the stent 2 months later via gastroscopy and only repeat exams and investigations in the case of recurrent pleural effusion. No recurrence of pleural effusion was seen during 4 years of follow-up.

Like a stent, the placement of transpapillary nasopancreatic drain can also facilitate healing of ductal disruptions by partially occluding the leaking duct or by traversing the pancreatic sphincter, thereby converting the high-pressure pancreatic duct system to a low-pressure system with preferential flow through the nasopancreatic drain. Downsides of a nasopancreatic drain are that they are uncomfortable to patients and there is a risk that the nasopancreatic drain may accidentally dislodge. A benefit of a nasopancreatic drain is the ability to easily obtain repeated pancreatograms to monitor the healing of ductal disruption without having to repeat ERCP. Moreover, a blocked nasopancreatic drain is opened up through flushing and aspiration, thus obviating the need for repeat ERCP and stent replacement as in the case of a blocked stent. Also, after demonstrating healing of duct disruption, a nasopancreatic drain can be easily removed without necessitating an endoscopy. Bhasin and colleagues [51] described the usefulness of endoscopic transpapillary nasopancreatic drain placement in ten patients with pancreatic ascites and effusion. Following placement of a nasopancreatic drain, the ascites and/or pleural effusion resolved in all patients within 4 weeks. All patients had partial pancreatic duct disruption, and the nasopancreatic drain bridged the disruption in eight of the ten (80%) patients.

Kozarek and colleague [63] investigated the role of endoscopic transpapillary pancreatic duct stent placement in nine patients with an external pancreatic fistula. The stents bridged the disruption in three patients, and fistulas successfully healed in eight (89%). Costamagna and colleagues [64] reported on 16 patients with postsurgical external pancreatic fistula using endoscopic transpapillary nasopancreatic drainage. Successful outcomes were achieved in 12 (75%) patients, and fistulas healed in 11 of these 12 patients with a mean time to closure of external pancreatic fistula of 8.8 days (range: 2–33 days. These studies suggest that external pancreatic fistula can be effectively treated by transpapillary stent and nasopancreatic drain placement, with the best results being obtained in patients with a partial pancreatic duct disruption that can be bridged. Figure 33.2 shows the management algorithm of internal pancreatic fistulas (pancreatic ascites and pleural effusion) [53].

In case of a postoperative pancreatic fistula, the timing of ERCP is controversial, but there is evidence that extending the period of conservative therapy beyond 3 weeks increases

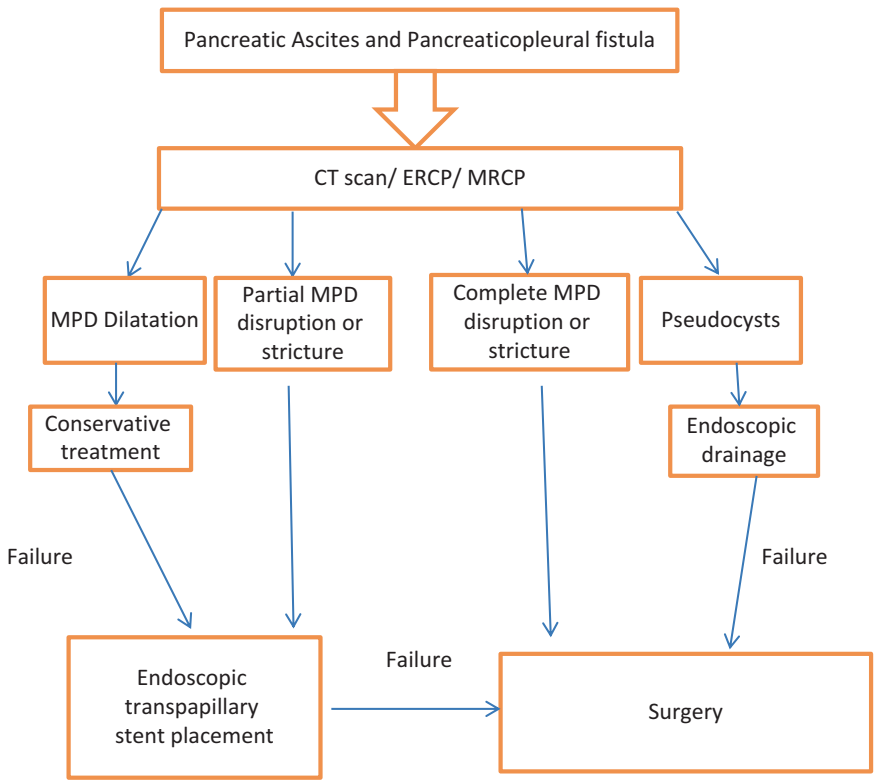

Fig. 33.2 Algorithm for the management of internal pancreatic fistula [53]

Table 33.6 Success rate of transpapillary drainage in patients with POPF

Study	Patients	Method	Success Rate
Costamagna [64]	16	Nasopancreatic drain	12/16 (75%)
Boerma [67]	15	Pancreatic duct stent	13/15 (87%)
Howard [65]	7	Pancreatic duct stent	7/7 (100%)
Kozarek [63]	9	Pancreatic duct stent	8/9 (89%)

the mortality rate [65, 66]. Most experts recommend ERCP when a fistula persists for at least 2 weeks. The first report on the use of pancreatic stents in the treatment of internal and external postoperative pancreatic fistula was published in 1993 [44]. The success rate of endoscopic pancreatic stenting in more recent series has been 75–100% with an average clinical success rate of 85% in a total of 47 patients [19]. The technique comprises of placing a 5–7 Fr diameter stent of variable length and preferably across the site of ductal disruption [63–65, 67]. Table 33.6 summarizes studies, which have used stents to treat postoperative pancreatic fistula with success rates.

A management algorithm for postoperative pancreatic fistula is shown in Fig. 33.3 [9].

Prophylactic endoscopic pancreatic stenting has been considered as a measure aimed to reduce the development of postoperative pancreatic fistula following distal pancreatectomy [68]. A pancreatic stent reduces the secretory pressure on the surgical closure [68, 69]. Prophylactic endoscopic pancreatic stenting is usually performed approximately 6 days before the distal pancreatectomy. The stent should be removed 1–2 weeks after the distal pancreatectomy to prevent any alterations to the pancreatic duct [70–72]. Abe and colleagues reported that routine preoperative pancreatic stenting was effective in preventing postoperative pancreatic fistula; of the nine patients who underwent this endoscopic procedure and subsequently underwent a distal pancreatectomy, none developed a postoperative pancreatic fistula [68]. At present, the available evidence is too scarce to routinely recommend the use of prophylactic endoscopic pancreatic stenting in this setting.

Complications

Several observational case studies have demonstrated that transpapillary drainage is safe and effective in patients with communicating pancreatic pseudocysts [3, 26, 29, 73, 74]. This route of drainage is physiologic, as it depends on the normal anatomic route of drainage of pancreatic juice and does not involve creation of an alternative non-physiological route of drainage such as in transmural drainage. The advantage of the transpapillary approach over the transmural drainage is the reduced risk of bleeding or perforation associated with transmural drainage. Transpapillary drainage however, carries risks associated with ERCP including post-ERCP pancreatitis, bleeding, and retroperitoneal perforation after sphincterotomy and also raises the risk of infection and stent-induced ductal changes mimicking chronic pancreatitis, especially in patients with acute pancreatitis or trauma and normal pancreatic duct [45, 47, 48, 75].

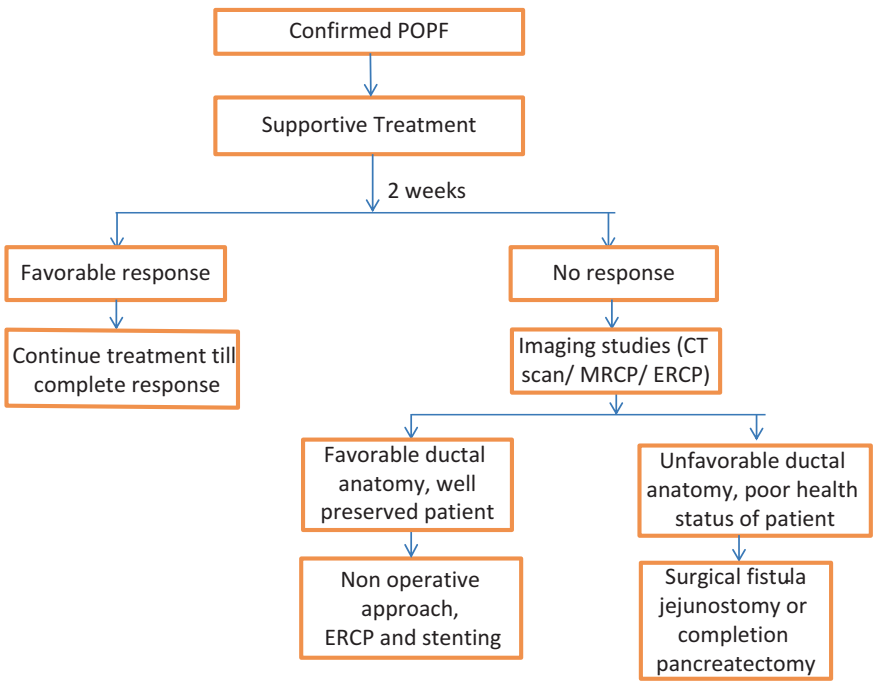

Fig. 33.3 Algorithm for the management of POPF [9]

Complications of Transpapillary Drainage
- Bleeding after sphincterotomy
- Post-ERCP pancreatitis
- Retroperitoneal perforation after sphincterotomy
- Secondary stent-induced changes and strictures in the part of the pancreatic duct that has been stented in particular at the proximal stent tip
- In- or outward plastic stent migration

Instruments and Accessories
- Ultrasound processor and linear echo endoscope
- 19 G EUS fine-needle device
- Long guidewire(s)
- Oasis 8 Fr stent pusher (to facilitate the introduction of a second guidewire)
- Cystotome (6 or 10 Fr)
- Dilation balloon (8 mm)
- Plastic double-sided pigtail pancreatic stents or fully covered metal expandable stents specifically designed for the drainage of fluid collections (lumen-opposing stents, e.g., Hot AXIOS stent, Boston, Scientific)

Transmural Drainage

Pseudocysts are the most common presentation of a pancreatic duct leak. Pseudocysts developing as a consequence of pancreatic duct disruption may be drained via the transpapillary or transmural route, or a combination of both. The transmural drainage of pseudocysts is achieved by placing one or, preferably, more stents through an endoscopically created fistulous tract between the pseudocyst and the gastroduodenal lumen. Internal drainage of pseudocyst contents leads to the collapse and resolution of the fluid-filled cavity, which eventually results in closure of the pancreatic fistula. Consideration of endoscopic pseudocyst drainage depends on several factors including the position of the fluid collection relative to the gastric or duodenal wall, the location of surrounding vascular structures, and the physical consistency of the cyst contents (solid components versus liquid only).

In general, pseudocysts that are adherent to the gastroduodenal wall, predominantly fluid filled, and without intervening blood vessels are amenable to endoscopic drainage. EUS provides detailed imaging of the pseudocyst wall and content that may not be possible to appreciate with alternative methods like transabdominal ultrasound or CT scan. Varices or retroperitoneal vessels situated between the gastroduodenal wall and the pseudocyst wall can be easily detected with EUS imaging. EUS can accurately identify intracystic solid debris and allows appropriate measures to be taken to avoid infection after drainage procedures. It also offers the advantage of excellent visualization of pancreas and peripancreatic areas and provides real-time guidance to advance the needle safely into the pseudocyst cavity without inadvertent puncture of any intervening blood vessels. Therefore, EUS-guided drainage should be considered in patients with non-bulging fluid collections, patients at high risk of bleeding complications, prior failed transmural attempt without EUS guidance, and collections inaccessible by standard endoscopic techniques (e.g., pseudocysts located at the tail end of the pancreas) [76, 77].

The Procedure

A linear echo endoscope is used, preferably with a large working channel, to search for the most optimal localization for draining the fluid collection. A puncture spot is chosen where the fluid collection is closest to the gastrointestinal wall while avoiding interposing blood vessels. The actual puncture of the fluid collection is done with either a 19 G EUS puncture needle or as a one-step procedure using the cystotome. The former approach has some advantage in certain situations in which it is more challenging to enter the collection, for example, in the case of infected necrosis with solid material and air. In such case, fluid can be aspirated to confirm the appropriate position of the needle, or contrast can be injected to delineate the fluid collection. Next, a long guidewire is introduced through the needle or the cystotome into the fluid collection letting it curl one or two times to secure its position. When a needle was used to enter the fluid cavity, it is now removed. In case the inner cystotome catheter was used to enter the fluid collection, the outer catheter is advanced into the cyst to widen the fistula, again using electrocautery. For this, the plug on the handle of the cystotome connecting it to the electrocautery device is disconnected from the inner and moved to the connector of the outer catheter. If a EUS needle was used to puncture the fluid collection, the puncture channel can be dilated immediately with an 8 mm dilation balloon that is inserted over the guidewire into the fluid collection. Many prefer to use the outer catheter of the cystotome (10 Fr) for this purpose using electrocautery because it may prove very difficult to pass the dilation catheter into the fluid collection when, for example, the wall of the fluid collection is well developed such as, for example, in the case of a pseudocyst. An added advantage of using the outer catheter of cystotome is that a second guidewire can be introduced into the fluid collection easily which greatly facilitates the placement of multiple plastic stents. Depending on indication and personal preference, either (multiple) plastic stents, usually double-pigtail 5–7 cm 8.5 Fr stents, are placed under fluoroscopic and endoscopic guidance. In case of an infected fluid collection, often also a nasocystic drain is inserted. Lately, the placement of lumen

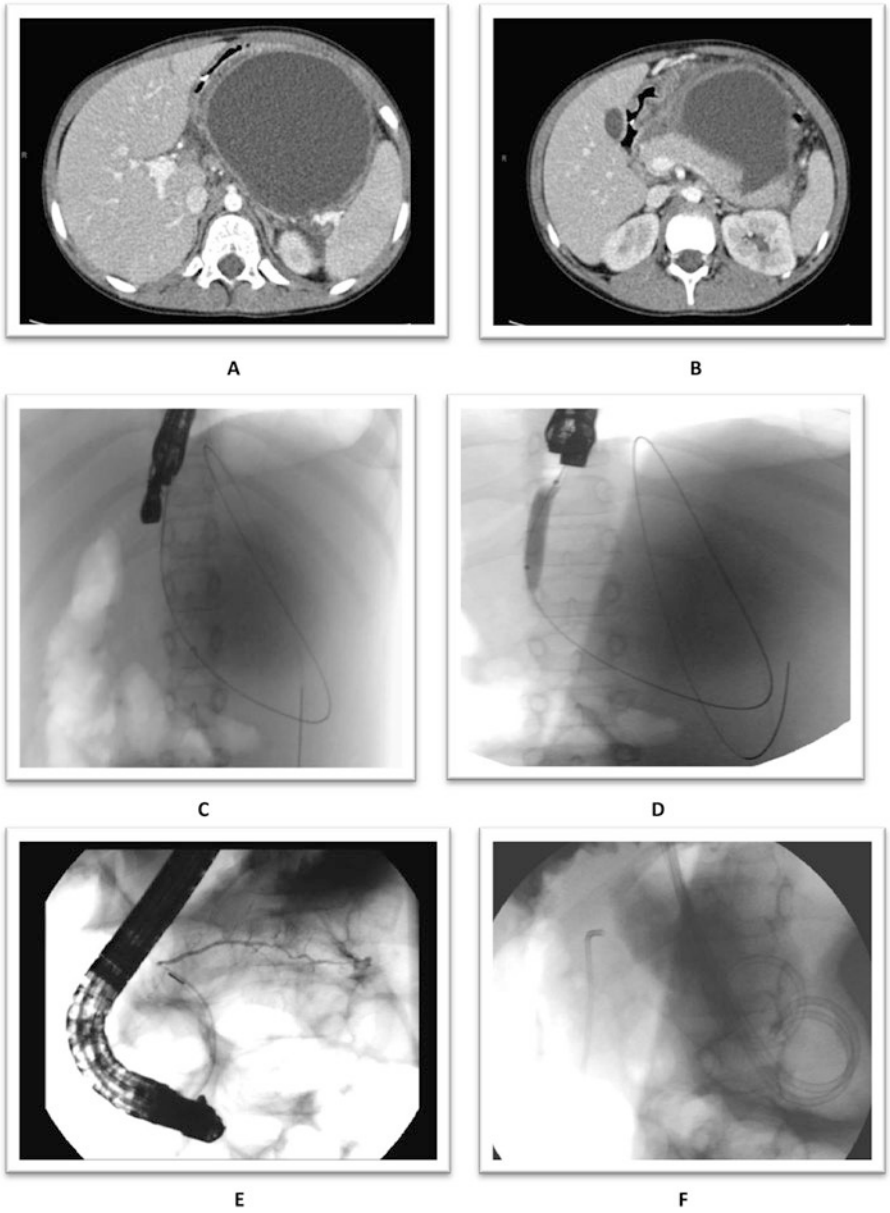

Fig. 33.4 A young female presented with a large pancreatic pseudocyst secondary to pancreatic trauma: (**a**) CT scan showing a large homogenous fluid collection; (**b**) partial rupture of pancreatic parenchyma in the tail area with communication with the cyst; (**c**, **d**) EUS-guided transmural drainage of the cyst; (**e**) ERCP, a leak in pancreatic tail clearly seen; (**f**) a 5 Fr 5 cm plastic stent placed transpapillary, three 7 Fr 7 cm double-pigtail plastic stents in pseudocyst

apposing metallic expandable stents has become more popular (see further).

Figure 33.4 demonstrates a large pancreatic pseudocyst secondary to a leak in pancreatic tail, managed with transmural and transpapillary drainage. The patient had immediate relief of pain post-procedure. After 1 week, the fluid collection had disappeared completely as seen on abdominal ultrasound. The pancreatic stent was removed after 3 weeks and the double pigtails after 3 months. During 2 years of follow-up, the patient had no complaints, and no recurrence of a fluid collection occurred.

Conventional wisdom has been to remove the transmural stents in 6–8 weeks after resolution of the pancreatic fluid collection is confirmed on a follow-up CT scan. However, this strategy is associated with recurrence in 10–30% of patients, usually within 1 year after stent removal [19, 78]. Although prolonged stenting is associated with better outcomes, most data is derived from retrospective studies, and the optimal duration of transmural stenting is still debated [78]. In patients with disconnected pancreatic duct syndrome, prolonged transmural stenting seems particularly important, because drainage of the pancreatic secretions from the excluded pancreatic segment requires a patent fistula tract. The usual approach in most of the expert centers is to keep two transmural stents in place for long periods with elective stent replacement after 3–5 years. The stents are exchanged earlier if the patient presents with a recurrent collection [79, 80]. In a randomized controlled study, Arvanitakis

and colleagues compared the clinical outcomes of leaving transmural stents in place indefinitely following drainage with removal of stents after resolution of the pancreatic fluid collection [81]. Five of 13 patients in the stent-retrieval group had recurrence of the same pancreatic fluid collection, whereas in the group with indwelling stents, there was no recurrence noted in any patients. Most patients with recurrence had pancreatic duct disruption. The investigators suggested that long-term transmural stent placement should be considered in patients with complete pancreatic duct disruption or a communicating pancreatic fluid collection in the setting of chronic pancreatitis.

Complications

Complications directly related to EUS-guided pancreatic fluid collection drainage occur in approximately 10% of patients and include bleeding at the site of cystenterostomy, pneumoperitoneum, and local or systemic infection [82]. Small-bowel obstruction secondary to migration of transmural double-pigtail stents has also been reported [83].

Complications of EUS-Guided Transluminal Drainage

- Bleeding after upsizing gastroduodenal-cystostomy fistula with cystotome of dilation balloon
- Delayed bleeding due to mechanical friction between distal stent end and cyst wall (has been reported with metal lumen-opposing stents)
- Leakage of cyst fluid into the abdominal cavity with temporary peritonitis (can usually be managed conservatively with adequate analgesic therapy for 2 or 3 days)
- Secondary infection of the drained fluid collection, in particular in the case a necrotic collection containing solid parts necessitating endoscopic debridement
- Secondary infection of the drained fluid collection due to in- or outward migration of stent(s)

Endoscopic Pancreaticoduodenostomy or Pancreaticogastrostomy

This technique is designed for reconnecting a completely disconnected pancreatic duct to the gastrointestinal tract lumen [84]. The role of endoscopic management of patients with complete pancreatic duct disruption is still debated. While the efficacy of transpapillary drainage with stenting has been shown in incomplete main pancreatic duct ruptures, its role is much more limited in the disconnected pancreatic duct syndrome. Usually the upstream duct cannot be accessed by ERCP and transpapillary interventions are futile. There is no consensus on the optimal endoscopic approach to treatment of disconnected pancreatic duct syndrome, but the procedure entails the creation of an endoscopic pancreaticoduodenostomy or pancreaticogastrostomy. Most studies are from expert centers and include a small number of patients and have limited duration of follow-up. Importantly, the procedural adverse events are not trivial.

The Procedure

Instruments and Accessories

- Ultrasound processor and linear echo endoscope
- 19 G EUS fine-needle device, preferably the EchoTip access needle (Cook Medical) to prevent shearing of the guidewire
- Long guidewire
- Cystotome (6 Fr)
- Dilation balloon (4, 6 mm)
- 5 or 7 Fr plastic stents pancreatic stents

Procedural steps for endoscopic pancreaticoduodenostomy or pancreaticogastrostomy include the following. First, the dilated upstream pancreatic duct is punctured from the stomach or duodenum under EUS guidance using a 19 G aspiration needle, preferably the EchoTip® Ultra HD Ultrasound Access Needle (Cook Medical, USA) to prevent sheering of the wire. A small amount of contrast is injected in order to opacify the pancreatic duct. Next, a 0.035-inch or smaller-caliber guidewire is advanced into the ductal system. The transmural tract is then dilated by using dilation catheters, balloons, or preferably a cautery device such as a cystotome. Once proper access has been established with a wide-enough fistulous tract connecting the stomach lumen to the dilated disconnected pancreatic ductal system, a double-pigtail stent of suitable caliber is deployed to drain the disconnected main PD into the stomach or the duodenum [15]. A limiting factor for performing this challenging procedure is the lack of dedicated accessories facilitating easy, stable, and secure access into the pancreatic duct. Moreover, the plastic endoprostheses trend to migrate relatively frequent. More data with larger cohorts of patients are needed to validate the promising preliminary findings from a few expert centers [15]. Figure 33.5 shows an algorithm for the endoscopic management of DPDS [79].

Complications

Complications related to endoscopic pancreaticoduodenostomy or pancreaticogastrostomy largely resemble those of EUS-guided transluminal drainage. Frequent stent migration is of particular note as this is often a reason for recurrent symptoms. This then necessitates a new procedure as the fistulous tract may close off relatively quickly unless there is sufficient flow of pancreatic juice to maintain open communications with the stomach lumen.

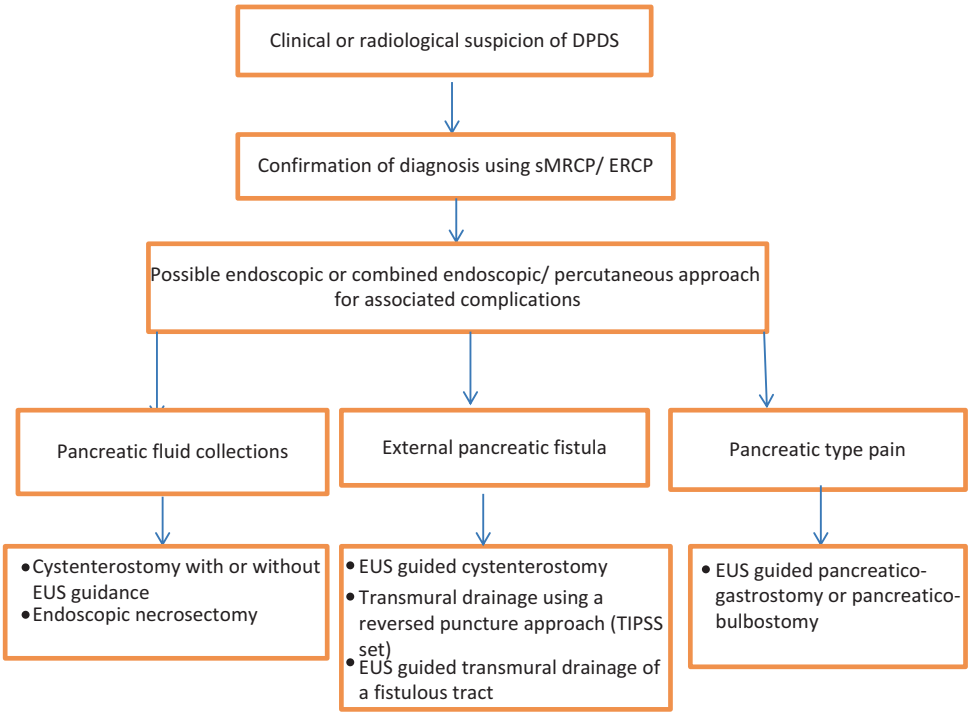

Fig. 33.5 Algorithm for endoscopic management of DPDS [80]

Complications of Endoscopic Pancreaticoduodenostomy or Pancreaticogastrostomy

- Bleeding during the creation of the gastropancreatostomy using the 6 Fr cystotome followed by balloon dilation
- Temporary leakage of cyst fluid into abdominal cavity with transient peritonitis (can usually be managed conservatively with adequate analgesic therapy for 2 or 3 days)
- Post-procedural pancreatitis
- Early partial stent migration, leakage, or occlusion leading to the formation of a peripancreatic fluid collection
- Early full stent migration leading to a clinical picture of a perforation with an acute abdomen and peritonitis necessitating endoscopic or surgical closure
- Late stent migration or occlusion with recurrence of symptoms
- Occurrence of secondary stent-induced changes and strictures in the part of the pancreatic duct that has been stented in particular at the distal stent tip and the entry point of the stent into the pancreatic duct

Novel Endoscopic Techniques and Approaches

Some patients have refractory fistulas that do not heal, even after optimal endoscopic management. Many patients with refractory pancreatic duct disruptions have large disruptions, disruptions located at the tail end of the pancreas, or complete pancreatic duct disruptions [15].

Patients with refractory fistulas may be treated with endoscopic glue or fibrin injection. Fibrin is a physiologic adhesive containing a combination of thrombin, fibrinogen, and calcium and does not promote foreign-body reaction or inflammation, but the exposure to pancreatic juice leads to rapid degradation, and, therefore, periodic injections are required to keep the fistula closed [85]. In contrast to fibrin, cyanoacrylate glue is a nonbiological compound that is more stable and is not degraded by pancreatic enzymes. Seewald and colleagues [86] assessed the safety and efficacy of endoscopic injection of N-butyl-2-cyanoacrylate into the fistulous tract combined with endoscopic transpapillary drainage in 12 patients with internal and external pancreatic fistula. The fistulas closed in eight (67%) patients, with a single injection in seven of these eight successfully treated patients. There were no complications, and none of the successfully treated patients had recurrence of the fistula. Fischer et al. [87] have shown successful closure of eight out of eight patients of postoperative pancreatic fistula with the use of fibrin glue. Advantages of N-butyl-2-cyanoacrylate are that it is possible to monitor the injection by mixing with lipiodol and it is more stable than fibrin glue. The potential complications are pancreatitis, pulmonary embolism, fever, and abscess formation. However, vascular embolization is less likely when being used for fistula closure. Another compound that has been used for closure of external pancreatic fistula is Glubran 2. This surgical glue

is composed of N-butyl-2-cyanoacrylate and methacryloxysulfolane and has lower toxicity and elicits lesser inflammatory response in comparison with N-butyl-2-cyanoacrylate glue. Mutignani and colleague [88] used endoscopic injection of Glubran 2 for closure of pancreatic fistula in four patients, three of whom had failed endoscopic drainage. The pancreatic duct disruption healed in three (75%) patients within 24 h of the procedure.

Endoscopic management of external pancreatic fistula without an associated pancreatic fluid collection can be extremely challenging. In a study by Arvanitakis et al., endoscopic or combined percutaneous and endoscopic treatment was performed in 16 patients with persistent external pancreatic fistula after previous unsuccessful conservative treatment [14]. Ten of the 16 patients had disconnected pancreatic duct syndrome. Two novel techniques were described by which a connection was established between the external pancreatic fistula tract and the duodenal or gastric cavity. The first one involved the transient filling of the fistula tract at the level of disconnection, rendering the virtual cavity transiently visible for EUS-guided drainage performed by a second operator. This resulted in a re-internalization of the fistula and closure of the external path [14, 79]. The other technique, performed under fluoroscopic control, used a TIPS (transjugular intrahepatic portosystemic shunt, TIPSS-200 set, Cook Medical) inserted over a guidewire into the external pancreatic fistula tract which was maneuvered to puncture the gastrointestinal tract under endoscopic and fluoroscopic control, thus creating a transmural drainage path. Both endoscopic and percutaneous procedures were performed by experienced endoscopists [14]. Irani et al. used this combined procedure using a TIPSS-200 set in ten patients with disconnected pancreatic duct syndrome and external pancreatic fistula; 70% of patients were successfully treated after a mean follow-up of 25 months [89].

There is also a report of sealing of an external pancreatic fistula by endoscopic deployment of coils (intravascular uses coil made of fibered platinum, 0.035 inches [0.89 mm] diameter, straight length 50 mm, coiled size 5 × 4 mm; Target Vascular, Boston Scientific, Ireland), but the safety and efficacy of this approach needs to be studied further [90]. An alternative approach to treating refractory pancreatic duct disruptions is placement of covered metallic stents. There have been case reports describing successful healing of refractory pancreatic fistulas by endoscopic insertion of self-expanding metallic stents [52, 91, 92]. Although placement of self-expandable metal stent appears to be an attractive option, stent-induced ductal and parenchymal changes limit its routine use; therefore, it should be used a last resort in difficult cases with no other feasible treatment options [93].

Conclusion

The current scientific evidence regarding clinical management of pancreatic duct leaks and disruptions is limited to case reports, case series, and expert opinion. Because of their complexity, pancreatic duct leak patients are best managed by a multidisciplinary hepato-pancreato-biliary team comprised of therapeutic endoscopists, interventional radiologists, and surgeons. The management of pancreatic fistula depends on the presence of symptoms, the characteristics and location of the ductal disruption, and the presence of associated complications such as infection. Distinct clinical manifestations must be recognized such as pancreatic ascites and pancreaticopleural fistula, disconnected pancreatic duct syndrome, and postoperative pancreatic fistula because all have their specifics and peculiarities with regard to medical, endoscopic, and surgical treatment. Careful attention to an optimal maintenance of hydration, nutrition, and electrolyte balance through the management of the disease process is of prime importance for a successful clinical outcome.

References

1. Kozarek RA, et al. Endoscopic transpapillary therapy for disrupted pancreatic duct and peripancreatic fluid collections. Gastroenterology. 1991;100(5 Pt 1):1362–70.
2. Bhasin DK, et al. Endoscopic management of pancreatic diseases. Indian J Gastroenterol. 1997;16(4):151–2.
3. Varadarajulu S, Noone TC, Tutuian R. Predictors of outcome in pancreatic duct disruption managed by endoscopic transpapillary stent placement. Gastrointest Endosc. 2005;61:568–75.
4. Pannegeon V, et al. Pancreatic fistula after distal pancreatectomy: predictive risk factors and value of conservative treatment. Arch Surg. 2006;141(11):1071–6.
5. Neoptolemos JP, London NJ, Carr-Locke DL. Assessment of main pancreatic duct integrity by endoscopic retrograde pancreatography in patients with acute pancreatitis. Br J Surg. 1993;80(1):94–9.
6. Kozarek RA. Endoscopic therapy of complete and partial pancreatic duct disruptions. Gastrointest Endosc Clin N Am. 1998;8(1):39–53.
7. Fulcher AS, Capps GW, Turner MA. Thoracopancreatic fistula: clinical and imaging findings. J Comput Assist Tomogr. 1999;23(2):181–7.
8. Zinner MJ, Baker RR, Cameron JL. Pancreatic cutaneous fistulas. Surg Gynecol Obstet. 1974;138(5):710–2.
9. Seetharam P, Rodrigues GS. Postoperative pancreatic fistula: a Surgeon's nightmare! An insight with a detailed literature review. JOP. 2015;16(2):115–24.
10. Rockey DC, Cello JP. Pancreaticopleural fistula. Report of 7 patients and review of the literature. Medicine (Baltimore). 1990;69(6):332–44.
11. Ondrejka P, et al. Isolated massive pleural effusion caused by pancreatico-pleural fistula. Z Gastroenterol. 2000;38(7):583–5.
12. Francois CJ, Demos TC, Iqbal N. Pancreaticothoracic fistulas: imaging findings in five patients. Abdom Imaging. 2005;30(6):761–7.
13. Pelaez-Luna M, et al. Disconnected pancreatic duct syndrome in severe acute pancreatitis: clinical and imaging characteristics and outcomes in a cohort of 31 cases. Gastrointest Endosc. 2008;68(1):91–7.

14. Arvanitakis M, et al. Endoscopic treatment of external pancreatic fistulas: when draining the main pancreatic duct is not enough. Am J Gastroenterol. 2007;102(3):516–24.
15. Varadarajulu S, Rana SS, Bhasin DK. Endoscopic therapy for pancreatic duct leaks and disruptions. Gastrointest Endosc Clin N Am. 2013;23(4):863–92.
16. Buchler MW, et al. Pancreatic fistula after pancreatic head resection. Br J Surg. 2000;87(7):883–9.
17. Bassi C, et al. Pancreatic fistula rate after pancreatic resection. The importance of definitions. Dig Surg. 2004;21(1):54–9.
18. Bassi C, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery. 2005;138(1):8–13.
19. Alexakis N, Sutton R, Neoptolemos JP. Surgical treatment of pancreatic fistula. Dig Surg. 2004;21(4):262–74.
20. van Berge Henegouwen MI, et al. Incidence, risk factors, and treatment of pancreatic leakage after pancreaticoduodenectomy: drainage versus resection of the pancreatic remnant. J Am Coll Surg. 1997;185(1):18–24.
21. Ban D, et al. Stapler and nonstapler closure of the pancreatic remnant after distal pancreatectomy: multicenter retrospective analysis of 388 patients. World J Surg. 2012;36(8):1866–73.
22. Ceroni M, et al. Amylase level in drains after pancreatoduodenectomy as a predictor of clinically significant pancreatic fistula. Pancreas. 2014;43(3):462–4.
23. Morgan KA, Adams DB. Management of internal and external pancreatic fistulas. Surg Clin North Am. 2007;87(6):1503–13. x
24. Itoh S, et al. Assessment of the pancreatic and intrapancreatic bile ducts using 0.5-mm collimation and multiplanar reformatted images in multislice CT. Eur Radiol. 2003;13(2):277–85.
25. Drake LM, Anis M, Lawrence C. Accuracy of magnetic resonance cholangiopancreatography in identifying pancreatic duct disruption. J Clin Gastroenterol. 2012;46(8):696–9.
26. Soto JA, et al. Traumatic disruption of the pancreatic duct: diagnosis with MR pancreatography. AJR Am J Roentgenol. 2001;176(1):175–8.
27. Subramanian A, Dente CJ, Feliciano DV. The management of pancreatic trauma in the modern era. Surg Clin North Am. 2007;87(6):1515–32. x
28. Gillams AR, Kurzawinski T, Lees WR. Diagnosis of duct disruption and assessment of pancreatic leak with dynamic secretin-stimulated MR cholangiopancreatography. AJR Am J Roentgenol. 2006;186(2):499–506.
29. Telford JJ, et al. Pancreatic stent placement for duct disruption. Gastrointest Endosc. 2002;56(1):18–24.
30. Kim HS, et al. The role of endoscopic retrograde pancreatography in the treatment of traumatic pancreatic duct injury. Gastrointest Endosc. 2001;54(1):49–55.
31. Barish MA, Yucel EK, Ferrucci JT. Magnetic resonance cholangiopancreatography. N Engl J Med. 1999;341(4):258–64.
32. Freeman ML. Adverse outcomes of ERCP. Gastrointest Endosc. 2002;56(6 Suppl):S273–82.
33. Blero D, Deviere J. Endoscopic complications--avoidance and management. Nat Rev Gastroenterol Hepatol. 2012;9(3):162–72.
34. Takishima T, et al. Pancreatographic classification of pancreatic ductal injuries caused by blunt injury to the pancreas. J Trauma. 2000;48(4):745–51. discussion 751-2
35. Blatnik JA, Hardacre JM. Management of pancreatic fistulas. Surg Clin North Am. 2013;93(3):611–7.
36. Klek S, et al. Enteral and parenteral nutrition in the conservative treatment of pancreatic fistula: a randomized clinical trial. Gastroenterology. 2011;141(1):157–63. 163 e1.
37. Heyland DK, et al. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. JPEN J Parenter Enteral Nutr. 2003;27(5):355–73.
38. Ho KM, Dobb GJ, Webb SA. A comparison of early gastric and post-pyloric feeding in critically ill patients: a meta-analysis. Intensive Care Med. 2006;32(5):639–49.
39. Gans SL, et al. Systematic review and meta-analysis of somatostatin analogues for the treatment of pancreatic fistula. Br J Surg. 2012;99(6):754–60.
40. Gomez-Cerezo J, et al. Pancreatic ascites: study of therapeutic options by analysis of case reports and case series between the years 1975 and 2000. Am J Gastroenterol. 2003;98(3):568–77.
41. Li-Ling J, Irving M. Somatostatin and octreotide in the prevention of postoperative pancreatic complications and the treatment of enterocutaneous pancreatic fistulas: a systematic review of randomized controlled trials. Br J Surg. 2001;88(2):190–9.
42. Ridgeway MG, Stabile BE. Surgical management and treatment of pancreatic fistulas. Surg Clin North Am. 1996;76(5):1159–73.
43. Fazel A. Postoperative pancreatic leaks and fistulae: the role of the Endoscopist. Tech Gastrointest Endosc. 2006;8(2):92–8.
44. Saeed ZA, Ramirez FC, Hepps KS. Endoscopic stent placement for internal and external pancreatic fistulas. Gastroenterology. 1993;105(4):1213–7.
45. Baron TH. Endoscopic drainage of pancreatic fluid collections and pancreatic necrosis. Gastrointest Endosc Clin N Am. 2003;13(4):743–64.
46. Samuelson AL, Shah RJ. Endoscopic management of pancreatic pseudocysts. Gastroenterol Clin N Am. 2012;41(1):47–62.
47. Smith MT, et al. Alterations in pancreatic ductal morphology following polyethylene pancreatic stent therapy. Gastrointest Endosc. 1996;44(3):268–75.
48. Sherman S, et al. Stent-induced pancreatic ductal and parenchymal changes: correlation of endoscopic ultrasound with ERCP. Gastrointest Endosc. 1996;44(3):276–82.
49. Raju GS, et al. Effect of a novel pancreatic stent design on short-term pancreatic injury in a canine model. Endoscopy. 2006;38(3):260–5.
50. Bhasin DK, Rana SS. Biodegradable pancreatic stents: are they a disappearing wonder? Gastrointest Endosc. 2008;67(7):1113–6.
51. Bhasin DK, et al. Endoscopic transpapillary nasopancreatic drainage alone to treat pancreatic ascites and pleural effusion. J Gastroenterol Hepatol. 2006;21(6):1059–64.
52. Bracher GA, et al. Endoscopic pancreatic duct stenting to treat pancreatic ascites. Gastrointest Endosc. 1999;49(6):710–5.
53. Chebli JM, et al. Internal pancreatic fistulas: proposal of a management algorithm based on a case series analysis. J Clin Gastroenterol. 2004;38(9):795–800.
54. Pai CG, Suvarna D, Bhat G. Endoscopic treatment as first-line therapy for pancreatic ascites and pleural effusion. J Gastroenterol Hepatol. 2009;24(7):1198–202.
55. Cicek B, et al. Endoscopic treatment of pancreatic fistulas. Surg Endosc. 2006;20(11):1706–12.
56. Kozarek RA, Jiranek GC, Traverso LW. Endoscopic treatment of pancreatic ascites. Am J Surg. 1994;168(3):223–6.
57. Oh YS, et al. Pancreaticopleural fistula: report of two cases and review of the literature. Dig Dis Sci. 2006;51(1):1–6.
58. Safadi BY, Marks JM. Pancreatic-pleural fistula: the role of ERCP in diagnosis and treatment. Gastrointest Endosc. 2000;51(2):213–5.
59. Neher JR, et al. Pancreaticopleural fistula in chronic pancreatitis: resolution with endoscopic therapy. Gastrointest Endosc. 2000;52(3):416–8.
60. Materne R, et al. Pancreaticopleural fistula: diagnosis with magnetic resonance pancreatography. Chest. 2000;117(3):912–4.
61. Shah HK, et al. Pancreatico-pleural fistula. Endoscopy. 1998;30(3):314.
62. Garcia-Ricart F, et al. Endoscopic management of a persistent pancreatopleural fistula. Gastrointest Endosc. 1997;46(4):359–61.
63. Kozarek RA, et al. Transpapillary stenting for pancreaticocutaneous fistulas. J Gastrointest Surg. 1997;1(4):357–61.
64. Costamagna G, et al. Endoscopic treatment of postsurgical external pancreatic fistulas. Endoscopy. 2001;33(4):317–22.
65. Howard TJ, et al. Contemporary treatment strategies for external pancreatic fistulas. Surgery. 1998;124(4):627–32. discussion 632-3

66. Lipsett PA, Cameron JL. Internal pancreatic fistula. Am J Surg. 1992;163(2):216–20.
67. Boerma D, et al. Endoscopic stent placement for pancreaticocutaneous fistula after surgical drainage of the pancreas. Br J Surg. 2000;87(11):1506–9.
68. Abe N, et al. Preoperative endoscopic pancreatic stenting for prophylaxis of pancreatic fistula development after distal pancreatectomy. Am J Surg. 2006;191(2):198–200.
69. Frozanpor F, et al. The effect of prophylactic transpapillary pancreatic stent insertion on clinically significant leak rate following distal pancreatectomy: results of a prospective controlled clinical trial. Ann Surg. 2012;255(6):1032–6.
70. Rieder B, et al. Endoscopic pancreatic sphincterotomy and stenting for preoperative prophylaxis of pancreatic fistula after distal pancreatectomy. Gastrointest Endosc. 2010;72(3):536–42.
71. Kozarek RA. Pancreatic stents can induce ductal changes consistent with chronic pancreatitis. Gastrointest Endosc. 1990;36(2):93–5.
72. Sugiyama M, et al. Endoscopic pancreatic stent insertion for treatment of pseudocyst after distal pancreatectomy. Gastrointest Endosc. 2001;53(4):538–9.
73. Bhasin DK, et al. Management of multiple and large pancreatic pseudocysts by endoscopic transpapillary nasopancreatic drainage alone. Am J Gastroenterol. 2006;101(8):1780–6.
74. Bhasin DK, et al. Endoscopic management of pancreatic pseudocysts at atypical locations. Surg Endosc. 2010;24(5):1085–91.
75. Baron TH, et al. Outcome differences after endoscopic drainage of pancreatic necrosis, acute pancreatic pseudocysts, and chronic pancreatic pseudocysts. Gastrointest Endosc. 2002;56(1):7–17.
76. Nasr JY, Chennat J. Endoscopic ultrasonography–guided transmural drainage of pseudocysts. Tech Gastrointest Endosc. 2012;14(4):195–8.
77. Kahaleh M, et al. Endoscopic ultrasound drainage of pancreatic pseudocyst: a prospective comparison with conventional endoscopic drainage. Endoscopy. 2006;38(4):355–9.
78. Cahen D, et al. Endoscopic drainage of pancreatic pseudocysts: long-term outcome and procedural factors associated with safe and successful treatment. Endoscopy. 2005;37(10):977–83.
79. Devie're J, Bouchard S. Endoscopic treatment for complex biliary and pancreatic duct injuries. J Dig Endosc. 2014;5:2–12.
80. Deviere J, Antaki F. Disconnected pancreatic tail syndrome: a plea for multidisciplinarity. Gastrointest Endosc. 2008;67(4):680–2.
81. Arvanitakis M, et al. Pancreatic-fluid collections: a randomized controlled trial regarding stent removal after endoscopic transmural drainage. Gastrointest Endosc. 2007;65(4):609–19.
82. Hookey LC, et al. Endoscopic drainage of pancreatic-fluid collections in 116 patients: a comparison of etiologies, drainage techniques, and outcomes. Gastrointest Endosc. 2006;63(4):635–43.
83. Varadarajulu S, Wilcox CM. Endoscopic placement of permanent indwelling transmural stents in disconnected pancreatic duct syndrome: does benefit outweigh the risks? Gastrointest Endosc. 2011;74(6):1408–12.
84. Arvanitakis M, et al. Endoscopic therapy for main pancreatic-duct rupture after Silastic-ring vertical gastroplasty. Gastrointest Endosc. 2005;62(1):143–51.
85. Engler S, Dorlars D, Riemann JF. [Endoscopic fibrin gluing of a pancreatic duct fistula following acute pancreatitis] Endoskopische Fibrinverklebung einer Pankreasgangfistel nach akuter Pankreatitis. Dtsch Med Wochenschr. 1996;121(45):1396–400.
86. Seewald S, et al. Endoscopic sealing of pancreatic fistula by using N-butyl-2-cyanoacrylate. Gastrointest Endosc. 2004;59(4):463–70.
87. Fischer A, et al. Endoscopic management of pancreatic fistulas secondary to intraabdominal operation. Surg Endosc. 2004;18(4):706–8.
88. Mutignani M, et al. External pancreatic fistulas resistant to conventional endoscopic therapy: endoscopic closure with N-butyl-2-cyanoacrylate (Glubran 2). Endoscopy. 2004;36(8):738–42.
89. Irani S, et al. Resolving external pancreatic fistulas in patients with disconnected pancreatic duct syndrome: using rendezvous techniques to avoid surgery (with video). Gastrointest Endosc. 2012;76(3):586–93 e1-3.
90. Luthen R, Jaklin P, Cohnen M. Permanent closure of a pancreatic duct leak by endoscopic coiling. Endoscopy. 2007;39(Suppl 1):E21–2.
91. Gane E, Fata'ar S, Hamilton I. Management of a persistent pancreatic fistula secondary to a ruptured pseudocyst with endoscopic insertion of an expandable metal stent. Endoscopy. 1994;26(2):254–6.
92. Baron TH, Ferreira LE. Covered expandable metal stent placement for treatment of a refractory pancreatic duct leak. Gastrointest Endosc. 2007;66(6):1239–41.
93. Yamakado K, et al. Metallic stent placement in the pancreatic duct: an experimental study in the normal dog pancreas. J Vasc Interv Radiol. 2003;14(3):357–62.

Endoscopic Management of Pancreatic Pseudocysts

34

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Introduction

A pseudocyst is a persisting localized pancreatic or peripancreatic fluid collection that is generally rich in pancreatic enzymes. It is an encapsulated collection of fluid that lacks a true wall and is surrounded by a fibrous tissue wall without true epithelialization [10]. Pseudocysts are thought to form as a result of a leak from a disrupted pancreatic duct, or more commonly a side branch, and are frequently asymptomatic. They can be sequelae of severe acute pancreatitis or of chronic pancreatitis. Symptomatic pseudocysts can be managed endoscopically, radiologically, or surgically [9]. Pancreatic necrosis and cystic neoplasms can cause diagnostic dilemmas. This chapter focuses on the endoscopic management of pancreatic pseudocysts.

Incidence and Etiology of Pseudocysts

Pseudocysts occur after an acute attack of pancreatitis in approximately 10% of cases. The incidence of pseudocysts in the general population has been reported to be 0.5–1 per 100,000 adults per year [50]. In a study of 926 patients with non-alcoholic acute pancreatitis, 5% were noted to have pseudocyst formation 6 weeks after an acute attack of pancreatitis [32]. In their study, Kourtesis et al. [27] followed 128 consecutive patients with acute pancreatitis by computed tomography (CT) imaging, and 37% developed some type of acute fluid collection in the vicinity of pancreas. The majority of these acute fluid collections resolved spontaneously, and only 15 (12%) patients progressed to the development of symptomatic pseudocysts. Another study has reported a 7% overall incidence of pseudocysts as a complication of acute pancreatitis [22]. Although often radiologists and physicians loosely use the term, "pseudocyst," for anything remotely cystic associated with pancreatitis, the revised Atlanta classification system [6] categorizes fluid collections under 4 weeks old, without solid material, as "acute pancreatic fluid collections" (PFC); these have no necrosis and are without a well-defined wall. After 4 weeks, if PFCs have not resolved, and when these generally develop a wall, assuming they demonstrate no/minimal necrotic material (i.e., generally under 30% solid), they are then referred to as "pseudocysts." In contrast, collections more than 4 weeks old that contain a significant amount of solid or semisolid necrotic material, with or without liquid, are termed, "walled-off necrosis (WON)."

Although there is a lack of precise long-term data on the incidence of pseudocyst development in patients with chronic pancreatitis, it has been reported that around 30–40% patients with chronic pancreatitis develop pseudocysts in their lifetime [9].

Pseudocysts have been reported more commonly after alcohol-induced than after non-alcohol-related pancreatitis [39]. In a study of 357 patients with pancreatic pseudocysts, alcohol was reported to be a causative factor in 251 cases (70%), biliary tract disease in 28 (8%), blunt or penetrating abdominal trauma in 21 (6%), operative trauma in one case (0.3%), and idiopathic in 56 (16%) [51].

Practical Considerations

- Majority of the acute fluid collections resolve spontaneously, and only 7–12% patients progress to symptomatic pseudocysts.

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Pathogenesis and Classification

Pseudocysts are generally formed due to rupture of the pancreatic duct or one of its side branches either by trauma or pancreatitis. This leads to extravasation of pancreatic juice that results in an acute fluid collection. Peripancreatic fluid can also sometimes form from edema, but usually does not result in an actual pseudocyst. Most patients with pseudocysts have demonstrable connections between the cyst and the main pancreatic duct or the side branch, but some lose their connection as the fibrosis walls off the area. Although necrosis is sometimes associated with these severe cases of pancreatitis, pseudocysts can occur without pancreatic necrosis; again, the pseudocysts themselves should have no substantial necrosis within the collection.

Liquified necrosis (postnecrotic pancreatic fluid collection, PNPFC) can mimic a pseudocyst, but generally is associated with a different natural history, different risk of infection, and different approach to management. They are usually not truly fluid-filled, but often have solid components and a semisolid gelatinous makeup that sometimes mimics fluid on imaging, especially CT (computed tomography) (Figs. 34.1 and 34.2). PNPFCs can persist beyond a month and evolve into "walled-off necrosis" (WON), which can be confused with a pseudocyst. T2-weighted MRI (magnetic resonance imaging) and ultrasound (US) are modalities that are better at differentiating solid from liquid contents.

In a patient with chronic pancreatitis, most often due to alcohol abuse, pseudocyst formation can occur by acute exacerbation of underlying disease (with the same mechanism as above) or by progressive ductal obstruction due to either downstream ductal stricturing or intraductal stone or protein plug formation. This prevents drainage of pancreatic juices into the small bowel. Elevation in upstream intraductal pressure predisposes to ductal leakage, with accumulation of peripancreatic fluid.

As mentioned above, many patients develop some type of acute pancreatic fluid collection (PFC) after acute pancreatitis, but this fluid collection is termed a pseudocyst only if it persists beyond 4–6 weeks and is surrounded by a fibrous tissue without true epithelialization [10, 39] and has no significant solid component. Pseudocysts can be sterile or infected; spontaneous infection of pseudocysts is rare and, when it occurs, is generally either due to contamination by an intervention or seeding from bacterial translocation or other causes of bacteremia. Spontaneous infection is even more rare for acute fluid collections not contaminated by intervention.

Pseudocysts were initially classified by D'Egidio and Schein [16] in 1991. They described three types of pseudocysts based on pancreatic duct anatomy, presence of communication between the cyst and the pancreatic duct, and underlying etiology of pancreatitis (acute or chronic). Type 1 was described as one that follows an acute attack of

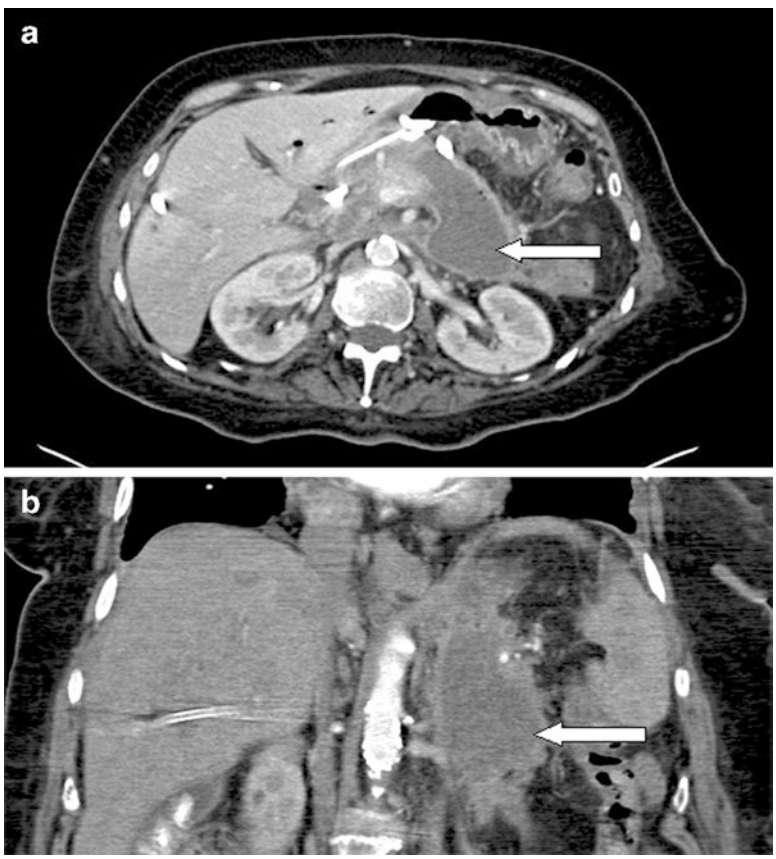

Fig. 34.1 CT images after endoscopic cystogastrostomy appearing to demonstrate a new or persisting collection (*arrow*) near a drained cyst. This hypodense lesion appeared to be fluid-filled on CT, surrounded by a brighter hyperdense capsule, and was reported as a "pseudocyst." It was subsequently shown by MRI to be solid/semisolid walled-off necrosis (*WON*). (**a**) Axial image. (**b**) Coronal image

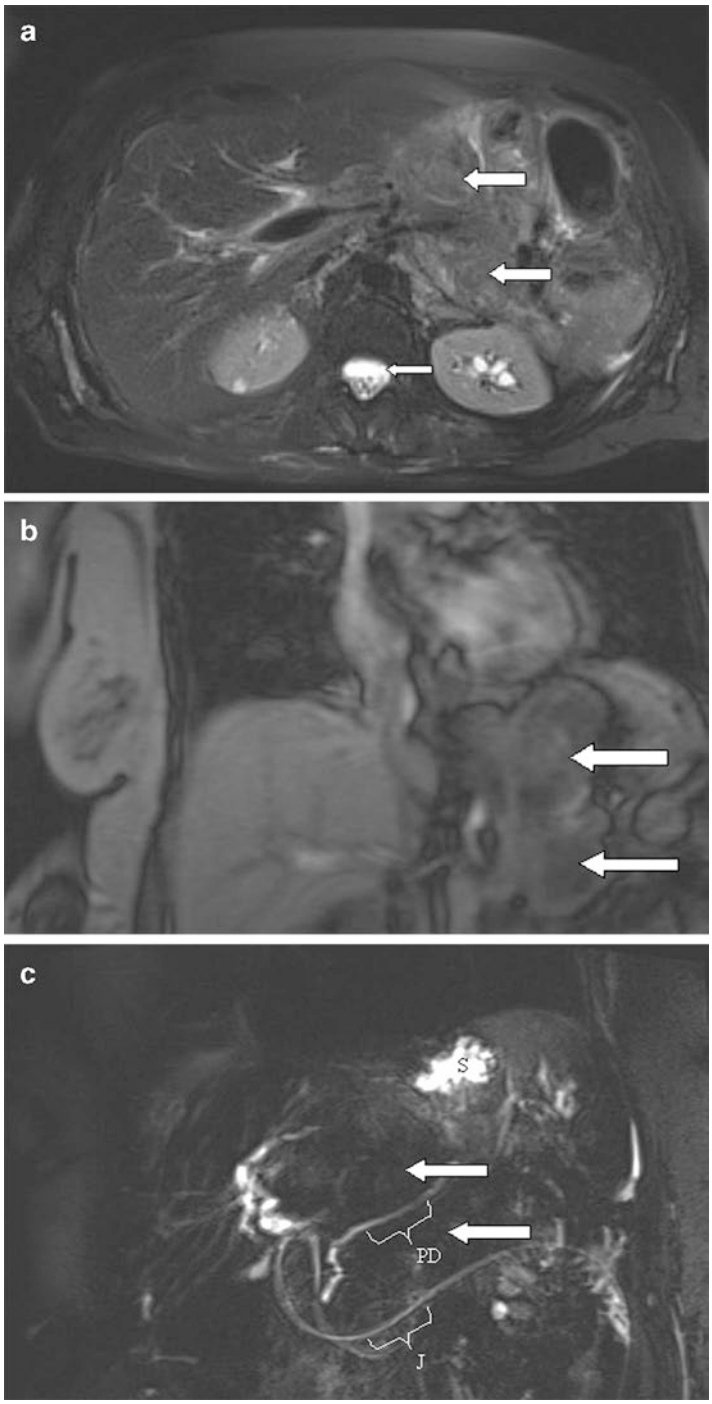

Fig. 34.2 T2-weighted MRI images in which stagnant fluids such as ductal or luminal fluid and cerebral spinal fluid (*small arrow*) appear white (high signal) showing that the "cyst" in Fig. 34.1 was not fluid-filled, but rather solid/semisolid pancreatic necrosis (mildly low signal) (*large arrows*). The heavily T2-weighted MRCP shows bright fluid in the stomach (*S*), and in the pancreatic duct (*PD*), but no bright fluid at all around the pancreas. A jejunal tube is also seen (*J*). (**a**) Axial image. (**b**) Coronal image. (**c**) MRCP image

pancreatitis and has normal duct anatomy and only rarely communicates with the pancreatic duct. Type 2 pseudocysts follow an episode of acute-on-chronic pancreatitis and often have duct-pseudocyst communication with a diseased pancreatic duct, but the duct is not strictured. Type 3 cysts, referred to as "retention" pseudocysts, occur as a result of chronic pancreatitis and are uniformly associated with duct stricture/obstruction and pseudocyst to duct communication. This classification has variable use in current practice.

To help guide decisions regarding surgical vs. non-surgical therapy, Nealon and Walser [36] classified pseudocysts based entirely on pancreatic duct anatomy. They described seven types of pseudocysts: type 1 has normal main duct with no communication with the cyst. Type 2 also has a normal main duct, but with duct-cyst communication. Type 3 has an otherwise normal main duct, but with stricture(s) and no duct-cyst communication. Type 4 has an otherwise normal main duct, with stricture(s) and duct-cyst

communication. Type 5 has a complete cutoff duct, with a duct that is otherwise normal, with no communication with the cyst. Type 6 occurs in chronic pancreatitis (abnormal pancreatic duct), but has no duct-cyst communication. Type 7 occurs in the presence of chronic pancreatitis (abnormal pancreatic duct) and has duct-cyst communication. Ductal communication, a critical part of this classification, may be difficult to discern with noninvasive imaging, but dynamic secretin-stimulated MRCP (magnetic resonance cholangiopancreatography) and EUS (endoscopic ultrasound) are promising. It is seldom necessary to use invasive and high-risk studies such as endoscopic retrograde cholangiopancreatography (ERCP) for this purpose.

Clinical Presentation and Diagnosis

A careful history regarding the duration of the cyst, whether pancreatitis was present and whether an etiology of the pancreatitis is known, and whether other suspicious symptoms are present (that might suggest this could be a cystic neoplasm) are very important factors to decide the best management.

History, Physical Examination, and Laboratory Evaluations: Narrowing the Differential

Pseudocysts can present with a wide range of clinical problems depending upon the location and size of the fluid collection and the presence of infection. Patients with pseudocysts may be completely asymptomatic; or they can present with abdominal pain, anorexia and/or nausea and/or weight loss, abdominal mass effect from a large cyst pressing on the gastric outlet leading to persistent nausea/vomiting and gastric outlet obstruction, compression of the splenic vein with splenomegaly and left upper quadrant pain, or jaundice due to compression of the bile duct. The weight loss that can result from nausea and pain can be confusing regarding the differential diagnosis of a cystic tumor. Patients also can present with other complications of pseudocysts, such as infection, bleeding into the cyst or splenic artery pseudoaneurysm, rupture of the cyst, or thrombosis of the splenic or portal vein with bleeding or non-bleeding gastric varices [19]. Serum laboratory tests have limited utility, and results depend on the clinical presentation and etiology of underlying pancreatitis. By the time a pseudocyst is found, serum pancreatic enzymes from the acute pancreatitis have usually returned to normal or near-normal. A white blood count may alert one to the possibility of infection, although persistent minor elevations in the white count are common and can be due to coexisting smoldering pancreatitis.

Pseudocysts are usually identified by cross-sectional imaging studies, such as CT done for an evaluation of the severity of an attack of pancreatitis or for persistent symptoms like fever, vomiting, or abdominal pain, after an attack. Once a pancreatic cyst is identified by an imaging modality, the most important point is to differentiate pseudocysts from necrosis and from cystic neoplasms of the pancreas not related to pancreatitis (the most common cyst in patients without pancreatitis), and this could pose a difficult diagnostic and therapeutic dilemma for clinicians.

Unlike in other abdominal organs, most incidental cysts in the pancreas that are not pseudocysts are in fact cystic neoplasms, some of which have malignant potential (Fig. 34.3).

Practical Considerations

- Postnecrotic pancreatic fluid collection (PNPFC) is generally associated with a different natural history, different risk of infection, and different approach to management.
- Pseudocysts can be sterile or infected; spontaneous infection of pseudocysts is rare, and when it occurs, is generally either due to contamination by an intervention or seeding from bacterial translocation or other causes of bacteremia.

True "simple cysts" or congenital cysts of the pancreas are thought to be rare. It is crucial to differentiate pseudocysts from necrosis and other cystic lesions as management varies by the type of cystic lesion. History is often the most helpful element to help differentiate these lesions. Pancreatic fluid collections, pseudocysts (and PNPFCs or WON), usually follow an acute attack of pancreatitis, can present at any age, and can be located anywhere in the pancreas or its vicinity (although the tail and the neck are common areas of duct disruption). When they occur in the setting of chronic pancreatitis, there is often a history of heavy alcohol and smoking intake in the present or past, since alcohol and smoking are the etiology of the majority of non-genetic chronic pancreatitis cases. Abdominal trauma and family history can be other clues. If the pancreatitis appears otherwise idiopathic, one must consider the possibility that the cyst was present prior to the pancreatitis and that the pancreatitis occurred secondary to the cyst, rather than the cyst being due to pancreatitis; cystic tumors, especially ones that produce mucin which may obstruct the duct, can cause pancreatitis.

Practical Considerations

- Pseudocysts can present with a wide range of clinical problems depending upon the location and size of the fluid collection and the presence of infection.

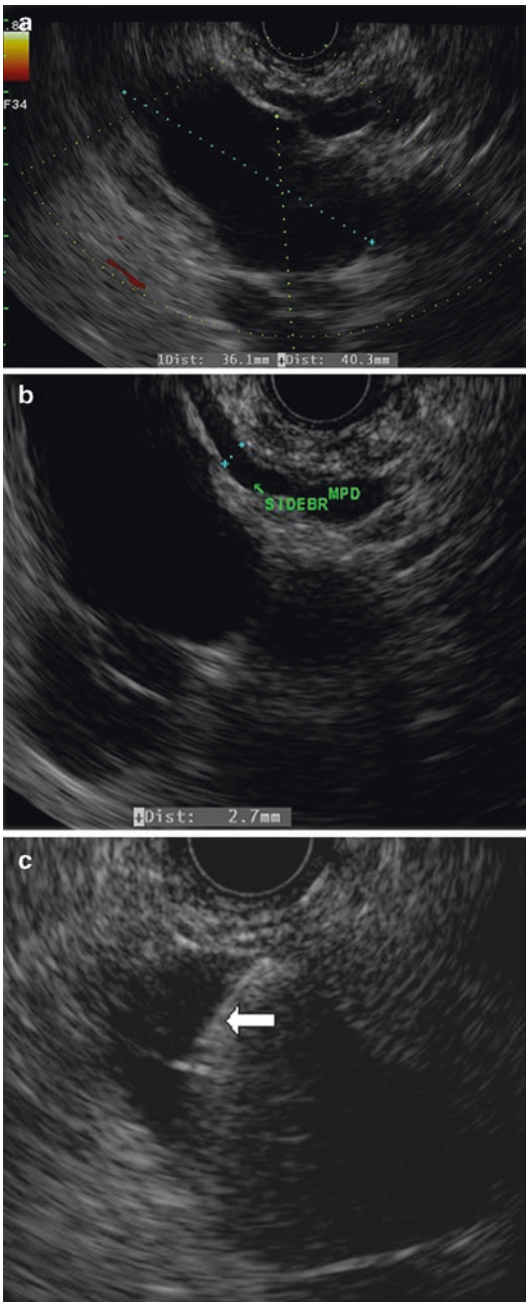

Fig. 34.3 Linear EUS of a slowly enlarging 3–4 cm Doppler-negative anechoic (cystic) lesion in the head of the pancreas in a middle-aged man without a history of pancreatitis. (**a**) A thin-walled cyst is seen with a dilated side branch (*SIDEBR*) from the main pancreatic duct (*MPD*) filling the cyst. (**b**) The lobular/tubular cyst morphology is consistent with a cluster of dilated side branches. (**c**) FNA with a 19 G needle (*arrow*) removed thick mucin consistent with a side branch variant IPMN. An intracystic brushing was obtained through the needle, but both fluid and brushing were acellular

Imaging Studies and Possible Fluid Sampling

Different imaging modalities can be used to evaluate pseudocysts of the pancreas. The imaging studies could include US, CT, MRI, ERCP, and EUS. Ultrasound (transabdominal conventional US or EUS) and T2-weighted MRI (with or without T2-weighted MRCP sequences) are the best modalities for confirming or refuting solid components and necrosis mimicking a pseudocyst (Fig. 34.2). Both modalities are superior to CT in distinguishing solid material from fluid. CT can often misclassify necrosis, or sometimes even a solid mass, as a pseudocyst, because the Hounsfield units of murky fluid and solid material can overlap (Fig. 34.1). CT is generally insufficient, on its own, to proceed with management. Lastly, fine needle aspiration (FNA) by CT or EUS is available for equivocal lesions, but should be avoided in classical pseudocysts to avoid the risk of infection, unless therapeutic drainage is also planned; most classic pseudocysts do not need diagnostic aspiration.

Conventional Abdominal Ultrasound

On US, pseudocysts appear as an anechoic (black), round or oval, relatively smooth-walled, and well-defined structure (although some internal irregularity of the wall is common). Conventional US has certain limitations, especially when examining a relatively small lesion in the retroperitoneum, behind the stomach, especially in the presence of overlying bowel gas (ileus and gastric obstruction or distension often accompanies the acute pancreatitis), and is operator dependent [39]. The patient is often in significant pain, and because of this, the ability to press with the probe deeply on the abdomen, or roll the patient to get different views, may be limited. Generally, the sensitivity of US for the detection of moderate-sized pancreatic pseudocysts ranges from 75% to 90%, which is generally inferior to CT (sensitivity >90%). Again, US is one of the best modalities for distinguishing solid from liquid, and so significant solid debris within the cystic lesion generally implies necrosis (or more rarely, neoplasia). At the same time, US can also reliably detect cholelithiasis (arguably the best test for this) and biliary dilation. Again, this exam can be limited when the patient is in considerable pain or is distended.

CT, MRI, and ERCP

CT and MRI are very sensitive diagnostic modalities for pancreatic pseudocysts. In a patient with recent history suggestive of pancreatitis, finding a round, thick-walled, fluid-filled structure in the vicinity of pancreas is very suggestive of a pseudocyst. The major limitations of CT are its poor ability to distinguish fluid from necrosis, its inability to differentiate pseudocysts from cystic neoplasm of the pancreas, and the risks of intravenous contrast [44]. It is also poor at assessing ductal communication and pancreatic strictures or irregularity that may point to a diagnosis of chronic pancreatitis and help with treatment planning. Although not as good as EUS, it has reasonable sensitivity for pancreatic calcifications.

MRI/MRCP is superior to CT in depicting debris within pseudocysts and differentiating cysts from solid lesions (Figs. 34.1 and 34.2). Also, it can give detailed imaging of

the pancreatic duct and bile duct. MRCP has some other advantages over CT including its superiority to detect choledocholithiasis [41], strictures, bleeding within the pseudocyst, and assessing duct to cyst communication (especially when secretin is given to stimulate pancreatic juice flow).

ERCP is not required to diagnose the pseudocyst, but it definitely has a role in the endoscopic therapy of the pseudocysts as described in the treatment section. Because of its risk of post-procedural pancreatitis, or worsening of existing pancreatitis, and the risk of contaminating the cyst with dye, which can lead to infection, ERCP is best avoided unless pancreatic ductal therapy is planned, temporary stenting of an externally compressed and obstructed biliary tree is needed, or removal of bile duct stones (that may have led to the attack of pancreatitis) is needed.

EUS and Possible Fine Needle Aspiration with Fluid Analysis

EUS is generally not the initial test used to diagnose pancreatic pseudocysts, but has a great role in further evaluation of cystic lesions diagnosed by other imaging modalities. It is arguably the imaging modality of choice to distinguish pseudocyst from other pancreatic cystic lesions in the equivocal scenarios described above. Again, EUS is one of the best imaging modalities to distinguish solid from liquid, to rule out significant debris/necrosis. It is also excellent at excluding an adjacent mass if there are suspicious symptoms such as weight loss. With EUS, very high-resolution images of the pancreas can be obtained due to the proximity of the pancreas to the stomach and duodenum; this proximity avoids intervening air and allows the use of higher-frequency high-resolution probes as compared with conventional US (because shallower depths of penetration are needed). This results in superior and probably unmatched ductal and parenchymal imaging.

EUS can be especially helpful when the cystic lesion is thought to possibly represent a cystic neoplasm, for example, cases wherein the cyst may have preceded the pancreatitis, cases involving elderly patients or unexplained pancreatitis, cases with constitutional symptoms such as weight loss, and cases without a clear history of pancreatitis. EUS can look at cyst morphology and duct communication and is very sensitive for picking up underlying chronic pancreatitis in those without a clear pancreatitis history.

A principal advantage of EUS as compared to MRI or CT is its capability of adding real-time EUS-guided FNA. In cases with an atypical imaging appearance, cases involving a cyst without a clear attack of pancreatitis, or cysts associated with a solid mass, EUS-guided fine needle aspiration (of the cyst or mass) may be needed. In contrast, if the cystic lesion has a pseudocyst-like morphology on EUS and is in the setting of explained (e.g., alcoholic) pancreatitis, FNA is not generally needed and should be avoided to reduce the risk of infection.

Cyst morphology and fluid analysis (amylase/lipase, mucin, carcinoembryonic antigen [CEA], and cytology) are used to further clarify cystic lesions that are equivocal. Fluid analysis of pseudocysts classically shows low CEA levels (although there is marked overlap with neoplasia) [13, 46], high amylase (signifying ductal communication) and inflammatory cells on cytology, and little to no mucin. Serous cystadenomas are most commonly seen in elderly women and make up 32–39% of all pancreatic cystic neoplasms [12]. On EUS, these cysts appear to have a cluster of microcysts, sometimes adjacent to a larger cyst, and often have central hyperechoic scar. Fluid analysis from these type of cysts classically shows no mucin, low amylase (no duct communication), very low CEA levels, and classically, monomorphic cuboidal cells on cytology (although the fluid is unfortunately often acellular). Cysts with malignant potential include intraductal papillary mucinous neoplasms (IPMN) and mucinous cyst neoplasms. The accuracy of EUS and MRCP for identifying small side branch IPMNs solely on morphology is improving. EUS-guided FNA and fluid analysis, when needed, show high CEA (>192 ng/mL), mucin, and high amylase/lipase levels (as they generally communicate with the main duct); cytological analysis is usually acellular or negative, but may be positive if malignant [13]. Mucinous cystadenomas are most commonly seen in middle-aged women and typically have macrocysts (>2 cm), are often unilocular, and generally have no communication with the pancreatic duct. Features suggestive of malignant transformation are thickened septations, thickened or irregular cyst walls, and the presence of mural nodules or mass; size and/or growth are associated with malignant potential. Fluid analysis shows high CEA, mucin, and low amylase levels; cytologic analysis may have atypical or neoplastic cells, but, again, is often negative or acellular.

The safety of EUS-guided FNA of cysts is well-established when the cyst is accessed with a single puncture and is drained dry. The risk of pancreatitis after EUS-guided FNA is only 2–3%, with the risk of infection less than 1% and intracystic hemorrhage less than 1% [23, 31]. To decrease the risk of infection, intra-procedural antibiotics are administered before or during the procedure and then often followed by antibiotics by mouth for 3–5 days post-procedure. The risk is likely higher if drainage is incomplete (more common in large cysts with thick fluid) or if debris or necrosis is present. Therefore, very large cysts, especially ones with debris, should generally not be aspirated for diagnosis unless the need for diagnostic sampling is justified, and ideally, a drain can also be placed simultaneously.

Practical Considerations

- Conventional ultrasound is one of the best modalities for distinguishing solid from liquid, and so significant solid debris within the cystic lesion generally implies necrosis (or more rarely, neoplasia).
- The major limitations of CT are its poor ability to distinguish fluid from necrosis, its inability to differentiate pseudocysts from cystic neoplasm of the pancreas, and the risks of intravenous contrast.
- MRI/MRCP is superior to CT in depicting debris within pseudocysts and differentiating cysts from solid lesions.
- EUS is generally not the initial test used to diagnose pancreatic pseudocysts.
- EUS is one of the best imaging modalities to distinguish solid from liquid, to rule out significant debris/necrosis and at excluding an adjacent mass, and to obtain FNA.

Treatment of Pancreatic Pseudocysts

Preprocedural Assessment

Most acute PFCs and pseudocysts resolve with supportive medical care that includes intravenous fluids as needed, analgesics and antiemetics. For patients who can tolerate oral intake, a low-fat diet is suggested at least in the short-term. Pancreatic non-enteric coated enzyme capsules (30–50,000 lipase units per meal) that release enzymes in the proximal small bowel and stimulant negative feedback to the pancreas are likely helpful in some patients, although the literature to support this is admittedly weak [11]. Octreotide is used very rarely to decrease pancreatic secretions in refractory ongoing leaks. For patients who cannot tolerate oral intake, nutrition can be provided via nasojejunal feeding or a percutaneous (direct or via a percutaneous gastrostomy) J-tube, for 4–8 weeks; total parenteral nutrition (TPN) is an option, but is a far inferior way of feeding due to higher rates of adverse metabolic and infectious events seen in randomized trials [1, 20, 25, 34, 53].

It is important to make sure that the cyst has "matured" from a PFC to a pseudocyst, with a well-developed wall, which generally takes at least 4 weeks. Interventional therapies, especially endoscopic ones, have better results, and fewer complications, when this is the case. In addition, it is important to allow sufficient time for the cyst to have a chance to spontaneously resolve, as most do. Before contemplating therapy, the pseudocyst should be associated with persisting symptoms. Although size does not matter, generally cysts under 4 cm in size do not cause significant symptoms (i.e., one should consider the possibility that any ongoing pain may be more likely due to ongoing/smoldering pancreatitis). An exception to this includes cysts in the head, where biliary or duodenal compression can occur with smaller diameter cysts. Nevertheless, placing a pigtail drain, by any means, into a cyst that is under 3–4 cm in size is technically difficult and often not feasible.

For cysts that do not resolve spontaneously with supportive medical management and become symptomatic or lead to development of a complication (gastric outlet obstruction, infection of the cyst, biliary obstruction), some type of drainage procedure will be required. The options for drainage include surgical, percutaneous, or endoscopic techniques. Before attempting any type of drainage, there are a few critical issues that need to be addressed.

First of all, it is important to consider alternative diagnoses (especially if there is no history of pancreatitis, idiopathic pancreatitis, etc.), especially a cystic neoplasm, as discussed above. Placing a transcutaneous or transluminal drain into a cystic neoplasm needs to be avoided, as it delays the neoplastic diagnosis and may seed the peritoneum with neoplastic fluid.

It is also important to distinguish pseudocyst from WON. In the latter, although treatment is similar to pseudocysts when asymptomatic or resolving, and not infected, conservative treatment is generally preferred given that treating WON with debridement or necrosectomy is more difficult than simply draining a pseudocyst. If complications occur, such as infection, then intervention is needed. Surgical treatment has been generally preferred for WON over transcutaneous or endoscopic drainage and debridement/lavage. However, in experienced hands, endoscopic drainage with endoscopic intracystic debridement (endoscopic necrosectomy) can be considered, selectively, especially in patients who are poor surgical candidates. The response rate is expected to be lower than in patients with sterile pseudocysts, and the adverse event rates are higher [8, 21]. However, recent data on endoscopic necrosectomy is encouraging, and the endoscopic approach may be comparable to minimally invasive surgical necrosectomy in terms of outcomes and cost [26].

It is important to exclude a pseudoaneurysm (usually of the splenic artery running near the cyst or in the cyst wall) which occurs in approximately 10% of patients with a pseudocyst [17, 40]. The presence of a pseudoaneurysm is suggested by unexplained gastrointestinal bleeding, sudden expansion of a pseudocyst, or an obscure drop in hematocrit. Severe and even fatal hemorrhage can occur following endoscopic drainage in patients with an unsuspected pseudoaneurysm. CT or MRI before drainage should help rule out a pseudoaneurysm, and if a suspicion is raised, angiography should be undertaken first. Without preprocedural arterial embolization, a pseudoaneurysm is a contraindication to

transluminal drainage. In a study of 57 patients considered for endoscopic drainage of pancreatic pseudocysts, pseudoaneurysms were detected in five patients prior to the drainage procedure. These patients were treated with a multidisciplinary approach, including embolization or resection [33].

Surgical Drainage

Surgery is usually definitive, but is not generally first-line treatment. It could be done either open or in selected experienced centers, laparoscopically; open surgery carries a significant risk of morbidity and mortality (25% and 5%, respectively). Surgical treatment of pseudocysts can be accomplished by providing a communication between the pseudocyst cavity and the stomach or small bowel; or surgical treatment can involve resecting it entirely, often including the part of the pancreas that is leaking into it. In centers with the appropriate expertise, endoscopic management of pancreatic pseudocysts is often considered first, and surgical drainage is reserved for those patients not meeting criteria for endoscopic drainage, those who fail endoscopic management or have recurrence following successful endoscopic drainage, those that have a disconnected duct or tight downstream stricture that cannot be traversed with a stent, or those that have equivocal lesions (i.e., resection of a possible cystic tumor). In a retrospective study [2] of 94 patients in which 42 patients underwent internal surgical drainage and 52 patients underwent percutaneous pseudocyst drainage, seven were surgically managed patients, and four percutaneously treated patients had complications (16.7% vs 7.7%). A significantly higher mortality rate was associated with surgical therapy (7.1%) than with percutaneous therapy (0%) ($P < 0.05$). However, subsequent operation was required in 19.2% of the percutaneous drainage group compared with only 9.5% of the surgical group ($P > 0.05$).

Percutaneous Drainage

In this procedure, an external drainage is obtained by placement of drainage catheter percutaneously into the fluid cavity; this is not always feasible anatomically, especially in the head of pancreas. US or CT is used to guide the catheter placement; symptomatic pseudocysts that may not be accessible endoscopically can be handled this way in many cases. Catheter drainage is continued until the flow rate falls to 5–10 mL/day. The mean duration of drainage can be up to 6 weeks; longer durations of indwelling catheters can lead to pancreaticocutaneous fistula. This technique, though usually successful, carries a high risk of infection; in one series, it was reported to occur in 48% of the patients [2]. It can also be associated with significant patient discomfort, and the catheter can clog and may require repositioning and exchange. Percutaneous drainage is more likely to be successful in patients with normal pancreatic ducts without downstream stricture and no communication between the duct and the cyst. It should not generally be performed in patients with cysts containing bloody or solid material, unless dilation of the tract and insertion of larger bore catheters, with or without continuous irrigation, are planned. It is sometimes used preoperatively in some patients who are clearly going to need surgical resection for some reason, to make surgery technically easier.

Practical Considerations

- It is important to make sure that the cyst has "matured" from a PFC to a pseudocyst, which generally takes at least 4 weeks.
- For cysts that do not resolve spontaneously with supportive medical management and become symptomatic require some type of drainage procedure.

Although clearly second line for mature pseudocysts, percutaneous drainage is a helpful option for less well-defined early acute pancreatic fluid collections (PFCs) that are very symptomatic and cannot wait until they resolve or mature. Because they are not mature enough to be called pseudocysts, they may not be appropriate for endoscopic transluminal drainage, and large ones may not be anticipated to resolve with transpapillary drainage alone (>3–4 cm). In these cases, the drain is usually placed, and often, an ERCP is then performed to rule out downstream ductal pathology, bridge any disruption, and place a transpapillary pancreatic stent if ductal communication with the PFC is present. If the stent encourages transpapillary drainage, the drainage through the percutaneous catheter should quickly slow down, allowing the percutaneous catheter to be removed within days or weeks. Again, complete disruptions, or percutaneous drains that persistently drain over the coming weeks despite the above, should be referred for surgery, to avoid a long-term drain that may lead to a fistula.

Endoscopic Drainage

Pseudocysts can be managed endoscopically with transluminal drainage (cystogastrostomy, cystoduodenostomy) or by facilitating transpapillary drainage with a stent and/or pancreatic sphincterotomy. Endoscopic transluminal drainage is considered to be a preferred therapeutic approach for qualifying mature pseudocysts as it is less invasive, avoids the

need to care for an external drain, and also has a high long-term success rate.

In patients with relatively small pseudocysts (less than 4–6 cm) communicating with the main pancreatic duct, transpapillary drainage with a temporary pancreatic stent may be tried as initial therapy, with or without a pancreatic sphincterotomy. A transluminal (transgastric or transduodenal) drainage approach is used in larger, well-circumscribed, mature, and symptomatic pseudocysts directly adjacent to the gastroduodenal wall (usually less than 1 cm separation between gastric and cyst lumens), without contraindications. Cross-sectional imaging helps assess the pseudocyst relationship to the gastrointestinal luminal wall. An immature pseudocyst wall is usually thin and poorly adherent to the gastrointestinal lumen; this may increase the risk of free perforation with endoscopic intervention. Endoscopic drainage should be delayed in such cases when possible.

Efficacy and Cost-Effectiveness of Endoscopic Management

The landmark success of endoscopic transmural pseudocyst drainage in the setting of chronic pancreatitis was reported in 1989 [15]. The technical success rate of the drainage procedure has since been reported to be up to 97%, with definitive resolution in more than 80% [14]. In cases of pancreatic necrosis and solid debris (what we now call WON), the success rate is significantly lower and is close to 60%. However, as mentioned above, in patients who are not good surgical candidates, endoscopic drainage and debridement can be considered [8, 21, 29]. One must be aware that for this WON indication, several procedures are often needed, usually as an inpatient, and often with an endoscopically placed nasocystic irrigation catheter (or with combined technique of endoscopic and percutaneous drainage catheter), to allow flushing out of the cyst contents between procedures.

Single stents through a small cystogastrostomy often result in inadequate drainage, leading to infection and a poor outcome. Failure can also occur due to untreated underlying downstream pancreatic ductal obstruction, unexpected necrotic debris that may otherwise have needed extensive endoscopic necrosectomy and lavage, and/or due to unexpected septations that do not allow drainage of some parts of the cyst.

Vilmann et al. [49] and Giovannini et al. [18] first described the single step EUS-guided cystogastrostomy in 1998. However, the routine use of EUS to guide endoscopic transmural drainage for bulging (Fig. 34.4) pseudocysts remains controversial. Although a randomized trial did not show a difference in success rates or complication rates [24], a meta-analysis [37] has concluded that EUS-guidance, on average, results in higher procedural technical success. In particular, it is required in cases of non-bulging pseudocysts; as such, EUS is often required for the cysts that are located in the tail, which often do not cause endoscopically visible luminal compression [43, 48]. These tail cysts are usually drained through the proximal stomach, and EUS guidance helps in this location in the avoidance of the nearby spleen, splenic vessels and collaterals or varices, and diaphragm. In addition, as mentioned previously, EUS is also helpful as a second opinion prior to drainage in detecting unexpected solid debris, assessing the distance between the gastrointestinal lumen and the pseudocyst lumen in determining the maturity of the pseudocyst wall. MR can perform most of these functions very well, however, except perhaps the ruling out of small intramural vessels, and is more widely available. When the cyst is very large (>6–8 cm), MR is also arguably more likely to be effective at assessing cyst contents and its relationship to other structures, as the back wall of the cyst will usually be too far away to be seen well with EUS. In large cysts, cross-sectional imaging and EUS are often complementary.

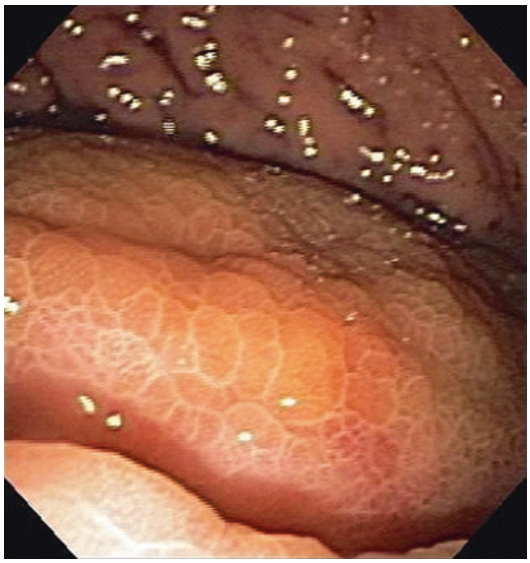

Fig. 34.4 An endoscopic view demonstrating a bulge in the body of the stomach from a compressing pseudocyst, with overlying congested mucosa

Practical Considerations

- Surgical drainage is usually definitive, but is not generally the first-line treatment. It carries a significant risk of morbidity and mortality.
- Percutaneous drainage is usually successful, carries a high risk of infection.
- Endoscopic transluminal drainage is considered to be a preferred therapeutic approach for qualifying mature pseudocysts as it is less invasive, avoids the need to care for an external drain, and also has a high long-term success rate.

A retrospective study compared EUS-guided cystogastrostomy with surgery in patients with uncomplicated pancreatic pseudocysts [47]. No significant differences were found in rates of treatment success (100% vs 95%, $p = 0.36$), procedural complications (none in either cohort), or reinterventions (10% vs 0%, $p = 0.13$) between surgery and EUS-guided cystogastrostomy. The post-procedure hospital stay for EUS-guided cystogastrostomy was significantly shorter than for surgical cystogastrostomy (mean of 2.65 vs 6.5 days, $p = 0.008$). The average direct cost per case for EUS-guided cystogastrostomy was significantly less than surgical cystogastrostomy ($9077 vs $14,815, $P = 0.01$; cost savings of $5738 per patient). In another more recent study of 122 patients who underwent EUS-guided drainage by using plastic stents, the overall treatment success was 94.3%. Most patients (83.6%) required only one intervention, while 10.7% required more than one intervention, and 5.7% failed treatment [5].

Technique of Cystogastrostomy/Duodenostomy

The endoscope (by visual bulge – Fig. 34.4) or EUS scope (by ultrasound image) is used to detect an optimal site of puncture of pseudocyst via the gastric or duodenal wall. EUS and color Doppler can be used to identify a vessel-free site for the puncture; alternatively, a miniprobe can be used to confirm that a borderline endoscopic bulge actually corresponds to an underlying cyst. The puncture is then made with either a large-caliber EUS needle (which ideally can accommodate a guide wire) or a fine sclerotherapy needle; a cystogram is performed under fluoroscopy. In the case of EUS guidance, a cystogram may not be necessary, but practically, even a faint cystogram can help anticipate the size and location of the wire loop on fluoroscopy (to make sure the wire is staying within cyst lumen). If a 19 G needle has been used, a wire (0.025- or 0.035-in. by 450-cm) can be passed through the needle and into the cyst. A 22G needle can also be used; however, it only accommodates a 0.017 or 0.021 in. wire. Wires can shear on the needle's sharp bevel while it is withdrawn, so they should be withdrawn with great care. This risk can also be lowered through the use of a blunt-ended trocar-style needle which has a sharp stylet that is removed after the puncture and before the wire insertion (EchoTip Access needle; Cook Medical Bloomington, IN). Lastly, a needle-knife sphincterotome or a 10F cystotome (6F cystotome not available in USA) (Fig. 34.5) can be used to burn a hole through the gastric wall and into the cyst cavity using the same site through which the transgastric cystography was performed, followed by a wire through the catheter. A large gauge (0.035″ or a 0.025″) guide wire is generally chosen as it provides more stability for accessories exchanges, and a generous amount of wire is generally curled up a few times in the cyst cavity under fluoroscopic guidance.

After wire access is achieved (Fig. 34.6), an ERCP cannula or a dilating balloon is used to dilate the entry site (blunt dissection) (Fig. 34.7), or cautery can be used to enlarge the hole (regular or needle-knife sphincterotome, or a cystotome); the former "cautery-free" technique may be associated with a lower bleeding risk, especially delayed bleeding [35]. A randomized trial comparing mechanical and electrocautery initial tract dilation in 47 patients with pseudocysts showed more adverse events with electrocautery ($n = 4$) than with mechanical dilation ($n = 1$) [30]. All patients who had adverse events had no luminal bulge and had vessels in the gastric-pseudocyst wall. The size of the balloon used for dilation of the tract is based on the size of the cyst, presence of necrotic material, proximity of vessels and viscosity of the aspirated pseudocyst fluid, but is generally 6–10 mm. After dilation of the tract, a large amount of fluid can rapidly drain into the lumen, which requires aggressive prompt suctioning via the endoscope to prevent pulmonary aspiration. Then, a double pigtail catheter (generally 7–10 F) is placed over the guide wire (Fig. 34.8), followed by recannulation alongside the first stent, replacing a wire in the cyst, and placing a second (or third) stent. Double lumen catheters, such as a balloon stone extraction catheter or a Howell biliary introducer, can be used to place two wires into the cyst to begin with, without having to recannulate to place the second wire. The disadvantage of this approach is that only a 7F stent will fit down a therapeutic channel when a second wire is beside the stent. If the cyst fluid appears very thick or particulate in consistency, then a nasocystic catheter to provide prolonged lavage of the cyst, for inpatients, can be considered to decrease the risk of stent/tract occlusion and infection.

Recently a few reports have evaluated the use of transluminal fully covered self-expandable metal stents (FCSEMS) for pseudocyst drainage. However, there are no comparison studies to suggest clinical necessity and cost effectiveness of plastic versus metal stents. A prospective study of 20 patients with pseudocysts treated by FCSEMS (Wallflex, Boston Scientific Corp, Natick, MA) had complete resolution of the pseudocyst in 70%, with 15% adverse events and 15% stent migration rate [38]. A new lumen-apposing metal stent (Axios, Xlumina Inc., Mountain View, CA) has also been used for cystogastrostomy drainage with varying success. A multicenter prospective cohort study of 15 patients with pseudocysts and 46 patients with WON used a lumen-apposing metal stent. Pseudocysts resolved in 93% of the patients (81% resolution in WON) with overall adverse events in 9% and stent migration rate in 10.5% cases [52]. A lumen-apposing, self-expanding metal stent incorporated in an electro cautery enhanced delivery system (Hot Axios) for EUS-guided drainage of PFCs has recently become available. In a retrospective study of 93 patients with PFCs (80% with complex collections with necrosis), penetration of the

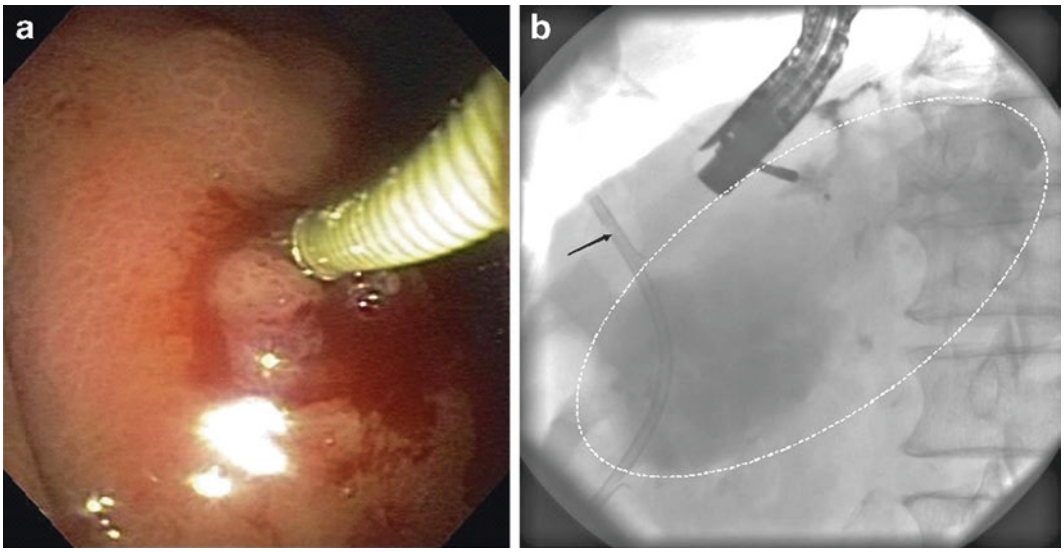

Fig. 34.5 A cystotome entering a pseudocyst through the gastric wall (**a**) after performing a partial transgastric cystogram (*dotted line*) using a fluoroscopically guided sclerotherapy needle inserted into the endoscopic bulge. (**b**) A biliary stent (*arrow*) had already been placed to relieve compression of the biliary tree by the cyst

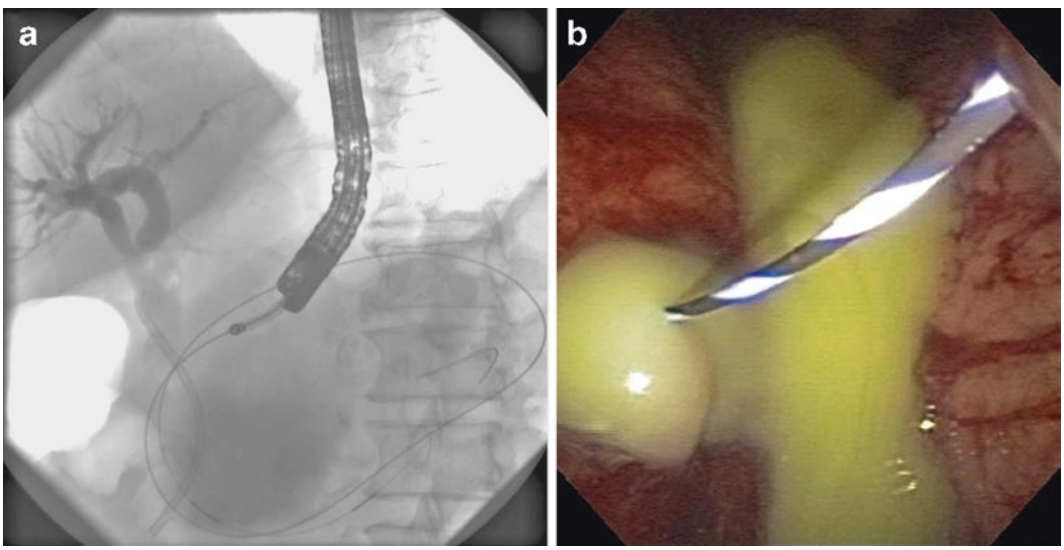

Fig. 34.6 Wire access to the cyst through the gastric wall. Wire coiled in the pseudocyst seen by fluoroscopy (**a**), with drainage of pseudocyst contents into the stomach around the wire seen endoscopically (**b**)

PFC was accomplished directly with this device in 74.2% of patients, and successful stent placement was accomplished in all but 1 patient, mostly without fluoroscopic assistance. Complete resolution of the PFC was achieved in 86 cases (92.5%), with no recurrence during follow-up. Treatment failure occurred in 6 patients with major adverse events reported in 5 patients [42]. With advancement in technology endoscopic drainage of pancreatic fluid, collection may become technically easier; however, placement of plastic stents provides effective drainage of pseudocysts, at significantly less expense than FCSEMS (Figs. 34.9 and 34.10).

All patients receive a short course of antibiotics. If patients have concomitant biliary obstruction due to pseudocyst compression, they are usually treated with temporary biliary stent placement, with a subsequent repeat cholangiogram and removal of the biliary stent at a second ERCP a few months later. Although not mandatory, a pancreatogram is often helpful to exclude downstream ductal obstruction, exclude main duct disruption, and assess for a significant active duct leak in order to determine if a temporary pancreatic stent would be helpful. Transmural drainage allows the disconnected pancreatic segment to drain via an enteral bypass into the GI lumen while stents are left in place.

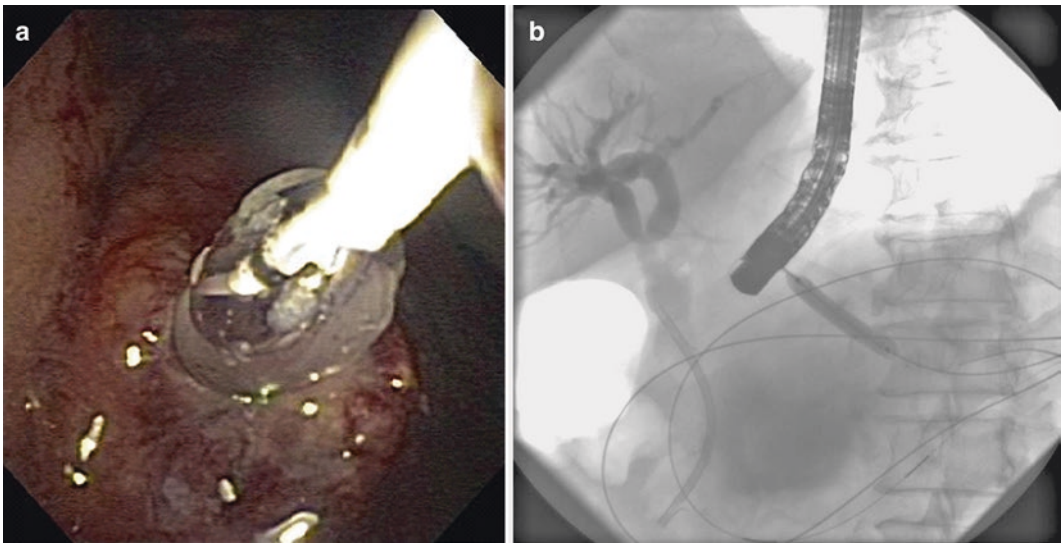

Fig. 34.7 An endoscopic (**a**) and fluoroscopic (**b**) view of a hydrostatic 6 mm balloon used to dilate the cystogastrostomy tract over a wire

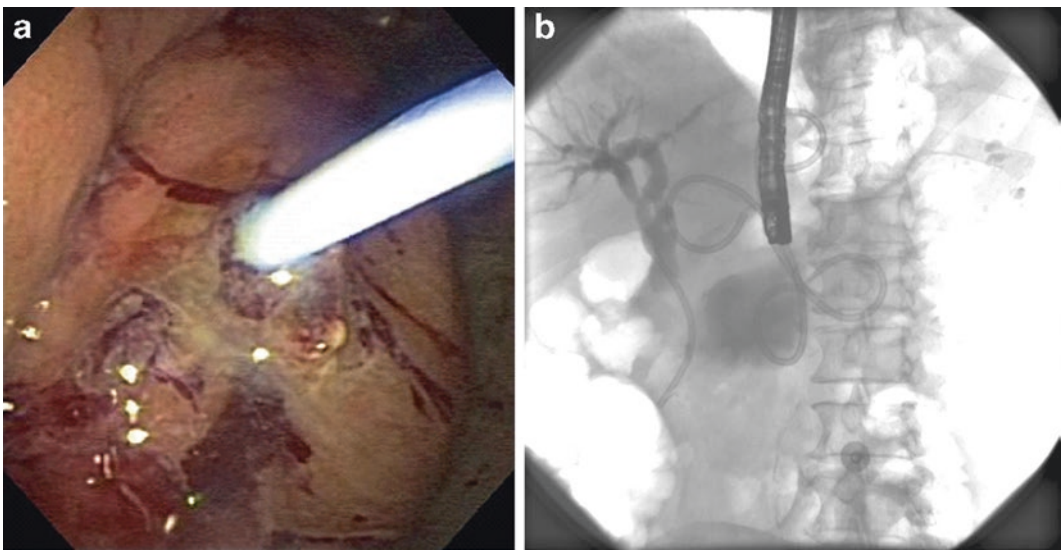

Fig. 34.8 A cystogastrostomy stent (**a**) was placed over the guide wire after balloon dilation, followed by placement of a double pigtail stent connecting the gastric lumen and the cyst lumen (**b**)

Recurrence is high after the transluminal stents are removed if an active leak is still present and downstream obstruction or disruption was not treated; in such cases, leaving stents may decrease the risk of recurrence [4]. Alternatively, instead of a direct pancreatogram, some prefer an MRCP in follow-up, after resolution of the cyst by transluminal drainage, to assess for pancreatic duct integrity, before removing transluminal stents; the large amount of fluid compressing the pancreas usually makes an MRCP pre-drainage inaccurate for this purpose. Periampullary edema can sometimes be so severe (due to active pancreatitis or due to venous congestion from compression) that the ampulla is obscured and ERCP with selective cannulation may be difficult or impossible.

A follow-up CT scan (or EUS or MRCP) in 1–2 months is then obtained. Assuming there is no significant residual collection, the stents can be removed at upper endoscopy with a snare. In patients whose pseudocysts have not resolved in 4–6 weeks, there are several options. First, one can wait. Second, one can assess the pancreatic duct for obstruction or disruption by pancreatography (ERCP or MRCP), with transpapillary stenting as needed. Third, one can dilate the transluminal tract and empirically replace the stents, remove solid material with endoscopic necrosectomy, or attempt additional transmural puncture of loculated areas. Multiple endoscopic sessions may be required in cases of persistent necrosis, with snare, forceps or extraction basket removal of

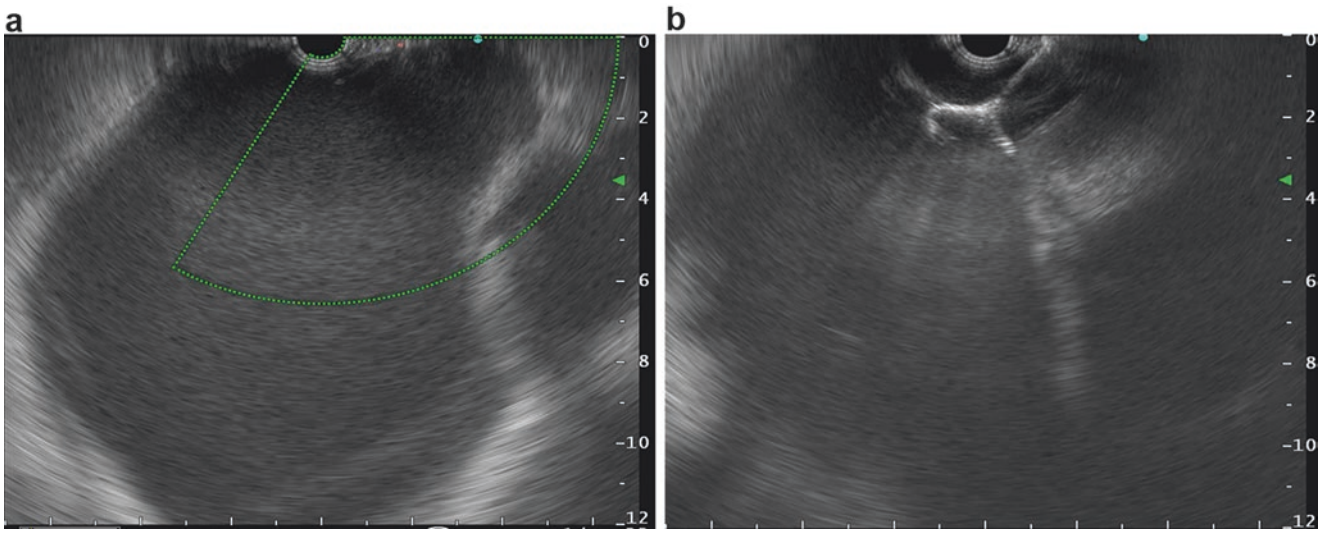

Fig. 34.9 EUS-guided cystogastrostomy image of the deploying lumen-apposing metal stent

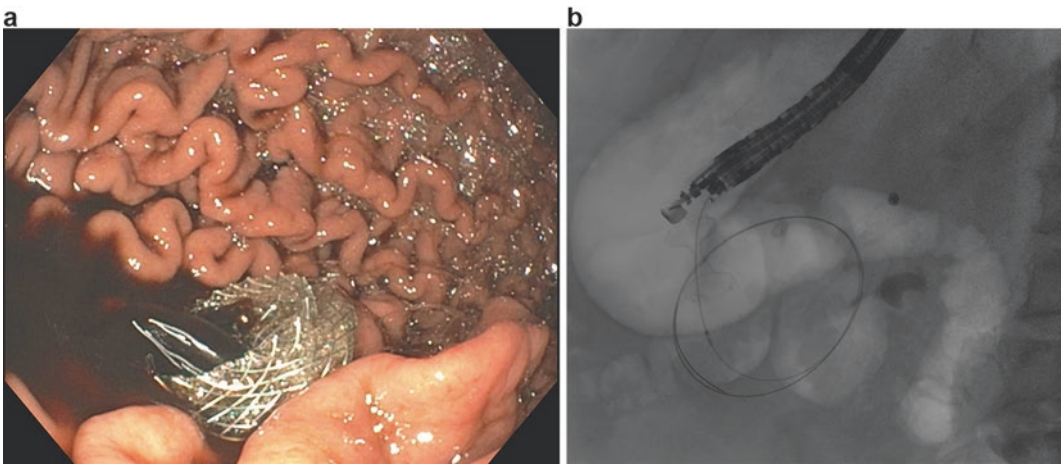

Fig. 34.10 An endoscopic (**a**) and fluoroscopic (**b**) view of the fully deployed lumen-apposing metal stent

necrotic debris under direct vision via the transluminal tract. Surgery should be considered for non-resolution of symptomatic pseudocysts, symptomatic recurrence without reversible factors, or in the presence of persistent symptomatic or infected walled off necrosis (WON).

Transpapillary Drainage

When a transpapillary pancreatic stent placement is needed, a pancreatic sphincterotomy is usually also performed, but is not mandatory, especially if chronic pancreatitis or intraductal stones are also present. Stones are removed when possible, and strictures are dilated and stented. If there is no obstruction, but a leak is demonstrated into the cyst from the duct, a small caliber stent is reasonable as a trial. It is controversial whether the stent inner tip should be placed in the duct (as it would be for a bile duct leak) or in the cyst itself; the latter provides more effective direct drainage, but stenting a blown out side branch into a larger caliber duct may prevent the side branch blowout from sealing over and, as such, may not be good in the long term. If the duct is partially disrupted, rejoining the duct with a stent over a wire, if the wire can bridge the disruption, is attempted [28, 45] (Fig. 34.11). Prophylactic and post-procedural antibiotics are provided for a few days given the unavoidable contamination of a sterile collection. The stent is generally pulled after satisfactory resolution of duct pathology on follow-up ERCP 1–2 months later.

If the cyst is accompanied by a complete main pancreatic duct disruption, it is unlikely that endoscopic therapy will ultimately succeed. Although the cyst may resolve, if one cannot reconnect the pancreas, the disconnected upstream pancreas will likely continue to cause obstructive symptoms (leak downstream from disruption) or cause the cyst to recur (leak upstream from disruption). Surgery should be strongly

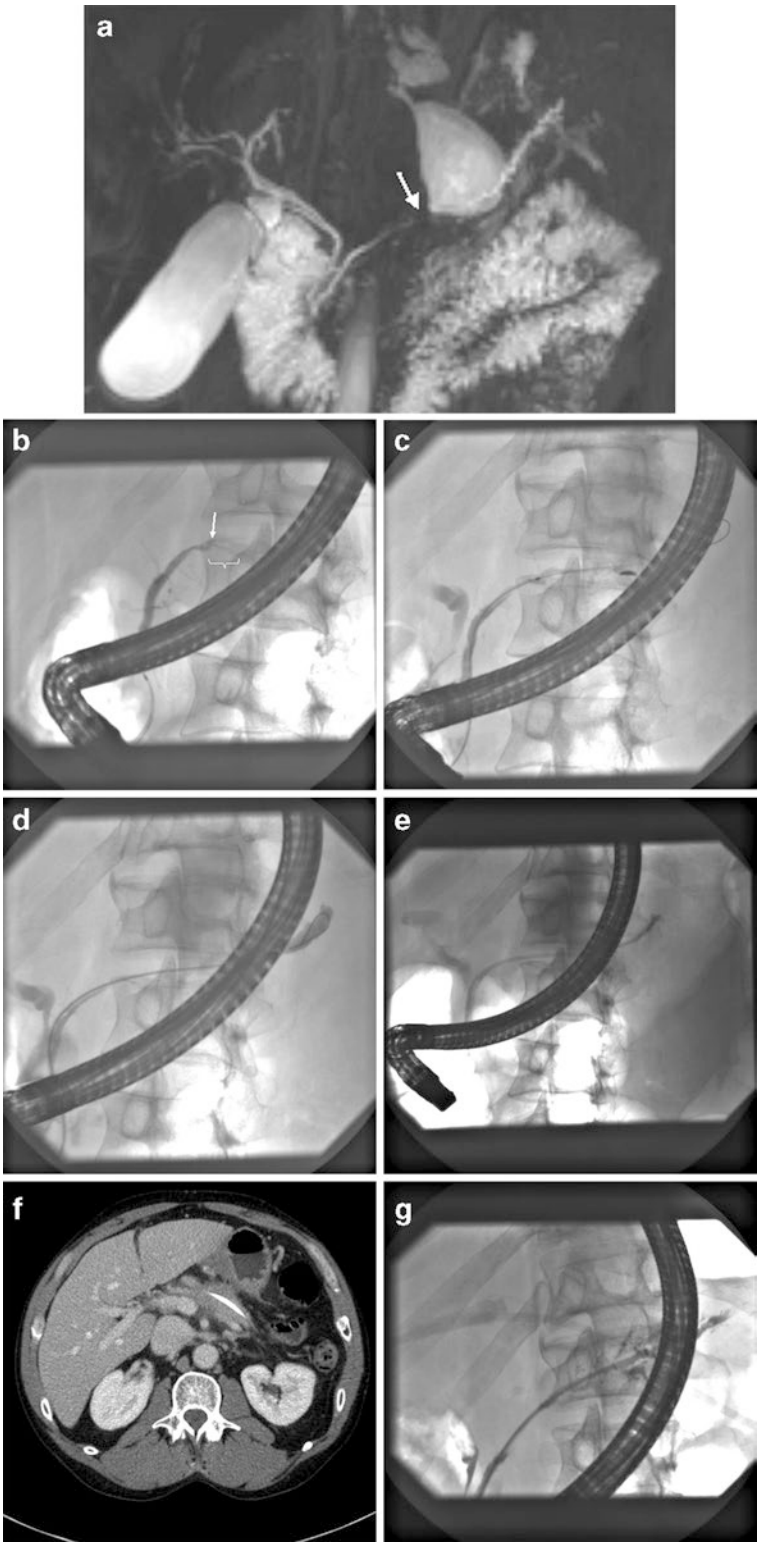

Fig. 34.11 A patient with alcoholic pancreatitis, persisting pseudocyst and pain. An image of a secretin-stimulated MRCP (**a**) and ERCP (**b**) leading to suspicion of a duct disruption (*small arrow*) as shown by a wisp of dye exiting from a partially cut-off pancreatogram in the body of the pancreas (*bracket*). The upstream duct (*PD*) appeared to be dilated on MRCP, and a wire was threaded across this area (**c**). Dye was injected to confirm that the wire was in the partially disconnected tail (**d**), and a stent was inserted (**e**). In follow-up, the cyst resolved on CT (**f**), and the pancreatic duct appeared to be reconnected (**g**)

considered in these cases. In selected cases, especially when the bulk of the disconnected tail is small, long-term transluminal stenting, perhaps with annual imaging thereafter, could be entertained as an alternative to surgery, hoping that the disconnected tail will atrophy over time. Long-term effectiveness and safety data on this approach are not available, so this should be a multidisciplinary decision, with the patient well-informed of the unknown outcomes.

Complications and Their Avoidance

Complications of endoscopic pseudocyst drainage include secondary infection, bleeding, perforation, and stent migration. The frequency of these has been reported around (11–37%) in literature [3, 8, 24]. Case selection is the key to reducing complications – not all apparent "cysts" reported on CT can or should be treated with endoscopic drainage.

Infection is the most common complication following endoscopic drainage of pseudocysts. The infection usually develops due to malfunction or obstruction of stents or due to significant unrecognized necrosis. Use of peri- and post-procedural antibiotics can help reduce this risk. Fortunately, the majority of infectious complications can be managed endoscopically, or with percutaneous drainage of loculated areas; cases of multiloculated infected necrosis often require surgery. Avoidance of this technique when there is significant necrosis, or early recognition of underlying pancreatic necrosis followed by extensive endoscopic debridement ("necrosectomy") and/or placement of nasal or percutaneous lavage drains in centers comfortable with these techniques, can reduce the need for surgical intervention for infection [7]. As stated above, inadequate drainage from small transluminal tracts and/or single stenting increases the risk of infection. FNAs that contaminate a cyst, without complete drainage, can also lead to infection.

Significant bleeding can occur due to inadvertent puncture of a submucosal vessel or varix; this can generally be prevented by use of an EUS-guided puncture. Although rare, the presence of a pseudoaneurysm can lead to fatal hemorrhage either by guide wire trauma as it coils along the inside of the cyst, erosion of a transluminal stent, or simply due to rapid changes in the cyst wall tension as the size of the cyst rapidly changes. Preprocedure imaging can usually detect this. One study suggested that blunt dissection with a dilating balloon over a wire that is placed through a needle after a needle puncture (i.e., a Seldinger technique), without cautery, has a lower risk than using cautery to enter the cyst and expand the cystogastrostomy lumen with a standard sphincterotome [35]. However, it is not clear if the higher risk of a cautery approach still applies when the diameter of the hole that is made with cautery is limited (such as a small entry with a needle-knife) or when the cutting is done with a circumferential cauterizing device such as a cystotome. The Seldinger technique can be difficult with a side-viewing scope as the tip of the 19 G needle can be damaged by the elevator, with cases of needle tip fragmentation into the cyst having been reported.

Perforation has been reported to occur in about 3% of cases [3, 21]. Perforation is more likely to occur when the pseudocyst wall is poorly defined by imaging studies or has a distance of greater than 1 cm from the intestinal lumen or if the cyst has not been present long enough to become adherent to the luminal structure into which it is being drained. Cystic tumors masquerading as pseudocysts are often not adherent to the GI lumen, because there is usually little or no inflammatory reaction around them, and as such, they are more likely to be associated with perforation or free-air. Usually, free-air can be managed conservatively, with antibiotics and fasting, but emergent percutaneous drainage or surgery may be required.

Conclusion

- Endoscopic drainage, with or without EUS guidance, can be considered a first-line cyst drainage modality for symptomatic pseudocysts (pancreatic fluid collections (PFCs) persisting more than 4 weeks) adjacent to the gastrointestinal wall without contraindications; EUS guidance is often needed for cysts located in the tail.
- Surgery is generally reserved for salvage therapy, for complicated cysts (e.g., with infection and/or significant necrosis), and for those cases associated with complete duct disruptions. In the latter, selected long-term transmural stents can be considered as an alternative to surgery, after a multidisciplinary discussion.
- Transpapillary drainage with a pancreatic stent and/or sphincterotomy is useful as monotherapy for small pseudocysts with ductal communication and is a useful adjunct to transluminal drainage when downstream ductal pathology exists.
- Acute PFCs, PNPFCs and WON, and cystic tumors can mimic pseudocysts, but require different interventions and have different considerations.
- Careful history-taking, waiting for cyst maturity, and US/MR/EUS imaging are key.
- Though recent data on endoscopic transluminal therapy for complicated pseudocysts (e.g., infected) or in symptomatic necrosis are very encouraging as being comparable to surgery in selected cases, the safety and superiority over surgery is not as clear as in uncomplicated pseudocysts.
- Expertise in the technique of transluminal endoscopic debridement of necrosis is limited to a small number of advanced endoscopists and centers, and often requires inpatient lavage and multiple procedures.

References

1. Abou-Assi S, Craig K, O'Keefe S. Prospective randomized trial of jejunal (EN) and intravenous (TPN) feeding in the management of acute pancreatitis. Gastroenterology. 2001;120:5.
2. Adams DB, Anderson MC. Percutaneous catheter drainage compared with internal drainage in the management of pancreatic pseudocyst. Ann Surg. 1992;215:571–8.

3. Antillon MR, Shah RJ, Stiegmann G, et al. Single-step EUS-guided transmural drainage of simple and complicated pancreatic pseudocysts. Gastrointest Endosc. 2006;63(6):797–803.
4. Arvanitakis M, Delhaye M, Bali MA. Pancreatic-fluid collections: a randomized controlled trial regarding stent removal after endoscopic transmural drainage. Gastrointest Endosc. 2007;65(4):609–19.
5. Bang JY, Wilcox CM, Trevino JM, et al. Relationship between stent characteristics and treatment outcomes in endoscopic transmural drainage of uncomplicated pancreatic pseudocysts. Surg Endosc. 2014;28(10):2877–83.
6. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62:102–11.
7. Baron TH, Thaggard WG, Morgan DE, et al. Endoscopic therapy for organized pancreatic necrosis. Gastroenterology. 1996;111(3):755–64.
8. Baron TH, Harewood GC, Morgan DE, et al. Outcome differences after endoscopic drainage of pancreatic necrosis, acute pancreatic pseudocysts, and chronic pancreatic pseudocysts. Gastrointest Endosc. 2002;56(1):7–17.
9. Boerma D, Obertop H, Gouma DJ. Pancreatic pseudocysts in chronic pancreatitis. Surgical or interventional drainage? Ann Ital Chir. 2000;71:43–50.
10. Bradley EL, Gonzalez AC, Clements JL Jr. Acute pancreatic pseudocysts: incidence and implications. Ann Surg. 1976;184(6):734–7.
11. Brown A, Hughes M, Tenner S, et al. Does pancreatic enzyme supplementation reduce pain in patients with chronic pancreatitis: a meta-analysis. Am J Gastroenterol. 1997;92(11):2032–5.
12. Brugge WR, Lauwers GY, Sahani D, et al. Cystic neoplasms of the pancreas. N Engl J Med. 2004;351:1218–26.
13. Brugge WR, Lewandrowski K, Lee-Lewandrowski E, et al. Diagnosis of pancreatic cystic neoplasms: a report of the cooperative pancreatic cyst study. Gastroenterology. 2004;126(5):1330–6.
14. Cahen D, Rauws E, Fockens P, et al. Endoscopic drainage of pancreatic pseudocysts: long-term outcome and procedural factors associated with safe and successful treatment. Endoscopy. 2005;37:977–83.
15. Cremer M, Deviere J, Engelholm L. Endoscopic management of cysts and pseudocysts in chronic pancreatitis: long-term follow-up after 7 years of experience. Gastrointest Endosc. 1989;35(1):1–9.
16. D'Egidio A, Schein M. Pancreatic pseudocysts: a proposed classification and its management implications. Br J Surg. 1991;78:981–4.
17. El Hamel A, Parc R, Adda G, et al. Bleeding pseudocysts and pseudoaneurysms in chronic pancreatitis. Br J Surg. 1991;78(9):1059–63.
18. Giovannini M, Bernardini D, Seitz JF. Cystogastrostomy entirely performed under endosonography guidance for pancreatic pseudocyst: results in six patients. Gastrointest Endosc. 1998;48(2):200–3.
19. Gouyon P, Levy P, Ruszniewski P, Zins M, et al. Predictive factors in the outcome of pseudocysts complicating alcoholic chronic pancreatitis. Gut. 1997;41:821–5.
20. Hernandez-Aranda JC, Gallo-Chico B, Ramirez-Barba EJ. Nutrition support in severe acute pancreatitis. Controlled clinical trial. Nutr Hosp. 1996;11:160.
21. Hookey LC, Debroux S, Delhaye M, et al. Endoscopic drainage of pancreatic-fluid collections in 116 patients: a comparison of etiologies, drainage techniques, and outcomes. Gastrointest Endosc. 2006;63(4):635–43.
22. Imrie CW, Buist LJ, Shearer MG. Importance of cause in the outcome of pancreatic pseudocysts. Am J Surg. 1988;156:159–62.
23. Jacobson BC, Baron TH, Adler DG, et al. ASGE guideline: the role of endoscopy in the diagnosis and the management of cystic lesions and inflammatory fluid collections of the pancreas. Gastrointest Endosc. 2005;61:363–70.
24. Kahaleh M, Shami VM, Conaway MR, et al. Endoscopic ultrasound drainage of pancreatic pseudocyst: a prospective comparison with conventional endoscopic drainage. Endoscopy. 2006;38(4):355–9.
25. Kalfarentzos F, Kehagias J, Mead N, et al. Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized prospective trial. Br J Surg. 1997;84:1665.
26. Khreiss M, Zenati M, Clifford A, et al. Cyst gastrostomy and necrosectomy for the management of sterile walled-off pancreatic necrosis: a comparison of minimally invasive surgical and endoscopic outcomes at a high-volume pancreatic center. J Gastrointest Surg. 2015;19(8):1441–8.
27. Kourtesis G, Wilson SE, Williams RA. The clinical significance of fluid collections in acute pancreatitis. Am Surg. 1990;56:796–9.
28. Kozarek RA, Ball TJ, Patterson DJ, et al. Endoscopic transpapillary therapy for disrupted pancreatic duct and peripancreatic fluid collections. Gastroenterology. 1991;100(5 Pt 1):1362–70.
29. Kruger M, Schneider AS, Manns MP, et al. Endoscopic management of pancreatic pseudocysts or abscesses after an EUS-guided 1-step procedure for initial access. Gastrointest Endosc. 2006;63(3):409–16.
30. Lakhtakia S, Gupta R, Nagar A, et al. A randomized controlled trial comparing tapered catheter vs 6 Fr cystotome for safe EUS guided drainage of non-bulging pseudocyst with collaterals [abstract]. Gastrointest Endosc. 2010;71:AB 136–7.
31. Lee LS, Saltzman JR, Bounds BC, et al. EUS-guided fine needle aspiration of pancreatic cysts: a retrospective analysis of complications and their predictors. Clin Gastroenterol Hepatol. 2005;3(3):231–6.
32. Maringhini A, Uomo G, Patti R, et al. Pseudocysts in acute nonalcoholic pancreatitis: incidence and natural history. Dig Dis Sci. 1999;44:1669–73.
33. Marshall GT, Howell DA, Hansen BL, et al. Multidisciplinary approach to pseudoaneurysms complicating pancreatic pseudocysts. Impact of pretreatment diagnosis. Arch Surg. 1996;131(3):278–83.
34. McClave S, Greene L, Snider H, et al. Comparison of the safety of early enteral vs parenteral nutrition in mild acute pancreatitis. JPEN. 1997;21:14.
35. Mönkemüller KE, Baron TH, Morgan DE. Transmural drainage of pancreatic fluid collections without electrocautery using the Seldinger technique. Gastrointest Endosc. 1998;48(2):195–200.
36. Nealon WH, Walser E. Main pancreatic ductal anatomy can direct choice of modality for treating pancreatic pseudocysts (surgery versus percutaneous drainage). Ann Surg. 2002;235:751–8.
37. Panamonta N, Ngamruengphong S, Kijsirichareanchai K, et al. Endoscopic ultrasound-guided versus conventional transmural techniques have comparable treatment outcomes in draining pancreatic pseudocysts. Eur J Gastroenterol Hepatol. 2012;24(12):1355–62.
38. Penn DE, Draganov PV, Wagh MS, et al. Prospective evaluation of the use of full covered self-expandable metal stents for EUS-guided transmural drainage of pancreatic pseudocysts. Gastrointest Endosc. 2012;76:679–84.
39. Pitchumoni CS, Agarwal N. Pancreatic pseudocysts. When and how should drainage be performed? Gastroenterol Clin N Am. 1999;28:615–39.
40. Pitkaranta P, Haapiainen R, Kivisaari L, et al. Diagnostic evaluation and aggressive surgical approach in bleeding pseudoaneurysms associated with pancreatic pseudocysts. Scand J Gastroenterol. 1991;26(1):58–64.
41. Romagnuolo J, Bardou M, Rahme E, et al. Magnetic resonance cholangiopancreatography: a meta-analysis of test performance in suspected biliary disease. Ann Intern Med. 2003;139(7):547–57.
42. Rinninella E, Kunda R, Dollhopf M, et al. EUS-guided drainage of pancreatic fluid collections using a novel lumen-apposing metal stent on an electrocautery-enhanced delivery system: a large retrospective study. Gastrointest Endosc. 2015;82:1039–46.
43. Seewald S, Ang TL, Teng KC, et al. EUS-guided drainage of pancreatic pseudocysts, abscesses and infected necrosis. Dig Endosc. 2009;21(Suppl 1):S61–5.
44. Siegelman SS, Copeland BE, Saba GP, et al. CT of fluid collections associated with pancreatitis. AJR Am J Roentgenol. 1980;134:1121–32.

45. Telford JJ, Farrell JJ, Saltzman JR, et al. Pancreatic stent placement for duct disruption. Gastrointest Endosc. 2002;56(1):18–24.
46. van der Waaij LA, van Dullemen HM, Porte RJ. Cyst fluid analysis in the differential diagnosis of pancreatic cystic lesions: a pooled analysis. Gastrointest Endosc. 2005;62:383–9.
47. Varadarajulu S, Lopes TL, Wilcox CM, et al. EUS versus surgical cyst-gastrostomy for management of pancreatic pseudocysts. Gastrointest Endosc. 2008;68:649.
48. Varadarajulu S, Wilcox CM, Tamhane A, et al. Role of EUS in drainage of peripancreatic fluid collections not amenable for endoscopic transmural drainage. Gastrointest Endosc. 2007;66(6):1107–19.
49. Vilmann P, Hancke S, Pless T, et al. One-step endosonography-guided drainage of a pancreatic pseudocyst: a new technique of stent delivery through the echo endoscope. Endoscopy. 1998;30(8):730–3.
50. Wade JW. Twenty-five year experience with pancreatic pseudocysts. Are we making progress? Am J Surg. 1985;149:705–8.
51. Walt AJ, Bouwman DL, Weaver DW, Sachs RJ. The impact of technology on the management of pancreatic pseudocyst. Fifth annual Samuel Jason Mixter lecture. Arch Surg. 1990;125:759–63.
52. Walter D, Will U, Sanchez-Yague, et al. A novel lumen-apposing metal for endoscopic ultrasound-guided drainage of pancreatic fluid collections: a prospective cohort study. Endoscopy. 2015;47:63–7.
53. Windsor ACJ, Kanwar S, Li AGK, et al. Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. Gut. 1998;42:431.

Instruments and Accessories for Endoscopic Ultrasound

35

Olaya Brewer-Gutierrez and Vikesh K. Singh

Introduction

Endoscopic ultrasound (EUS) was first introduced in the early 1980s as a diagnostic procedure using radial array echoendoscopes. EUS increasingly evolved to a therapeutic procedure that requires a linear array echoendoscope. Radial array echoendoscopes are largely used for cancer staging, evaluation of submucosal lesions, and for a morphologic assessment of the pancreas and bile ducts. Linear array echoendoscopes allow for tissue acquisition for cytology and histology as well as emerging applications such as augmented imaging techniques (e.g., elastography). The therapeutic capabilities of EUS include the placement fiducials for stereotactic body radiation therapy, drainage of pseudocysts and walled-off necrosis as well as the gallbladder, creation of communications between different areas of the gastrointestinal tract, and pancreaticobiliary ductal system (e.g., excluded stomach in Roux-en-Y gastric bypass, enteroenterostomy, choledochoduodenostomy). This chapter will review the instruments and accessories that serve as the basis of modern EUS clinical practice.

Instruments

Radial Echoendoscope

Radial-array echoendoscopes (RA-EUS) are used only for diagnostic EUS examinations and thus have limited applications because tissue sampling and therapeutic interventions are not possible. The 360° scanning range of the RA-EUS produces an image in a plane perpendicular to the long axis of the echoendoscope as a full panoramic view. The scan is in a plane perpendicular to the axis of the echoendoscope resulting in images similar to an axial CT "slice." The transducer appears in the center of the image.

The three major manufacturers of RA-EUS are Fujifilm Endoscopy (Fujinon, Wayne, NJ), Olympus (Olympus America, Center Valley, Pa), and Pentax (Pentax of America, Montvale, NJ). The echoendoscopes are similar in shape. The endoscopic camera is end-viewing on the Pentax and Fujinon echoendoscopes, whereas an oblique view (55°) in the Olympus echoendoscope. They vary in shaft diameters. Fujinon has the slimmest (11.5 mm) and most flexible scope, whereas the Olympus RA-EUS has the widest diameter (13.8 mm) at the junction of the shaft and the US transducer [1].

Main indication of RA-EUS is to assess benign or malignant mucosal or submucosal lesions in the gastrointestinal tract including esophageal, gastric, duodenal, and colorectal masses, liver, and those of the pancreatobiliary system. The use of color Doppler helps to differentiate blood vessels from any tubular structures such as the bile and pancreatic ducts or structures like lymph nodes. Another indication is the evaluation of cholelithiasis and choledocholithiasis.

Practical Considerations

- Ultrasound scanning area of 360°
- Varying ultrasound frequencies (from 5 MHz up to 12 MHz)
- Color and power Doppler
- Channel diameter 2.2 mm
- Only for diagnostic purposes

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Linear Echoendoscope

The curvilinear array echoendoscope (CLA-EUS) produces images in a plane parallel to the long axis of the echoendoscope, usually in a sector between 100° and 180°. The scan images are similar to a transabdominal US. This is important for tissue acquisition and therapeutic interventions since EUS needles are advanced from the distal tip of the echoendoscope in the same plane as the US image. This allows for simultaneous and continuous visualization of the target lesion and the needle as it is advanced out of the accessory channel. All CLA-EUS instruments have an elevator at the distal end of the working channel that allows a better control of the angle of exit of EUS needles or any devices from the working channel.

Three major manufacturers, Fujifilm, Olympus America, and Pentax, produce linear-array echoendoscopes. All transducers have a curved design and are located distal to the oblique-viewing endoscopic camera lens. The echoendoscopes differ on the tip design, flexibility, and working channel sizes (Table 35.1) [1].

The main indication of CLA-EUS is to perform fine needle aspiration (FNA) to obtain tissue specimens for cytology and histology. Any cyst or mass is contiguous with the wall of the upper and lower gastrointestinal tract, including the liver and pancreatobiliary system. Nowadays, EUS has evolved to a therapeutic modality and has been used increasingly for drainage of pancreatic walled-off necrosis (WON), treatment of cystic lesions of the pancreas, localized therapy of pancreatic tumors, and new techniques involving EUS-guided gallbladder, bile duct, and pancreatic duct drainage when conventional ERCP fails and enterostomies in cases of gastric outlet obstruction.

Forward Viewing Curved-Linear Echoendoscope

The primary limitation of the traditional CLA-EUS is that all devices exit the accessory channel oblique to the scope axis, which can deform the device and increase the difficulty of the procedure. The forward-viewing curved linear array EUS (FV-EUS) TGF-UC180J (Olympus America, Center Valley, PA) expands the treatment options for interventional EUS procedures. This echoendoscope provides a zero-degree accessory channel, forward-viewing endoscopic optics, and a transducer design that enables excellent resolution and penetration. Any device exits the working channel parallel to the longitudinal axis of the echoendoscope which allows an easy passage. Ultrasound scanning area is 90° and the working channel is 3.7 mm, without an elevator. Traditional CLA-EUS has 180° scanning ultrasound area and the working channel has an elevator. The potential benefit of this echoendoscope could be the ability to target areas in the GI tract difficult to access with an oblique-viewing endoscope and avoid the need of changing to a forward-viewing scope [2].

A summary of the key benefits would be:

- Short distal tip: the distal tip design allows potentially easier handling, intubation, and maneuverability.
- Straight working channel: the straight working channel provides direct accessory delivery to the region of interest with greater puncture force and control.
- Extensive angulation: the 180° up angulation is wider than any other ultrasound scope which could provide better access and visibility to areas that traditionally have been difficult to observe.
- Auxiliary water channel: flushes away any residue for a clear view at all times and eliminates the need of a balloon.

The available evidence of the performance of the FV-EUS is mostly based on single-center studies with small number of patients, without direct comparative studies with the standard CLA-EUS. There has been only one randomized, multicenter, controlled trial that compared the CLA-EUS and the FV-EUS for pancreatic pseudocyst drainage. The study reported no substantial advantages when the FV-EUS was used, with more time needed to identify the optimal pseudocyst access site compared with the oblique-viewing echoendoscope [3].

A prospective, randomized, crossover trial by Ippei et al. comparing the standard CLA-EUS and the FV-EUS in FNA of upper GI subepithelial lesions failed to show differences in the diagnostic yield between the two echoendoscopes. However, the tissue sample area in patients with gastrointestinal stromal tumors was larger, and the procedure time was significantly shorter with the FV-EUS than with CLA-EUS. This may be due to a more efficacious positioning and targeting of the lesion and easier use of the 19-gauge needle due to the design of the echoendoscope [4].

Table 35.1 CLA-EUS

Producer	Model	Scanning range (°)	Frequencies (MHz)	Working channel (mm)	Distal tip diameter (mm)
Olympus	GF-UCT180	180	5, 6, 7.5, 10, 12	3.7	14.6
Olympus	UCT140-AL5	180	5, 6, 7.5, 10,12	2.8	14.2
Pentax	EG-3870UTK	120	5, 6.5, 7.5, 9, 10	3.8	12.8
Fujinon	EG-530UT2	124	5, 7.5, 10, 12	3.8	13.9

Practical Considerations

- Ultrasound scanning area of 90°
- Short distal tip
- Channel diameter 3.7 mm
- Extensive angulation to 180°

More studies are needed to better characterize the advantages and disadvantages of the FV-EUS compared with the CLA-EUS. Additionally, several areas of use of this echoendoscope need to be further investigated, such as its potential for therapeutic and interventional procedures as well as for natural orifice transluminal endoscopic surgery [5].

EUS Miniprobe

EUS miniprobes are flexible high US probes that can be advanced through the working channel of some echoendoscopes. They consist of a flexible shaft with a central wire that drives rotation of a mechanical transducer at the tip. The transducer is surrounded by oil that serves as an acoustic interface with tissue, providing 360° imaging perpendicular to the axis of the probe [6]. The outer diameter of these probes vary between 1.7–3.4 mm. Compared to standard echoendoscopes, their scanning frequency can be between 12 and 30 MHz, allowing for improved differentiation of the wall layers of the GI tract. The conventional RA-EUS produces an image of the GI tract wall consisting of five sections or layers which are the innermost, medial layer (lumen) known as the superficial mucosal layer, the second layer that corresponds to the lamina propria or deep mucosa, the third layer known as the submucosa, the fourth layer referred to as the muscularis propria, and the fifth layer known as the adventitia in the esophagus and serosa in the stomach, duodenum, and part of the rectum. The high-frequency miniprobes provide a more detailed ultrasound image of the gut wall with 9 to 11 layers: the first and second layers correspond to the interface with the lumen and mucosal epithelium; the third and fourth layers correspond to deep mucosa (lamina propria); the fifth and sixth layers correspond to the muscularis mucosae interface and muscularis mucosae; the seventh layer is the submucosa; the eighth layer is the inner layer of the muscularis propria; the ninth layer corresponds to connective tissue and the interface between the muscle layers; the tenth layer corresponds to the outer layer of the muscularis propria; and the eleventh layer is the serosa/adventitia.

Nevertheless, whenever the frequency is higher, the depth of penetration is lower, limiting the usefulness of the probe beyond the discrimination of wall layers. Moreover, their cost is high and their durability is low. Acoustic coupling between the probe and tissue can be achieved by several methods, including close apposition of the probe to tissue with air aspiration, instillation of liquid into the gut lumen, use of a condom over the tip of the endoscope, and use of a balloon sheath over the probe [6]. Before use, the tip of the catheter should be rotated outside the body to ensure even distribution of the immersion oil.

Current manufacturers of high-frequency EUS probes include Fujifilm Endoscopy and Olympus.

The main indication of EUS probes is for imaging of benign or malignant superficial neoplasms of the esophagus, stomach, and duodenum as well as small subepithelial mass lesions of the GI tract. In addition, wire-guided US probes are available for intraductal evaluation of the pancreatic and biliary ducts. Nonetheless, the limited depth of tissue penetration makes ultrasound probes inadequate for complete TNM staging of gastrointestinal tumors. The staging accuracy of ultrasound probes in patients with superficial esophageal, gastric, and colorectal carcinoma has been reported to widely vary from 60% to 90% [6].

Accessories

Fine Needle Aspiration (FNA) and Fine Needle Biopsy (FNB) Needles

EUS enables sampling masses of the middle and inferior mediastinum, which are adjacent to the esophagus; cystic or

Table 35.2 EUS-FNA needles

Producer	Model	Needle size (Gauge)	Minimum working channel (mm)	Sheath size (Fr)
Boston scientific	Expect	19, 22, 25	2.8 (19 ga), 2.4 (22, 25 ga)	5.49 (19 ga), 4.95 (22 ga), 4.56 (25 ga)
Cook	EchoTip Ultra	19, 22, 25	2	5.19–4.2 (19 ga), 5.19 (22, 25 ga)
Medtronic	Beacon	19, 22, 25	2.8	7.5
Olympus	EZshot2 and EZshot 3	19, 22, 25 (only EZshot2)	2.8	5.55
Medi-globe GmbH	SonoTip pro	19, 22, 25	3.2	6.3 (19 ga), 5.4 (22, 25 ga)
ConMed	ClearView	19, 22, 25	3.2	6.3 (19 ga), 5.4 (22, 25 ga)

solid lesions of the pancreas, which are adjacent to the stomach and duodenum; perirectal lesions; subepithelial lesions of the upper gastrointestinal tract; upper abdominal masses; and lesions located in the left kidney, left adrenal gland, and left lobe of the liver by fine needle aspiration (FNA) or core biopsy (FNB).

Several needles are available to perform EUS-FNA (Table 35.2). All needles have four main components: a metal needle, a stylet, a sheath, and a handle for controlling the length of the sheath and needle. The sheath size varies from 4 to 7.5 Fr in diameter, and needle size ranges from 25 to 19-gauge. The needle length is up to 8 to 9 cm. The most commonly used needle size is 22-gauge [7]. Some endoscopists prefer inserting the needle with the stylet fully inserted, whereas others prefer stylet withdrawal about 1–2 cm before puncture.

In a trial were eight commonly used EUS needles were compared, there was no significant difference in the ratings and rankings of these needles between endosonographers and radiologists. Overall, one prototype needle was rated as the best, ranking 10% to 40% higher than all other needles ($P < 0.01$). Among the commercially available needles, the EchoTip Ultra® needle and the ClearView® needle were top choices. The EZ Shot 2® needle was ranked statistically lower than other needles (30–75% worse, $P < 0.001$) [7].

EUS-FNA is a convenient, minimally invasive, and safe procedure. The diagnostic accuracy of EUS-FNA for pancreatic cancer ranges from 78% to 95% with a sensitivity and specificity of 85% to 95% and 95% to 98%, respectively; however, needle types, needle sizes, lesion location, number of passes, endoscopist skill, and presence of rapid onsite cytologic evaluation (ROSE) can impact the outcome of an EUS-FNA procedure [8]. Moreover, FNA is limited by a small sample size that may be insufficient for immunohistochemistry or a histological diagnosis. Therefore, specialized needles have been designed to acquire larger "core" specimens that preserve tissue architecture for a histologic diagnosis and immunohistological staining. These are the FNB-needles (Table 35.3).

Table 35.3 EUS-FNB needles

Producer	Model	Needle size (Gauge)	Minimum working channel (mm)	Sheath size (Fr)
Boston scientific	Acquire	22, 25	2.8 (19 ga), 2.4 (22, 25 ga)	4.95 (22 ga), 4.56 (25 ga)
Cook	EchoTip ProCore	19, 20,22, 25	2 (19, 22, 25 ga), 3.7 (20 ga)	4.8 (19 ga), 7.95 (20 ga), 5.2 (22, 25 ga)
Medtronic, Covidien	SharkCore	19, 22, 25	2.8	7.5

A prospective, randomized study aimed to compare the utility of the 22G EUS-FNB (EchoTip ProCore®, Cook Medical Inc., Bloomington, IN, US) with the 22G EUS-FNA for collecting adequate histological core samples in patients with GI subepithelial tumors (SETs); the rates of obtaining macroscopically and histologically optimal core samples with EUS-FNB in patients with GI SETs were 92% and 75%, respectively, which were superior to those with EUS-FNA (30% and 20%). Furthermore, the median number of needle passes required to obtain macroscopically optimal core samples using EUS-FNB was significantly lower (2 vs 4) than that using EUS-FNA. The technical performance and safety profile of EUS-FNB were comparable to that of EUS-FNA. Thus, the diagnostic sufficiency rate was higher for EUS-FNB than for EUS-FNA (75% vs 20%) [9].

A new EUS-FNB needle (SharkCore®, Medtronic, Sunnyvale, CA, US) has been introduced, which has a novel needle tip shape in an attempt to improve diagnostic accuracy, tissue yield, and to potentially obtain a core tissue sample via EUS. The needle tip design incorporates two sharp points of different lengths and a multifaceted bevel in an attempt to capture additional tissue, preferably as a core (Fig. 35.1).

A trial of 15 patients undergoing EUS-FNB with the SharkCore® needle was performed, and it was compared to EUS-FNA in 15 patients who underwent EUS-FNA. The SharkCore needle required fewer needle passes to obtain diagnostic adequacy than the standard needle ($P < 0.001$) [10]. The SharkCore needle required 1.5 passes to reach adequacy, whereas the standard needle required 3 passes. For cases with cell blocks, the SharkCore needle produced diagnostic material in 85% of cases (95% confidence interval (CI), 54–98), whereas the standard needle produced diagnostic material in 38% of the cases (95% CI, 9–76). The SharkCore needle produced actual

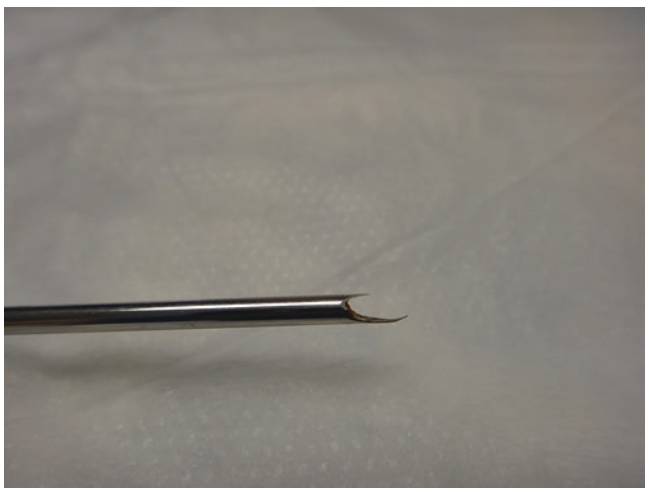

Fig. 35.1 SharkCore® FNB needle. The tip design incorporates two sharp points of different lengths and a multifaceted bevel

tissue cores 82% of the time (95% CI, 48–98), but the standard needle produced no tissue cores (95% CI, 0–71) ($P = 0.03$) [11].

Micro Forceps

Recently introduced, through the needle single-use micro forceps, the Moray® (US endoscopy, Mentor, OH) micro forceps is designed to be used in EUS procedures using most 19-gauge FNA needles to enhance sampling from lesions in the gastrointestinal tract for more definitive diagnosis and targeted therapy. Currently, data supports its use for the diagnosis of pancreatic cystic neoplasm only.

The micro forceps have serrated jaws with a maximum opening of 4.3 mm and a spring sheath allowing for use in angulated positions. The diameter of the sheath is 2.4 Fr and the device length is 230 cm.

A few studies have reported on the safety and utility of this micro forceps. Shakhatreh MH et al. reported a case series of two patients who had large pancreatic cystic lesions in the pancreatic head. Linear EUS was performed, and tissue samples were obtained with the micro forceps through a 19-gauge needle. In both patients, mucinous columnar epithelium lined the cystic walls. One patient underwent surgical resection, and the other elected surveillance. Examination of the surgical specimen from the first patient confirmed the cyst was a side-branch intraductal papillary mucinous neoplasm (IPMN) [12].

Prospective controlled trials are needed to further assess the accuracy and safety of this new device.

Lumen-Apposing Metal Stents (LAMS)

Practical Considerations

- The micro forceps require passage through a 19-gauge FNA needle.
- Serrated jaws with a maximum opening of 4.3 mm and 2.4 Fr spring sheath.
- Data supports its use in the diagnosis of cystic neoplasms of the pancreas only.

In the past, EUS-guided transluminal drainage was performed using plastic or fully covered self-expandable metallic stents (FCSEMS) used in endoscopic retrograde cholangiopancreatography (ERCP) which did not seal the layers between the targeted tissues increasing risk of leakage. Also, stent migration was a frequent adverse event (AE) since stents could not be anchored.

A newly developed LAMS were designed for transluminal drainage sealing the cavities and overcoming the risk of AE such as leak and migration. Current indications for the use of LAMS include drainage of the gallbladder in patients unfit for cholecystectomy and for pancreatic fluid collections, including pseudocysts and WON. In addition to these drainage procedures, LAMS has been used for the creation and maintenance of enteroenterostomies, including gastrojejunostomy for malignant gastric outlet obstruction and gastrogastrostomy for papillary access in patients with Roux-en-y gastric bypass. The potential complications related to LAMS deployment are partial or failed stent expansion, stent collapse, device failure including failure to deliver the stent, stent migration/dislodgement, adverse reaction to implant and/or delivery system (e.g., abdominal or back pain, nausea, infection, fever, chronic inflammation/foreign body reaction), minor or excessive bleeding (requiring intervention), leakage of pseudocyst or bowel contents/peritonitis, tissue damage during stent implantation and/or removal, ulceration or erosion of mucosal or organ wall linings, pneumoperitoneum, and perforation.

There are various types of LAMS (Table 35.4). Currently, the AXIOS™ stent (Boston Scientific, Marlborough, MA) is the only commercially available LAMS in the United States. It consists of double-walled flanges that are perpendicular to the lumen and hold the tissue walls in apposition. Fully expanded, the flange diameter is approximately twice that of the stent lumen. The stent flanges are designed to distribute pressure evenly on the luminal wall. The stent is made of braided nitinol wire and is fully covered to prevent tissue ingrowth and tract leakage as well as enable removability. Depending on the target for drainage, the AXIOS™ stent has been custom designed for this purpose with lumen diameters of 10 and 15 mm for trans-enteric drainage of adjacent organ/collections [13]. Additionally, the stent serves as an access port for endoscopy-guided therapy, irrigation, and debridement.

Recently, the 10-Fr AXIOS™ stent delivery system has been modified to combine a diathermic ring and cut-wire to provide easy access into target tissue through the GI tract

Table 35.4 Technical characteristics of the lumen apposing metal stents

Producer	Model	Internal diameter (mm)	Length (mm)	Flange diameter (mm)
Boston scientific	AXIOS	10, 15	10	21, 24
Leufen medical	Aix	10, 14	20	14/16, 18/20
M.I. Tech	Hanarostent BCF	10, 12	30, 40	25
TaeWoong medical	Spaxus	8, 10, 16	20	25
TaeWoong medical	Nagi	10, 12, 14, 16	10, 20, 30	22, 24, 26, 28

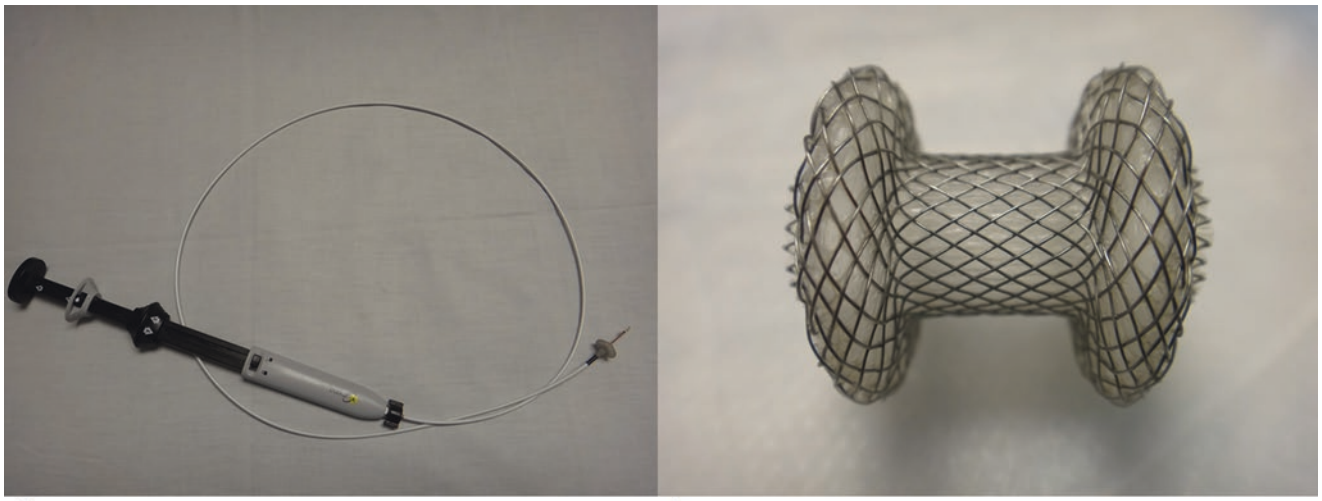

Fig. 35.2 (**a**) AXIOS™ cautery enhanced delivery system composed of a catheter, the catheter lock, the catheter control hub, and the catheter deployment hub. (**b**) Expanded stent

wall and obviate the need for dilation to deploy the stent (Fig. 35.2).

EUS-guided drainage has become the primary management modality for symptomatic pancreatic fluid collections (PFCs). Although the overall long-term clinical success of plastic stents for the drainage of pseudocysts is high, trials have demonstrated that the success rates depends on the type of PFC. Plastic stents are prone to early occlusion when draining WON, leading to PFC infection and the need for repeat endoscopic therapy [14]. FCSEMS have also shown efficacy in drainage of WON but are limited by their small luminal diameter, which can become occluded with debris, and by the inability to pass the endoscopes through the FCSEMS for debridement procedures [15]. Placement of larger caliber diameter stents may enable effective resolution of PFCs and particularly WON.

In a retrospective study by Siddiqui et al. with 82 cases of PFCs, 14 pancreatic pseudocysts (PPs), and 68 WON, long-term success with endoscopic therapy of PPs by using LAMSs was achieved in all patients (100%) and 88.2% for WON [14]. In another study by Sharaiha et al., technical success for placement of the LAMS in 124 patients with WON was achieved in all (100%), and clinical success with successful endoscopic eradication of the WON was achieved in 86.3% [15].

EUS-guided gallbladder drainage (EUS-GBD) is a relatively new approach with limited published data [2]. In a multicenter prospective study by Walter et al., where the authors determined the feasibility and safety of the use of LAMS for EUS-GBD in high-risk surgical patients with acute cholecystitis, 30 patients were included. Technical success was achieved in 27 of 30 patients (90%) and clinical success in 26 of 27 patients (96%). LAMS removal was performed in 15 of 30 patients (50%) after a mean of 91 days. In 15 patients (50%), no LAMS removal was performed because of death, significant tissue overgrowth, or other causes. A total of 15 serious AE (50%) were reported, including four that were possibly stent-related or procedure-related (13%). Overall mortality was 23% (7/30), with 30-day mortality of 17% (5/30). The 30-day mortality in this study is comparable with the 30-day mortality or in hospital death of 15.4% after percutaneous transhepatic gallbladder drainage (PTGBD). However, the rate of nonfatal AE (n = 9, 30%) is substantially higher than reported for PTGBD (15%). One explanation for this high complication rate could be the relatively poor clinical condition of patients in the study [16].

Another application of LAMS is EUS-guided enteroenterostomies (EUS-EE). Surgical EE has been the standard treatment for gastric outlet obstruction (GOO) associated with good functional outcome and long-term relief of symptoms [17]. Nevertheless, it is associated with an increased risk of AE (mainly infections) and increased length of hospital stay. To date, there have only been two major techniques for EUS-EE, namely, water-filling technique and water-inflated balloon technique. Itoi et al. described the first prospective clinical study of EUS-guided double-balloon-occluded gastrojejunostomy bypass (EPASS) using a LAMS, in which the procedure was performed in 20 patients with malignant GOO. The double-balloon tube was correctly inserted into the jejunum across from the stomach in all cases. The technical success rate of stent placement was 90%. No stent occlusion or migration was observed in 18 cases during the follow-up period (median 100 days) [17].

In another study by Khashab et al., ten patients underwent EUS-EE. One patient had complete GOO and underwent successful direct EUS-GE. In the remaining nine patients, EPASS was attempted and was successful in eight. Thus, technical success occurred in nine patients (90%), and clinical success with resumption of solid oral intake was achieved in all nine patients (100%) [18].

Recently, a EUS-guided procedure for access to the major and minor papilla in patients with Roux-en-Y gastric bypass has been developed, termed internal EUS-directed transgastric ERCP (EDGE). This technique involves accessing the excluded stomach from the gastric pouch by placing a lumen-apposing metal stent (LAMS) across a fistula tract with EUS guidance, and subsequently performing conventional ERCP through the LAMS [19]. Patients with altered anatomy such as Roux-en-Y gastric bypass pose distinct challenges to performing ERCP. Deep enteroscopy-assisted ERCP has a success rate of 63% that is dependent on the length of the Roux limb. In a trial by Kedia et al., five patients had EUS-guided creation of a gastrogastric fistula or jejunogastric fistula via placement of a LAMS, and it was successful in all cases (100%). ERCP through the newly created fistula at the time of the index procedure was successful in three of five cases (60%). In two patients, there was an inability to pass the duodenoscope after placement of the LAMS. To avoid the risk of stent dislodgement, ERCP was postponed in these cases. There were no AE such as bleeding, perforation, peritonitis, or pancreatitis. There was an incidence of stent dislodgement during the procedure in three cases likely because of over dilation of the 15 mm stent lumen to 18 mm within an immature fistulous tract and/or traction on the stent from the endoscope [20]. Risk of dislodgement can be decreased by avoiding over dilation of the LAMS lumen (maximum 15 mm) and lubricating the shaft of the duodenoscope. In patients without an emergent need for ERCP, performing the EDGE procedure in two sessions can be considered if there is concern for the possibility of stent dislodgement during the index procedure. Another study published by Tyberg et al., in which 16 patients underwent EDGE, technical success was 100%. Clinical success was 90%; five patients were awaiting maturation of the fistula tract prior to ERCP, and one patient had an aborted ERCP due to perforation. One perforation occurred, which was managed endoscopically. Three patients experienced stent dislodgement; all stents were successfully repositioned or bridged with a second stent [21]. There are concerns associated with the utilization of EDGE. The procedure carries a risk of weight gain due to the formation of a gastro-gastric or enterogastric fistula, reversing the benefit of the surgical bypass. However, the fistula remains patent for only a short time before closure, and any weight gain would likely be outweighed by the benefit of the procedure.

EUS-Guided Fiducials Placement

Radiation therapy has an important role in the treatment of different locally advanced or metastatic malignancies and can be used alone or in conjunction with surgery and/or systemic chemotherapy. Fiducial markers are radiopaque spheres, coils, or seeds that are implanted into the targeted lesion for both localizing and tracking during radiotherapy. Traditional fiducials are cylindrical gold seeds, measuring 3 to 5 mm long and 0.75 to 1.2 mm in diameter, and are delivered using a 19-gauge needle. The new smaller and longer fiducial markers are 10 mm long and 0.28 or 0.35 mm in diameter and are available preloaded on a needle carrier delivery device for use with a 22-gauge needle. Fiducials can be placed surgically or percutaneously under ultrasound or computed tomography guidance or by EUS. EUS-guided fiducial placement has been reported for mediastinal tumors, prostate cancer, and gastrointestinal malignancies, including pancreatic cancers, hepatic malignancies, cholangiocarcinomas, as well as esophageal, gastric, and colon cancers [22]. Another indication would be to aid in parenchymal-sparing pancreatic surgery in cases of small pancreatic neuroendocrine tumors, since localization of these small tumors at surgery can be difficult [23].

Currently, the only Food and Drug Administration-approved fiducial needle is the EchoTip fiducial needle manufactured by Cook Medical (Bloomington, IN, US). This is a 22-gauge needle that contains four gold fiducial markers. Another preloaded fiducial needle model is currently being launched by Medtronic (Sunnyvale, CA, US). The Beacon® Fine Needle fiducial system in both 19 and 22-gauge needles comes preloaded with two fiducial markers [2] (Fig. 35.3).

In a study by Choi JH et al., 32 consecutive patients who were scheduled to receive radiation therapy for pancreatic and hepatic malignancies were referred for EUS-guided fiducial placement. All 32 patients had successful fiducial placement under EUS guidance. The mean number of fiducials placed per patient was 2.94 ± 0.24 (range, 2 to 3 seeds). Spontaneous fiducial migration was noted in one patient (3.1%). Of the 32 patients, 29 patients (90.6%) successfully underwent radiation therapy. One patient (3.1%) developed mild pancreatitis, requiring a 2-day prolonged hospitalization after fiducial placement. Five patients (15.6%) underwent same-session, EUS-guided fine needle aspiration for histologic confirmation at the time of fiducial placement, without any procedure-related AE [24].

Khashab MA et al. studied two kinds of commercially available fiducials: traditional fiducials (TFs) (5 mm length, 0.8 mm diameter) delivered by a 19-gauge needle and Visicoil fiducials (Core Oncology, Santa Barbara, Calif) (VFs) (10 mm length, 0.35 mm diameter) delivered by a 22-gauge needle. A total of 39 patients with locally advanced pancreatic cancer underwent EUS-guided placement of 103

Fig. 35.3 (**a**, **b**) The Beacon® Fine Needle fiducial system

fiducials (77 TFs, 26 VFs). Visibility was significantly better for TFs compared with VFs. The rates of fiducial migration were similar between them. There was no difference in the mean number of fiducials placed, indicating a similar degree of technical difficulty for TF and VF deployment [25].

The feasibility of EUS-guided fiducial placement with or without fluoroscopy for locally advanced and recurrent pancreatic cancer has been reported with technical success rates of 85–100% [22].

EUS Guided Radiofrequency Ablation

The Habib™ EndoHPB (Emcision, London, UK) is a novel endoscopic bipolar radiofrequency (RF) probe developed to ablate tissue in the gastrointestinal tract.

This probe consists of a 1 Fr wire that has a working length of 220 cm and can be passed through a standard 19 or 22-gauge EUS needle. Radiofrequency power is applied to the 20 mm electrode at the end of the wire to cauterize or coagulate tissue [2].

In a prospective, multicenter trial by Pai M et al., eight patients, six had a pancreatic cystic neoplasm (four a mucinous cyst, one had intraductal papillary mucinous neoplasm, and one a microcystic adenoma) and two had a neuroendocrine tumors (NET) in the head of pancreas. The mean size of the cystic neoplasm and NET were 36.5 mm (SD ± 17.9 mm) and 27.5 mm (SD ± 17.7 mm), respectively. The EUS-RFA was successfully completed in all cases. Among the six patients with a cystic neoplasm, post-procedure imaging in 3–6 months showed complete resolution of the cysts in two cases and 48.4% reduction [mean pre RF 38.8 mm (SD ± 21.7 mm) vs mean post RF 20 mm (SD ± 17.1 mm)] in size in three cases. In regards to the NET patients, there was a change in vascularity and central necrosis after EUS-RFA. No major complications were observed within 48 h of the procedure. Two patients had mild abdominal pain that resolved within 3 days [26].

This RF catheter can be used by the endoscopist for tumors in the bile duct and head of pancreas. It allows partial destruction of the tumor prior to stent insertion, which can result in longer stent patency by delaying tumor growth, and can also be used to clear obstructed metal stents.

An 18-gauge RFA needle and a VIVA RF generator (STARmed, Goyang, Korea) with a working length of 150 cm and a 10 mm electrode in the needle tip have also been studied in six patients with unresectable pancreatic cancer. The procedure was technically successful in all patients with the only adverse event being post-procedure pain in two patients [2].

Practical Considerations

- 1 Fr wire that requires a 19 or 22-gauge FNA needle
- 20 mm electrode at the tip of the wire
- Primary indication is for bile duct and pancreatic tumors

Confocal Laser Endomicroscopy

Confocal laser endomicroscopy (CLE) is a novel endoscopic method that enables imaging at a subcellular level of resolution during endoscopy, allowing up to 1000-fold magnification of tissue and providing an optical biopsy. CLE is based on tissue illumination with a low-power laser with subsequent detection of the fluorescence of light reflected from the tissue through a pinhole. The term confocal refers to the alignment of both illumination and collection systems in the

same focal plane. The laser light is focused at a selected depth in the tissue of interest, and reflected light is then refocused onto the detection system by the same lens. Only returning light refocused through the pinhole is detected. The light reflected and scattered at other geometric angles from the illuminated object or refocused out of plane with the pinhole is excluded from detection. This dramatically increases the spatial resolution of CLE allowing cellular imaging and evaluation of tissue architecture at the focal plane during endoscopy. Confocal imaging can be based on tissue reflectance or fluorescence. Confocal devices based on tissue reflectance do not require any contrast agents, but current prototypes using 2-photon strategies have relatively low resolution, which significantly compromise in vivo imaging and clinical utility. CLE by using topical and/or intravenous fluorescence contrast agents generates images with resolution similar to traditional histological examination. CLE systems have included through-the-scope probes or dedicated endoscopes with integrated CLE systems [27].

CLE is being primarily used for the evaluation of pancreatic cystic neoplasms (PCNs) since the differentiation of mucinous from non-mucinous cysts is important because mucinous cysts such as intraductal papillary mucinous neoplasm (IPMN) and mucinous cystic neoplasm (MCN) have malignant potential and may require interval surveillance or surgery, whereas non-mucinous cysts like serous cystadenoma (SCA) and pseudocysts are benign. The diagnosis of pancreatic cystic neoplasms (PCNs), which now depends on morphology, cytology, and fluid analysis, remains challenging [28].

A novel CLE probe that can be inserted through a 19-gauge FNA needle allows for needle-based CLE (nCLE) (AQ-Flex™ Celvizio®, Mauna Kea Technologies, Inc., Suwanee, GA). The depth of imaging is 40 to 70 μm, the maximal field of view is 325 μm, and resolution is 3.5 μm. The probe can be reused for as many as ten examinations [2].

The recent INSPECT (pilot study of in vivo identification of pancreatic cystic neoplasms with needle-based confocal laser endomicroscopy under endosonographic guidance) study assessed both the diagnostic potential of nCLE in differentiating cyst types and the safety of the technique. A total of 66 patients underwent nCLE imaging and images were available for 65. The presence of epithelial villous structures based on nCLE was associated with PCNs ($P = 0.004$) and provided a sensitivity of 59%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 50%. The overall complication rate was 9% and included pancreatitis ($n = 2$), transient abdominal pain ($n = 1$), and intracystic bleeding not requiring any further measures ($n = 3$) [28].

The DETECT (Diagnosis of Pancreatic Cysts: Endoscopic Ultrasound-guided, Through-the-Needle Confocal Laser-Induced Endomicroscopy and Cystoscopy) Trial evaluated the feasibility, safety, and diagnostic yield of the combination of cystoscopy and nCLE in the clinical diagnosis of PCNs in 30 patients. The procedure was technically successful with the exception of one probe exchange failure. In two patients (7%), post-procedure pancreatitis developed. Specific features associated with the clinical diagnosis of mucinous cysts were identified: mucin on cystoscopy and papillary projections and dark rings on nCLE. The sensitivity of cystoscopy was 90% (9/10), and that of nCLE was 80% (8/10), and the combination was 100% (10/10) in 18 high-certainty patients. On nCLE, villous structures defined as papillary projections and dark rings are both sensitive and specific for mucinous cysts. Of note, nCLE findings were heterogeneous, and these villous structures were focally seen. Therefore, authors needed to image multiple areas by moving the nCLE probe to reduce sampling errors [29].

In a study by Napoleon et al. 31 patients with a solitary pancreatic cystic lesion of unknown diagnosis were prospectively included at three centers. EUS-FNA was combined with nCLE. The final diagnosis was based on either a stringent gold standard (surgical specimen and/or positive cytopathology) or a committee consensus. Investigators reviewed nCLE sequences from patients with the most stringent final diagnosis and identified a single feature that was only present in serous cystadenoma (SCA). A superficial vascular network pattern visualized on nCLE was identified as the criterion. It corresponded on pathological specimen to a dense and subepithelial capillary vascularization only seen in SCA. The accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of this sign for the diagnosis of SCA were 87%, 69%, 100%, 100%, and 82%, respectively [30].

Practical Considerations

- CLE probe requires a 19-gauge FNA needle.
- The probe can be reused for as many as ten examinations.
- Primarily used for the evaluation of pancreatic cystic neoplasms (PCNs).

Another study aimed to describe nCLE interpretation criteria for the characterization of pancreatic masses, with histopathological correlation, and to perform the first validation of these criteria. A total of 40 patients were evaluated by EUS-FNA combined with nCLE for the diagnosis of pancreatic masses. Final diagnosis was based on EUS-FNA histology and follow-up at 1 year. The nCLE criteria were described for adenocarcinoma (dark cell aggregates, irregular vessels with leakages of fluorescein), chronic pancreatitis (residual regular glandular pancreatic structures), and neuroendocrine tumors (NET) (black cell aggregates surrounded

by vessels and fibrotic areas). A conclusive nCLE result was obtained in 75% of cases (96% correct). Statistical evaluation provided promising results, with high specificity and negative and positive predictive values for all types of pancreatic masses [31].

Currently the EUS needles that support the use of the nCLE are the 19-gauge EchoTip®, EZShot 2, 19-gauge Expect™ Needle Flex, SonoTip® Proc Control, SonoTip® II, and 19-gauge BNX fine needle aspiration system (Beacon). Other types of needles are not recommended.

Endoscopic Ultrasound Elastography

Elastography is an ultrasound modality that provides images and measurements related to tissue stiffness. The basis for elastography is the fact that many different pathologic processes, including inflammation, fibrosis, and cancer, induce alterations in tissue stiffness. Elastography evaluates tissue stiffness through the application of slight compression of the target tissue using an ultrasound transducer and recording the resulting tissue displacement in the examined field [32]. Physiologic vascular pulsations and respiratory movements provide the vibrations and compressions necessary for the recording. An image stable for at least 5 s is required for the final color pattern characterization because the colors can fluctuate.

There are two types of elastography: qualitative and quantitative. Qualitative elastography relies on the quantification of the compression-induced deformation of the structures in the B-mode image using the degree of deformation as an indicator of tissue stiffness. Elasticity (on a scale of 1 to 255) is depicted using a color map (red-green-blue), where hard tissue is shown in dark blue, medium hard tissue in cyan, tissue with intermediate hardness in green, medium soft tissue in yellow, and soft tissue in red [32, 33]. Quantitative elastrography uses a hue histogram or a strain ratio. The hue histogram is a graphical representation of the color distribution (hues) in a selected image field. Hue histograms are based on the qualitative EUS elastography data for a manually selected region of interest (ROI) within the standard elastography image. Strain ratio calculation is based on standard qualitative EUS elastography (EUS-E) data. Two different areas (A and B) are selected. Area A is selected so that it includes as much of the target lesion as possible without including the surrounding tissues. Area B is selected within a soft (red) reference area outside the target lesion, preferably the gut wall. The strain ratio is then calculated as the quotient of B/A [33].

EUS-E assess the elasticity of tumors in the proximity of the digestive tract that are hard to reach with conventional transcutaneous ultrasound probes, such as pancreatic masses and mediastinal or abdominal lymph nodes, thus improving the diagnostic yield of the procedure. The accuracy of EUS-FNA is affected by the selection of the targeted area within the lesion to be assessed. EUS-E can show the hardest areas within the lesion, thus being useful for the selection of the most suspicious area to be targeted for EUS-FNA. Although EUS-E at present cannot replace EUS-FNA for the diagnosis of a focal lesion located in the pancreas or for assessing enlarged lymph nodes, it still may be a useful adjunct for guiding further clinical management when EUS-FNA is negative or inconclusive. EUS-E is only applied to assess the elasticity of solid lesions based on its principles, while cystic lesions are usually shown as an artifact. The current clinical indications of EUS-E are mainly solid pancreatic lesions, submucosal GI masses, lymph nodes, focal left liver lesions, and left adrenal lesions [34].

The first study of EUS-E in pancreatic solid lesions was published in 2006 by Giovannini et al. A total of 24 pancreatic masses were analyzed using a subjective scoring system based on the different color patterns of the images. The lesions that appear mainly blue (harder) were classified as malignancies. Based on this classification, the sensitivity and specificity of the malignancy detection was 100% and 67%, respectively [35]. A subsequent multicenter trial in 2009, Giovanni et al. reported EUS-E findings in 121 cases with pancreatic masses. They used the classification they previously made, classifying scores of 1 and 2 as benign, and 3 to 5 as malignant. The sensitivity, specificity, positive predictive value, and negative predictive value of the differentiation between benign and malignant pancreatic masses were 92.3%, 80.0%, 93.3%, and 77.4%, respectively, and an overall accuracy of 89.2% [36].

Diagnosis of pancreatic exocrine insufficiency (PEI) is limited by methodological difficulties of pancreatic function tests. The probability of PEI in chronic pancreatitis (CP) increases as pancreatic fibrosis develops. Pancreatic fibrosis in CP may be quantified by EUS-E. In a prospective trial by Dominguez-Muñoz JE et al., the authors evaluated whether EUS-E could predict PEI in patients with CP. Diagnosis of PEI was based on the (13)C-mixed triglyceride breath test. EUS-E was performed. Two areas were selected for elastographic evaluation: area A corresponds to the pancreatic parenchyma and area B to a soft peripancreatic reference area. The strain ratio (SR) (quotient B/A) was considered the elastographic result. A total of 115 patients with CP of different etiologies were included; 35 patients (30.4%) had PEI. Pancreatic SR was higher in patients with PEI (4.89; 95% confidence interval, 4.36–5.41) than in those with a normal breath test result (2.99; 95% confidence interval, 2.82–3.16) ($P < 0.001$). A direct relationship was found between the SR and the probability of PEI, which increases from 4.2% in patients with an SR less than 2.5% to 92.8% in those with an SR greater than >5.5 [37].

EUS-E may be helpful for the differential diagnosis of benign and malignant lymph nodes or to select the more suspicious nodes to be targeted for EUS-FNA [34].

Currently EUS-E is available with Pentax echoendoscopes CLA-EUS EG-3870UTK and radial array EG-3670URK in combination with the HI VISION™ Preirus™ ultrasound scanner from Hitachi-Aloka (Wallingford, CT) and the

EU-ME2 ultrasound processor from Olympus (Center Valley, PA) with the Olympus EUS echoendoscopes.

The limitations of EUS-E are the following:

1. Both qualitative and quantitative methods are observer dependent with operator bias in the selection of ROI and areas for analysis, which could cause intra- and interobserver variability.
2. It is difficult to control the tissue compression by the endosonographer, and excessive pressure applied to the tissues can artificially increase their strain.
3. Since a high-frequency transducer is used in the EUS-E, the depth of penetration is limited; thus, only the organ or part of the organ near the GI tract can be imaged.
4. Presence of motion artifacts.
5. The strain value can be impacted by the vessels, cysts, and bones in the selected ROI.
6. The strain value may be also impacted if there is insufficient surrounding "normal tissue" [34].

Practical Considerations

- Elastography provides images and measurements related to tissue stiffness.
- Pathologic processes induce alterations in tissue stiffness.
- EUS-E is only applied to assess the elasticity of solid lesions.
- EUS-E is useful for the selection of the most suspicious area within a lesion to be targeted for EUS-FNA.

Emergent indications include the use of EUS-E for the characterization of lesions located in the liver, biliary tract, adrenal glands, and GI tract including subepithelial lesions and rectal lesions. Still, additional evidence is required to define the role of EUS-E in these clinical applications.

Conclusions

In conclusion, modern EUS clinical practice has evolve and presently has the capability of performing advanced therapeutic procedures that could only be resolved by surgery or interventional radiology in the past. This could represent less morbidity and mortality to patients. There are many different instruments and accessories that can be used to accomplish these interventions. The selection of the type of endoscopic ultrasound instrument as well as the specific type(s) of accessory(ies) will depend on the type of intervention planned.

References

1. ASGE, Technology Committee, Murad FM, Komanduri S, et al. Echoendoscopes. Gastrointest Endosc. 2015;82(2):189–202
2. Chapman C, Siddiqui U. New scopes, new accessories, new stents for interventional endoscopic ultrasound. Clin Endosc. 2016;49(1):41–6
3. Voermans R, Ponchon T, et al. Forward-viewing versus oblique-viewing echoendoscopes in transluminal drainage of pancreatic fluid collections: a multicenter, randomized, controlled trial. Gastrointest Endosc. 2011;74(6):1285–93
4. Ippei M, Ryoji M, et al. Forward-viewing versus oblique-viewing echoendoscopes in the diagnosis of upper GI subepithelial lesions with EUS-guided FNA: a prospective, randomized, crossover study. Gastrointest Endosc. 2015;82(2):287–95
5. Fuccio L, Attili F, et al. Moving EUS forward-viewing: ready for prime time? Gastrointest Endosc. 2015;82(2):296–8
6. ASGE Technology status evaluation report, Liu J, Carpenter S, et al. Endoscopic ultrasound probes. Gastrointest Endosc. 2006;63(6):751–4
7. Tang SJ, Vilmann AS, et al. EUS needle identification comparison and evaluation study (with videos). Gastrointest Endosc. 2016;84(3):424–33
8. Alper E, Onur İ, et al. Endoscopic ultrasound-guided tissue sampling: how can we improve the results? Turk J Gastroenterol. 2016;27(1):1–3
9. Kim GH, Cho YK, et al. Comparison of 22-gauge aspiration needle with 22-gauge biopsy needle in endoscopic ultrasonography-guided subepithelial tumor sampling. Scand J Gastroenterol. 2014;49(3):347–54
10. Kandel P, Tranesh G, et al. EUS-guided fine needle biopsy sampling using a novel fork-tip needle: a case-control study. Gastrointest Endosc. 2016;84(6):1034–9
11. Adler DG, Witt B, et al. Pathologic evaluation of a new endoscopic ultrasound needle designed to obtain core tissue samples: a pilot study. Endosc Ultrasound. 2016;5(3):178–83
12. Shakhatreh MH, Naini SH, et al. Use of a novel through-the-needle biopsy forceps in endoscopic ultrasound. Endosc Int Open. 2016;4(4):E439–42
13. Weilert F, Binmoeller K. Endoscopic ultrasound-assisted Pancreaticobiliary access. Gastrointest Endosc Clin N Am. 2015;25(4):805–26
14. Siddiqui A, Adler D, et al. EUS-guided drainage of peripancreatic fluid collections and necrosis by using a novel lumen-apposing stent: a large retrospective, multicenter U.S. experience. Gastrointest Endosc. 2016;83(4):699–707
15. Sharaiha RZ, Tyberg A, et al. Endoscopic therapy with lumen-apposing metal stents is safe and effective for patients with pancreatic walled-off necrosis. Clin Gastroenterol Hepatol. 2016;14(12):1797–803
16. Walter D, Teoh AY, et al. EUS-guided gall bladder drainage with a lumen-apposing metal stent: a prospective long-term evaluation. Gut. 2016;65(1):6–8
17. Itoi T, Ishii K, et al. Prospective evaluation of endoscopic ultrasonography-guided double-balloon-occluded gastrojejunostomy bypass (EPASS) for malignant gastric outlet obstruction. Gut. 2016;65(2):193–5
18. Khashab MA, Kumbhari V, et al. EUS-guided gastroenterostomy: the first U.S. clinical experience (with video). Gastrointest Endosc. 2015;82(5):932–8
19. Tyberg A, Nieto J, et al. Endoscopic ultrasound (EUS)-directed transgastric endoscopic retrograde cholangiopancreatography or EUS: mid-term analysis of an emerging procedure. Clin Endosc. 2016;50(2):185
20. Kedia P, Tyberg A, et al. EUS-directed transgastric ERCP for roux-en-Y gastric bypass anatomy: a minimally invasive approach. Gastrointest Endosc. 2015;82(3):560–5

21. Tyberg A, Nieto J, et al. Endoscopic ultrasound (EUS)-directed Transgastric endoscopic retrograde cholangiopancreatography or EUS: mid-term analysis of an emerging procedure. Clin Endosc. 2016;19:1–6
22. Chavalitdhamrong D, DiMaio CJ, et al. Technical advances in endoscopic ultrasound-guided fiducial placement for the treatment of pancreatic cancer. Endosc Int Open. 2015;3(4):E373–7
23. Law JK, Singh VK, et al. Endoscopic ultrasound (EUS)-guided fiducial placement allows localization of small neuroendocrine tumors during parenchymal-sparing pancreatic surgery. Surg Endosc. 2013;27(10):3921–6
24. Choi JH, Seo DW, et al. Fiducial placement for stereotactic body radiation therapy under only endoscopic ultrasonography guidance in pancreatic and hepatic malignancy: practical feasibility and safety. Gut Liver. 2014;8(1):88–93
25. Khashab MA, Kim KJ, et al. Comparative analysis of traditional and coiled fiducials implanted during EUS for pancreatic cancer patients receiving stereotactic body radiation therapy. Gastrointest Endosc. 2012;76(5):962–71
26. Pai M, Habib N, et al. Endoscopic ultrasound guided radiofrequency ablation, for pancreatic cystic neoplasms and neuroendocrine tumors. World J Gastrointest Surg. 2015;7(4):52–9
27. ASGE Technology Committee. Confocal laser endomicroscopy. Gastrointest Endosc. 2014;80(6):928–38
28. Konda VJ, Meining A, et al. A pilot study of in vivo identification of pancreatic cystic neoplasms with needle-based confocal laser endomicroscopy under endosonographic guidance. Endoscopy. 2013;45(12):1006–13
29. Nakai Y, Iwashita T, et al. Diagnosis of pancreatic cysts: EUS-guided, through-the-needle confocal laser-induced endomicroscopy and cystoscopy trial: DETECT study. Gastrointest Endosc. 2015;81(5):1204–14
30. Napoléon B, Lemaistre AI, et al. A novel approach to the diagnosis of pancreatic serous cystadenoma: needle-based confocal laser endomicroscopy. Endoscopy. 2015;47(01):26–32
31. Giovannini M, Caillo F, et al. Endoscopic ultrasound-guided needle-based confocal laser endomicroscopy in solid pancreatic masses. Endoscopy. 2016;48(10):892–8
32. Kamata K, Kitano M, et al. New endoscopic ultrasonography techniques for pancreaticobiliary diseases. Ultrasonography. 2016;35(3):169–79
33. Iglesias-Garcia J, Lindkvist B, et al. Endoscopic ultrasound elastography. Endosc Ultrasound. 2012;1(1):8–16
34. Cui XW, Chang JM, et al. Endoscopic ultrasound elastography: current status and future perspectives. World J Gastroenterol. 2015;21(47):13212–24
35. Giovannini M, Hookey LC, et al. Endoscopic ultrasound elastography: the first step towards virtual biopsy? Preliminary results in 49 patients. Endoscopy. 2006;38(4):344–8
36. Giovannini M, Thomas B, et al. Endoscopic ultrasound elastography for evaluation of lymph nodes and pancreatic masses: a multicenter study. World J Gastroenterol. 2009;15(13):1587–93
37. Dominguez-Muñoz JE, Iglesias-Garcia J, et al. EUS elastography to predict pancreatic exocrine insufficiency in patients with chronic pancreatitis. Gastrointest Endosc. 2015;81(1):136–42

Contrast-Enhanced Endoscopic Ultrasound (CE-EUS)

36

Roald F. Havre, Adrian Saftoiu, Manoop S. Bhutani, and Peter Vilmann

Introduction

Blood-pool ultrasound contrast agents (UCSs) have the ability to image blood flow in soft tissues, which can be visualized at capillary level. Color Doppler has been integrated in EUS equipment since the introduction of electronic transducers and is able to visualize blood flow and its direction in small arteries and veins but not blood flow in capillaries or perfusion. Visualization of perfusion by contrast agents represents a new step in flow imaging and may separate hyper- and hypoperfused areas in tissue. This may be useful for tissue characterization and identification of tumors or abscesses or to guide intervention and tissue sampling.

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Instruments and Accessories

How to Acquire CE-EUS Movies and to Analyze Them

In order to acquire data for a CE-EUS uptake, you need a standard electronic EUS endoscope and a scanner which is set up with software for contrast harmonic imaging mode. The contrast mode usually has a split-screen interface with one image showing the B-mode image and the other showing an image where the tissue signal is subtracted. This image will be tuned to visualize the nonlinear scattering of US by the contrast bubbles as they pass into the region of interest (ROI) by the feeding vessels and then into the capillaries before they are washed out by the veins. A bolus traction recording is used to visualize differences between the arterial phase and the venous phase and for liver scanning of the intermittent portal phase. The recording can be interpreted in real time, or the recording can be analyzed with use of dedicated software that can analyze the distribution of UCA in user-selected areas of the image plane (Fig. 36.2f). By this software it is possible to measure several parameters such as peak intensity, time to peak intensity, wash-in time, washout time, and area under the time-intensity curve (TIC). Another approach to do the contrast examination is to use the flash mode which emits a short train of high mechanical index (MI) US bursts, which serves to crush the contrast bubbles in the imaging plane and then record the influx of new contrast bubbles during the late (steady state) phase of contrast distribution. This is sometimes useful if the arterial phase has to be examined again, e.g., in the situation of multiple pancreatic or liver masses, without the need of injecting a second i.v. bolus of the contrast agent.

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Use of Contrast Agents in EUS

Second-generation UCAs are made of inert gases in small bubbles in a phospholipid layer. The size, gas, and the composition of phospholipids make the basic properties of the contrast agent such as size distribution and frailness. UCAs are often pegylated to counteract bubble coalescence [1]. The most used contrast agents in EUS, which we will focus on in this chapter, are phospholipid covered UCAs, sulfur hexafluoride (Sonovue®, Bracco), and perfluorbutane (Sonazoid®, GE Healthcare) that has been utilized in Japan and Korea [2–4].

UCAs are usually administered intravenously in a large cubital vein using an i.v. line of at least 22 G and gentle syringe pressure. The patient must be fasting as for any other upper endoscopic procedure, but no other preparation is required which enables the sonographer to use UCAs immediately during a procedure if indicated by the image findings. It is of importance to select an image section representing both the lesion of interest and some surrounding tissue for reference. It is also important that the image can be maintained in a stable position throughout the recording time especially if one intends to use post-processing software for time-intensity curve (TIC) analysis.

Practical Considerations

- The size, gas, and the composition of phospholipids make the basic properties of the contrast agents.
- The patient must fast as for any other upper endoscopic procedure.

The Procedure

The UCAs come as freeze-dried powder and are reconstituted by injecting saline/sterile water and shaking the vial. When using Sonovue in CE-EUS, injecting a full vial (4.8 ml) is recommended. The contrast mode image is usually shown side by side with the B-mode image in a split screen setting. Before the administration of contrast media, the contrast mode image should only be showing minor tissue elements. The contrast injection should be recorded for at least 60 s in order to be able to reevaluate or to analyze the injection sequence using a TIC. The first 30 s corresponds to the arterial phase in most organs, in the liver, this is followed by the portal venous phase (30–60 s) and, finally, a venous phase after 60 s. In other organs the venous phase starts usually immediately after the arterial phase at approximately 30 s. The passage time will vary from organ to organ and will overlap. As the contrast media enter in capillaries, the parenchyma of the insonified tissue increases in brightness (Fig. 36.1). The temporal difference in the signal intensity (brightness) from the surrounding parenchyma is an important feature. Early washout or a hypoenhancing focal lesion may be a sign of neoplastic disease (Figs. 36.1a, b and 36.2e, f).

In EUS, the US frequency is higher than in transcutaneous contrast-enhanced ultrasound (CEUS), 7.5–12 Mhz. With these frequencies, a lower portion of the gas-filled bubbles are recruited to oscillate and to return a visible, nonlinear signal to the US probe; hence, a higher dose is needed, and the contrast agent may still seem to have a modest increase in signal intensity as it flows through the scanning plane compared to the low-frequency transcutaneous probes.

The Mechanical Index (MI)

The mechanical index (MI) is defined as the peak negative pressure caused by the US wave divided by the square root of the frequency. This can be adjusted and should not be higher than 1.9 in any US scanning. MI is always available on the US scanner screen. Initially, US contrast agents were used as a color or power Doppler enhancer, and the scanning was performed with high MI (>0.5). Contrast agents can be thus used to visualize macrovasculature on B-mode or by color Doppler, acting as signal enhancers during a high-MI examination mode.

Using UCAs to visualize microvasculature and perfusion requires low MI settings and harmonic imaging protocols based on the second harmonic. Under low MI (0.1–0.3) the contrast bubbles do not break under influence of the US scanning, but they are brought into resonance and act as sound emitters. Consequently, the signal-to-noise ratio is improved and allows the depiction of microvascular signals, without tissue-induced artifacts. By pushing the flash button in contrast mode, a short train of pulses with high MI can be transmitted, and all contrast bubbles in the scanning plane can be broken. This may be useful for a reconsideration of the arterial phase in a different section or lesion after the bolus has passed and the UCAs remain in circulation for some time.

For safety intentions, using a low MI in contrast scanning produces less biological cell damage in biological models [5].

Practical Considerations

- When using Sonovue in CE-EUS, injecting a full vial (4.8 ml) is recommended.
- The contrast injection should be recorded for at least 60 s in order to be able to reevaluate or to analyze the injection sequence using a TIC.
- The first 30 s corresponds to the arterial phase in most organs.
- In the liver the arterial phase is followed by the portal venous phase (30–60 s) and finally, a venous phase after 60 s.

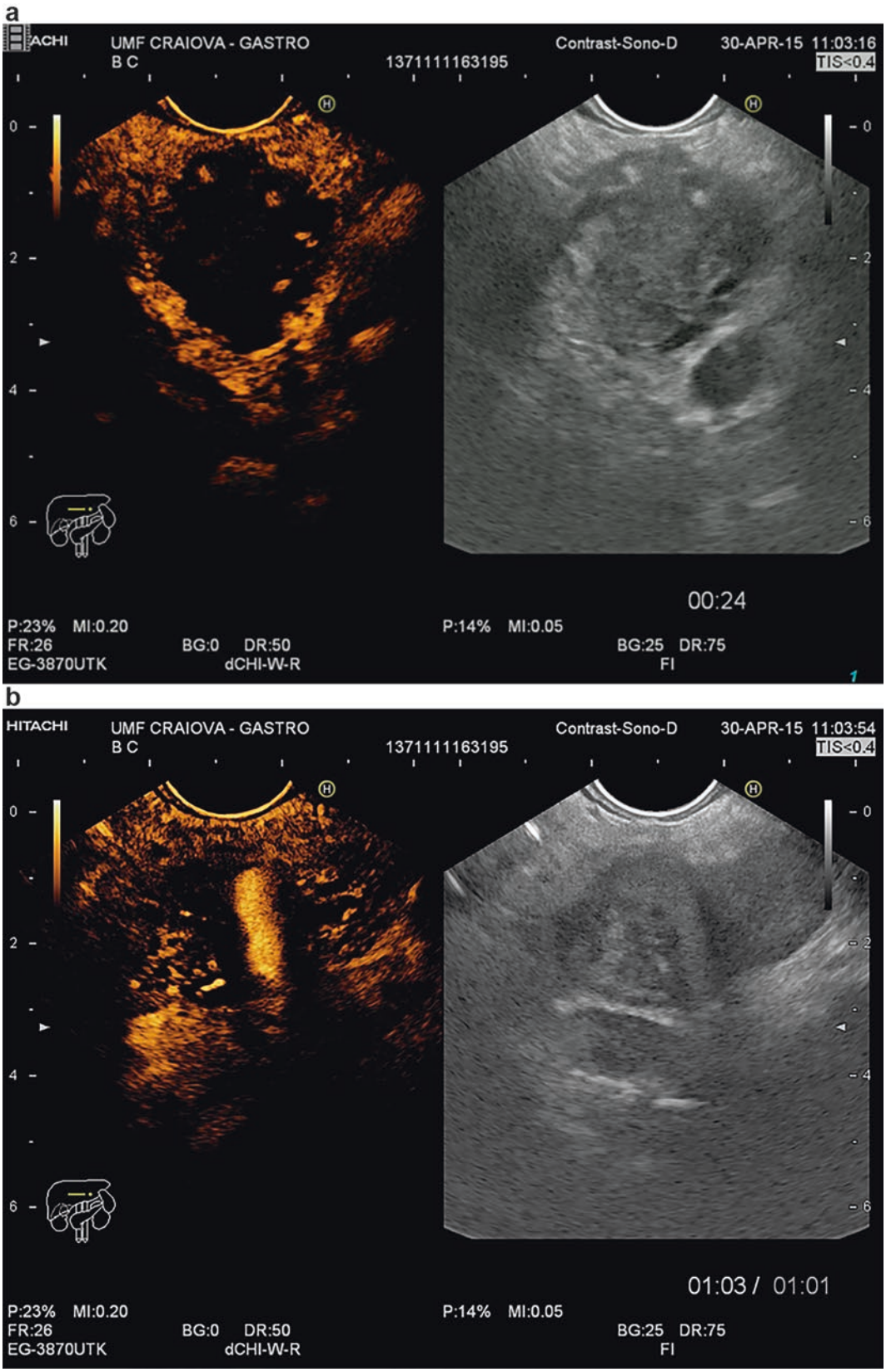

Fig. 36.1 EUS images of a pancreatic adenocarcinoma in (**a**). CE-EUS: hypoenhancing focal tumor with some arteries in the cross-sectional plane in the arterial phase (24 s after Sonovue administration). (**b**) Venous/late phase also showing a hypoenhancement in tumor and encasement of the splenic artery (1 min and 3 s). (**c**) Elastography (*left*) of the same tumor with histogram showing the distribution of strains recorded in the tumor area indicating that tumor tissue is harder than the surrounding tissue (Images: A. Saftoiu)

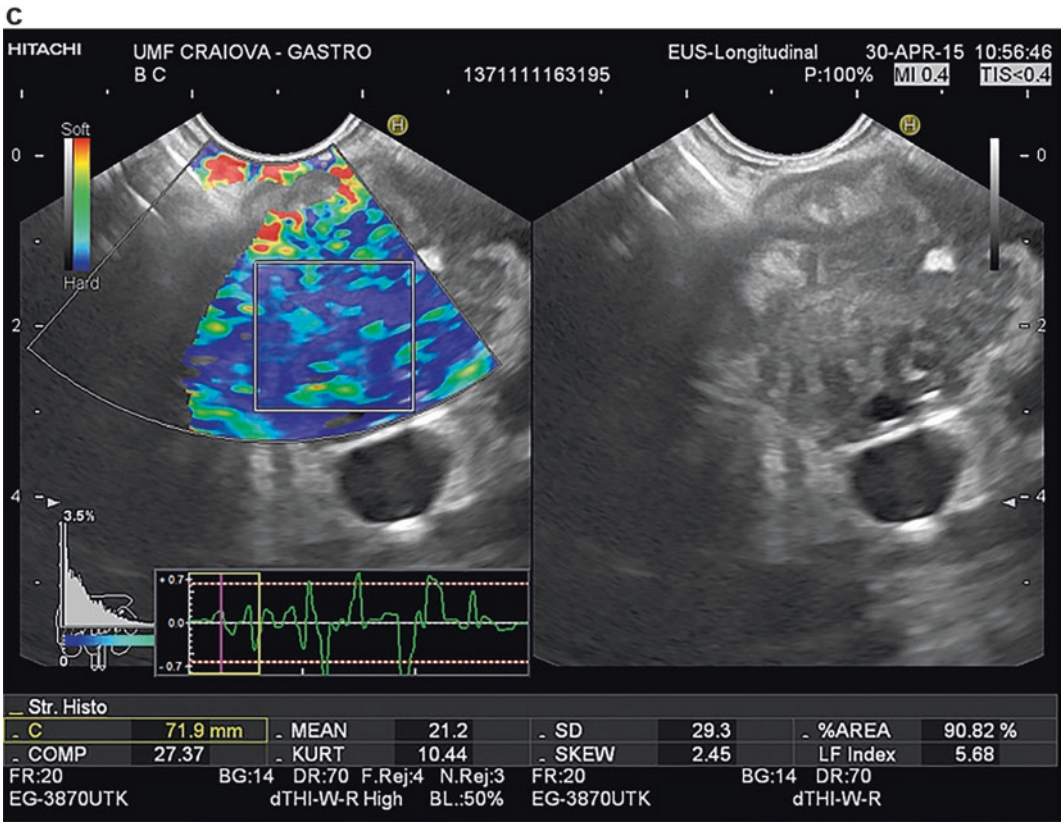

Fig. 36.1 (continued)

Safety of CE-EUS

The use of UCAs rarely causes allergic reactions. In a retrospective study of more than 23.000 administrations of Sonovue, only 0.002% experienced anaphylactoid reactions [6]. Similar good safety results have been described when UCAs have been used in stress-echo examinations [7]. With Sonazoid, allergic reactions may theoretically occur in patients with egg allergy as phosphatidyl sodium from egg (H-EPSNa) and sucrose are among the ingredients, but these are rare. The gases commonly used in UCAs are sulfur hexafluoride or perfluorobutane. They are inert gases and have low water solubility. Sulfur hexafluoride, SF6 (Sonovue, Bracco Imaging, Italy), is exhaled, and 80% of the injected gas is found in the exhaled air within 2 min, and elimination is complete after 15 min [2]. Perfluorobutane (Sonazoid, GE-Healthcare/Daiichi-Sankyo Company, Japan) has a half time of 2.7 min in the 2–15-min interval after injection and thereafter 7.3 min in the 15–30-min interval. After 2 h Sonazoid concentration falls under the detection limit in blood [8, 9]. The shell is made up of phospholipids that are similar to the constituents of biological membranes and are metabolized.

Using UCAs involves no radioactive substances or ionizing radiation. For Sonovue the circulating gas bubbles have an average diameter of 4.4 μm and a size distribution of 90%, between 1 and 10 μm [4]. Sonazoid has an average diameter of 2.6 micrometer, and only 0.1% is larger than 7 μm [3]. They act as transient circulating emitters of nonlinear RF signals when exposed to US frequencies of a low MI. The lower size distribution of Sonazoid may fit the higher frequencies used in EUS (7.5–12.5 MHz) better.

Practical Considerations

- Allergic reactions to Sonovue is rare.
- Allergic reactions to Sonazoid may occur in patients with egg allergy.

In a recent report of signal of disproportionate reporting (SDR) in Standardized Medical Queries of perflutren US contrast agents to the US Food and Drug Administration Adverse Event Reporting System, no disproportionate

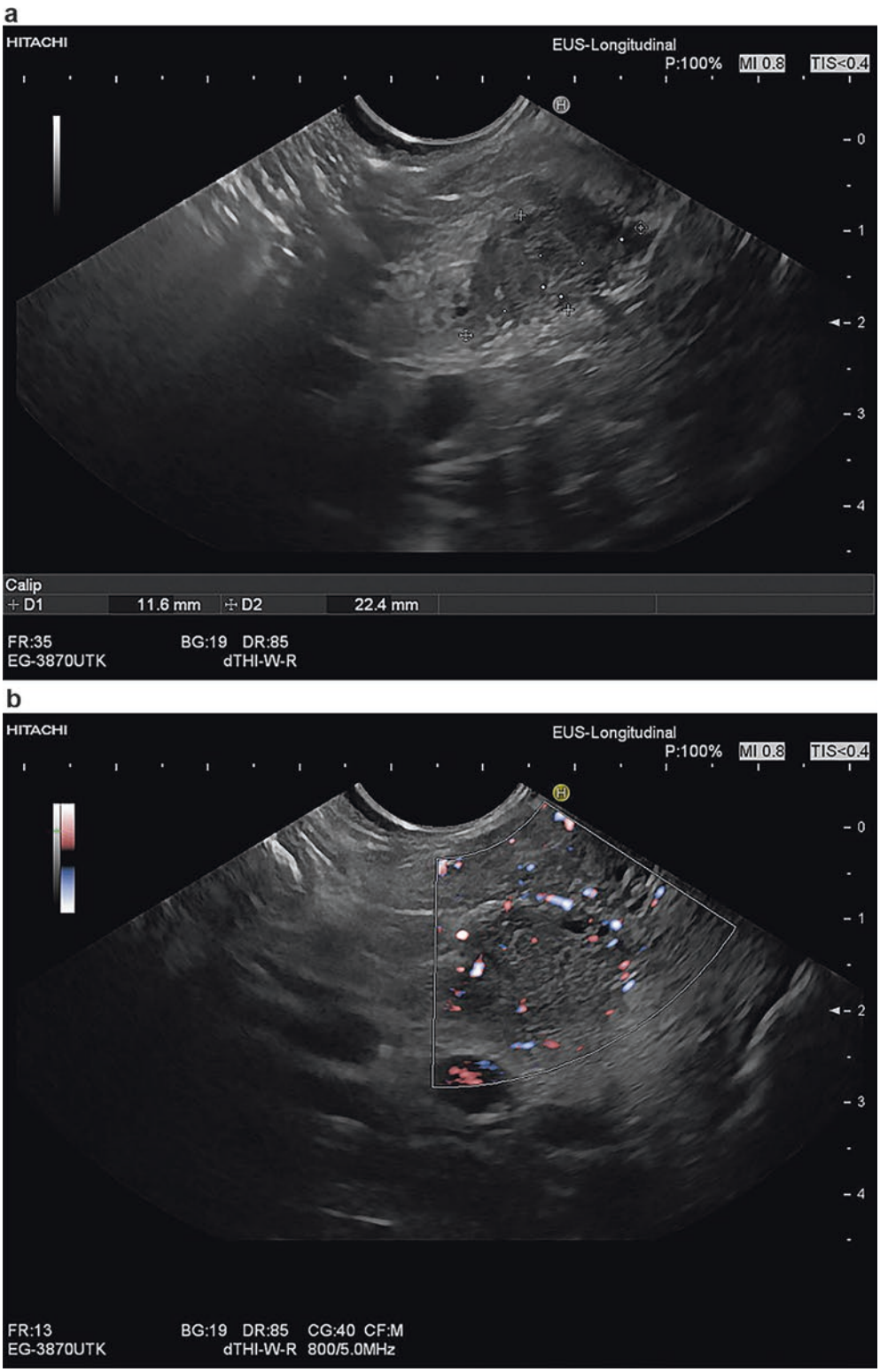

Fig. 36.2 EUS of a pancreatic focal lesion in the uncinate process. (**a**) B-mode image of hypoechoic solid lesion 22.4 × 11.6 mm with small cystic areas. (**b**) Color Doppler image of tumor section showing few vessels in the tumor area. (**c**) Pre-contrast CE-EUS image. (**d**) Arterial phase CE-EUS showing contrast uptake in the tumor but hypoenhancing compared to the reference tissue 18 s after Sonozoid bolus administration with a hypoechoic center. (**e**) Venous phase CE-EUS showing washout of Sonazoid in the tumor area, relative to the surrounding tissue (at 52 s). (**f**) Time-intensity curve of the contrast bolus uptake over 52.2 s in tumor area (*red*) and the reference pancreatic tissue (*yellow*). The tumor is hypoenhancing compared to the reference area in all phases. (**g**) Elastogram of tumor shows increased tissue hardness in the tumor area indicated by blue color. A strain ratio between the reference tissue and the lesion is measured by strain ratio to 3.35. (Histology: Moderately differentiated adenocarcinoma, pT3, N0.) (Images: R.F. Havre)

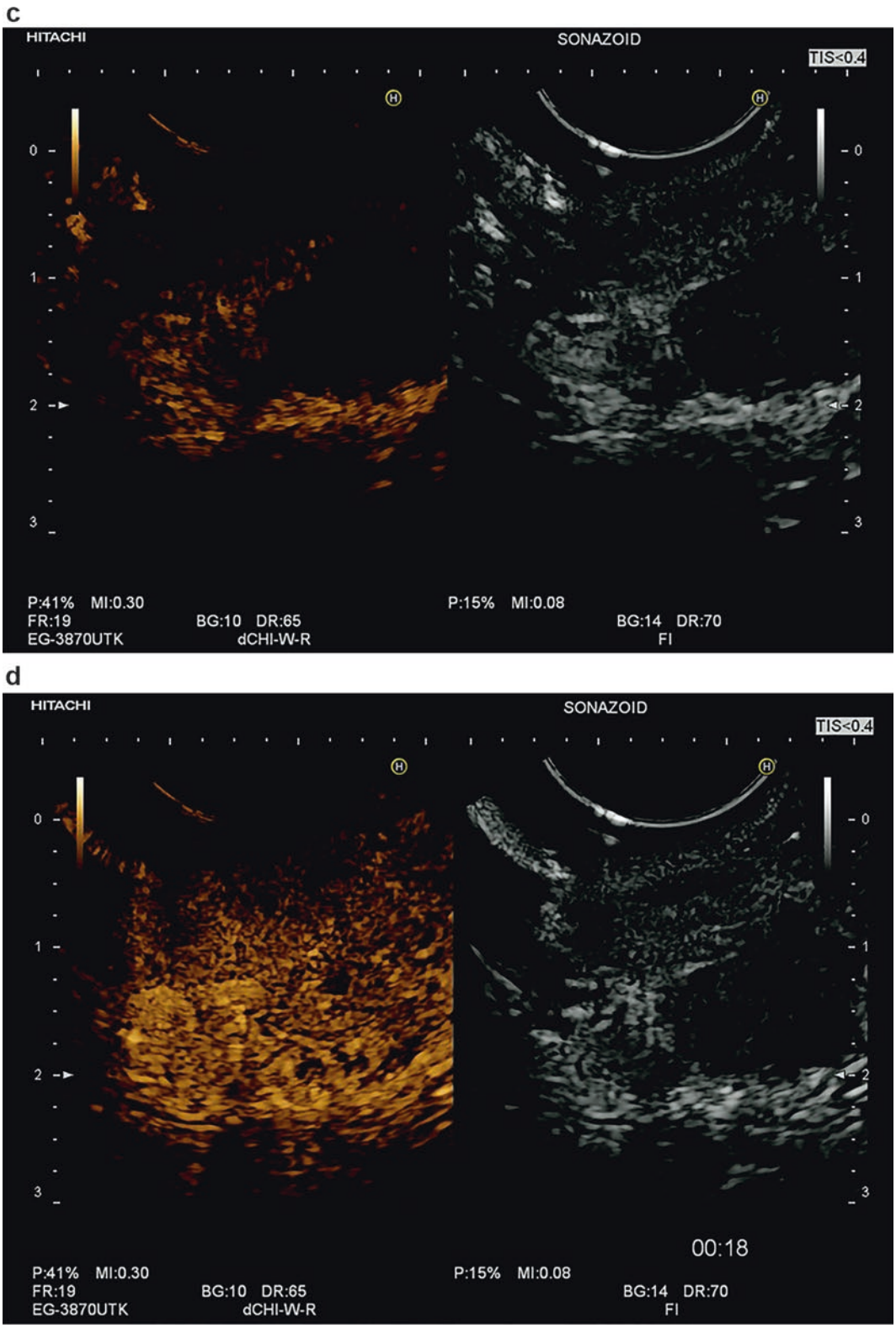

Fig. 36.2 (continued)

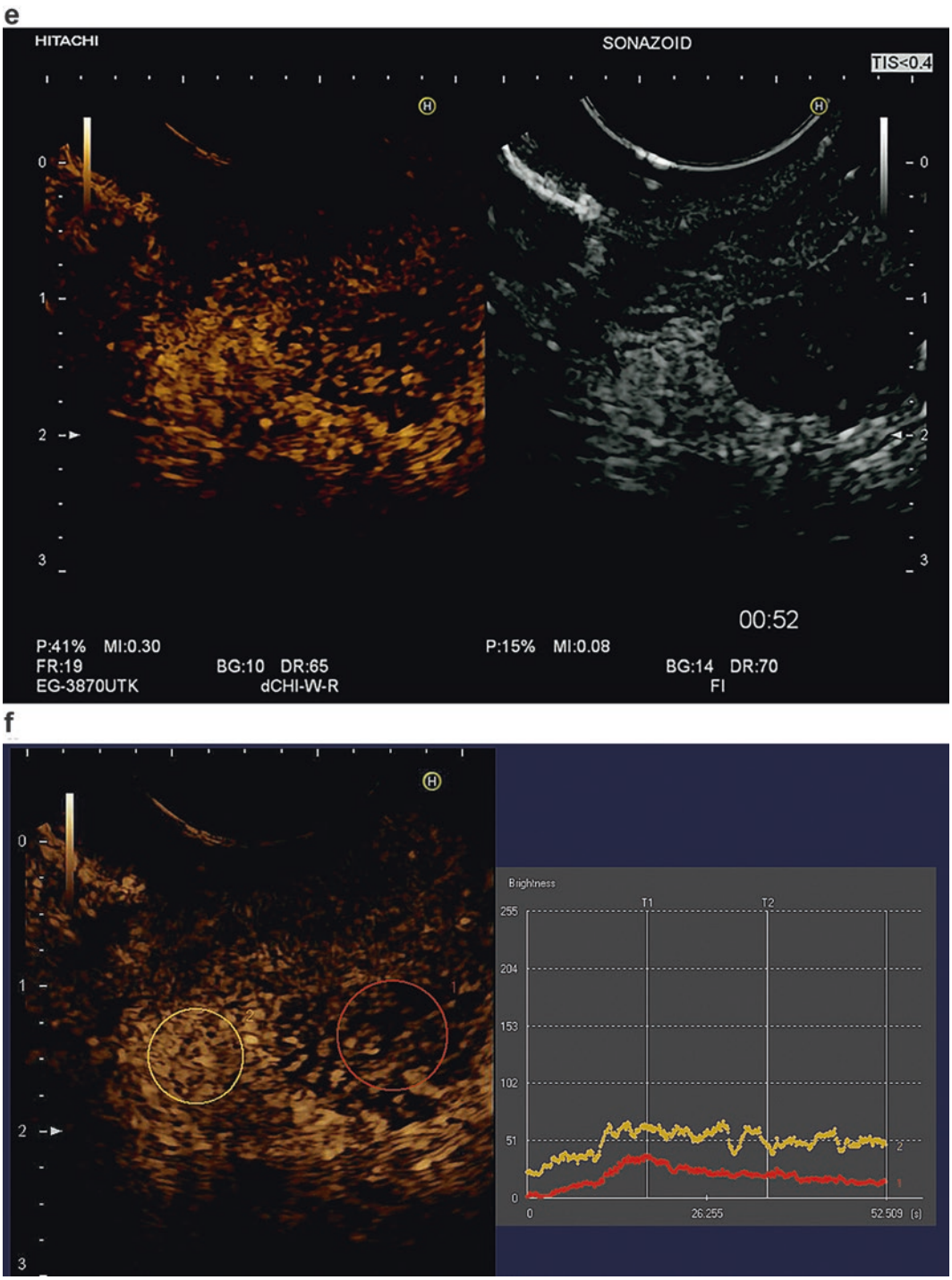

Fig. 36.2 (continued)

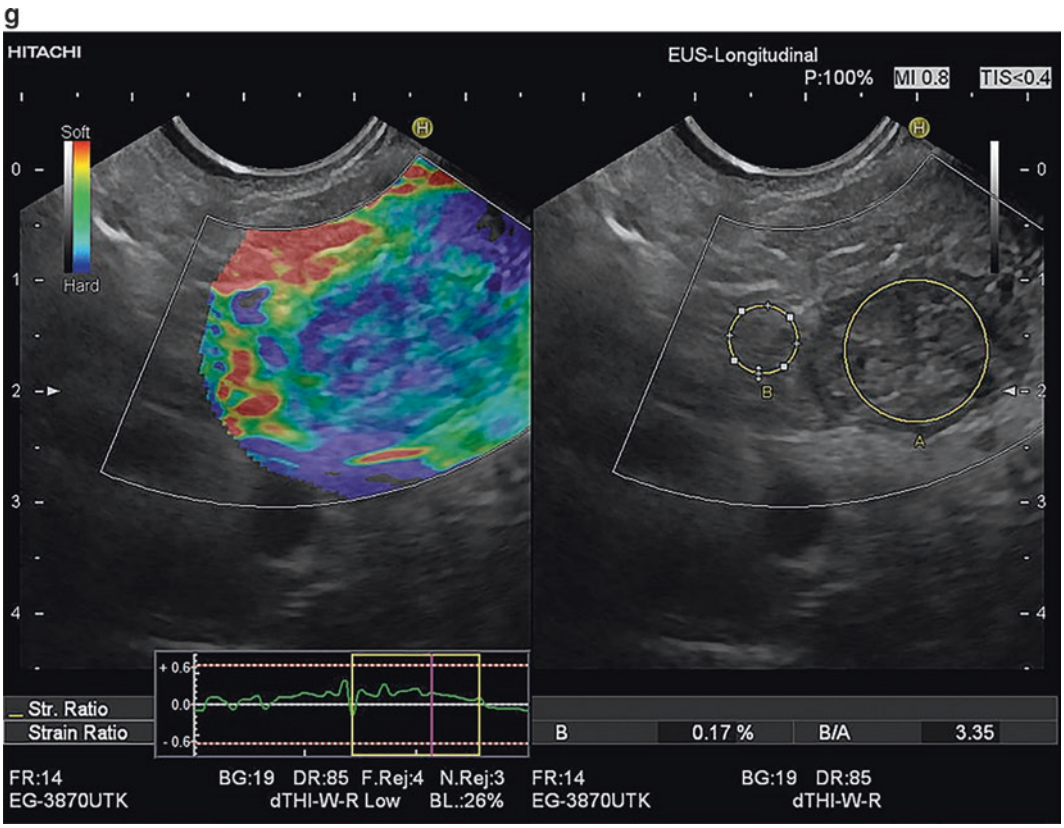

Fig. 36.2 (continued)

reporting was discovered, and no cases of deaths or cardiovascular infarctions were found [10]. Even if the safety seems to be well documented, it cannot be excluded that UCAs may exert biological effects to biological membranes even at low mechanical indexes. The effect called sonoporation may be caused by several mechanisms, linked to the rapid oscillation of the gas bubbles on nearby cell membranes. The effect is a transient increase in permeability of the cell wall or even transient creation of pores in the cell membrane, without destruction of the cell, with an effect dependent on the acoustic power used [5, 11, 12].

Clinical Indications of CE-EUS

Differentiation of Lymph Nodes by CE-EUS

The diagnostic accuracy of US for lymph node diagnosis is based on several parameters such as size, echogenicity, and border delineation. The diagnostic accuracy was improved when adding contrast agents in a transcutaneous approach, from 55% by B-mode US to 80% when using US contrast agent (sulfur hexafluoride) [13]. CE-EUS has been used in several studies in order to differentiate between malignant and benign mediastinal lymph nodes. Kanamouri et al. described benign lymph nodes as hyperenhancing with a homogeneous pattern and malignant lymph nodes typically with nonhomogeneous enhancement. Using time-intensity curves (TIC), the benign lymph nodes had a higher area under the curve (AUC) than the malignant lymph nodes. The authors found an increase in diagnostic accuracy by adding CE-EUS: the sensitivity, specificity, and accuracy rate of CE-EUS were 100%, 81.8%, and 92.0%, respectively [14]. Hocke et al. performed a larger prospective study of CE-EUS for differentiation between malignant and benign lymph nodes in the mediastinum and in the abdomen in 122 patients. They concluded that CE-EUS improved the specificity, but the sensitivity was not higher than the B-mode criteria, 60%. When lymphomas were excluded, the sensitivity increased to 73%. They concluded that CE-EUS could not replace EUS-FNA in diagnosing mediastinal lymph nodes [15].

Differentiation of Solid Pancreatic Lesions by CE-EUS

Focal pancreatic lesions may represent malignant tumors or a variety of benign lesions, which may not always be inflammatory lesions. In pancreatic surgery, 5–20% of lesions

resected show benign histology [16, 17]. Asymptomatic patients operated for pancreatic adenocarcinomas found as incidental findings have much higher 5-year survival [18]. Several studies have focused on CE-EUS in order to differentiate malignant and benign solid lesions of the pancreas. The studies have predominantly focused on the differentiation between inflammatory lesions and adenocarcinomas. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is considered the gold standard for diagnosing pancreatic solid focal lesions. In some countries this is used as a standard pretreatment procedure providing a tissue diagnosis, while for other countries this minimally invasive method is used for atypical lesions or locally advanced tumors. An image-based evaluation including B-mode, color Doppler, elastography, and CE-EUS may be useful whenever EUS-FNA is negative or considered contraindicated. Lesions that show hypoechogenicity, increased tissue stiffness, and low-contrast uptake or washout should still be considered for surgery (Figs. 36.1 and 36.2) [19].

Generally, adenocarcinomas tend to be hypoenhancing throughout the arterial and venous phases of a bolus tracking of UCA. Inflammatory lesions are often hyper- or isoenhancing (Fig. 36.3). Neuroendocrine tumors of the pancreas are frequently hyperenhancing [20].

In a meta-analysis from 2012, Gong et al. evaluated 12 studies with 1139 patients and found a pooled sensitivity of 94% and a pooled specificity of 89%, respectively. The area under the S-ROC curve was 0.9732. In the study a substantial heterogeneity in specificity was observed, probably due to different diagnostic standards using visual pattern recognition as well as more sophisticated post-procedure analyses such as TIC analysis. Also the patient selection was different in the selected studies [21].

Since then a prospective multicenter study by Saftoiu et al. included 167 patients with pancreatic carcinoma (PC) or chronic pancreatitis (CP) with a mass-forming lesion. The enhancement of the lesion of interest was analyzed categorically as hypo-, iso-, or hyperenhancing, with a dedicated software for TIC analysis (Vue-box) and by an artificial neural network analysis (NNA). In the visual categorical characterization, a sensitivity of 87% and specificity of 92.7% were reached, while after the NNA a sensitivity of 94.64% and a specificity of 94.44 were reached. Using Vue-box the parameter "peak enhancement" was the parameter that best differentiated the two entities [22].

Studies on Neuroendocrine Tumors

Ishikawa et al. found higher sensitivity of 95.1% for identifying pancreatic neuroendocrine tumors (pNET) using EUS with contrast-enhanced color Doppler mode. They compared with the sensitivity of MDCT (80.6%) and transcutaneous ultrasound (45.2%) [23]. Kitano et al. reported hyperenhancing pattern in pancreatic NETs in 78.9%, and Yamashita et al. found hyperenhancement in 6/8 in the early phase and in 5/8 in the late phase. Only 1/8 pNET was hypoenhancing in the late phase [24, 25].

Combining CE-EUS and EUS elastography imaging has proven useful in differentiating focal pancreatic lesions. EUS elastography has a high sensitivity but may be false positive [26]. The combined findings of harder lesion with low-enhancing or washout on CE-EUS had an accuracy of 93% in 25 of 50 consecutive patients with solid focal pancreatic lesions [19].

Differentiation of Solid Lesions in Chronic Pancreatitis

One of the main challenges in pancreatic EUS is to identify a malignancy in patients with chronic pancreatitis (CP). In CP the parenchyma of the pancreas often is seen as lobulated and hypoechogenic subdivided by more echogenic strands, which may be difficult to differentiate from tumors by B-mode EUS. The presence of other CP features such as cysts, increased pancreatic duct (PD) diameter, marked PD wall thickness, parenchymal and PD calcifications, or pseudocysts does not exclude a malignant lesion and may be similar to findings associated with pancreatic tumors. Patients with CP carry a small but significant increased risk for pancreatic adenocarcinoma [27]. Several studies have addressed this problem, although the prevalence of CP or subgroup of CP is varying in the studies, and only few report a prospective, intention-to-diagnose protocol, but rather results from patients with confirmed inflammatory or neoplastic lesions by surgery or follow-up. Imazu et al. reported in 2012 a case control study of a selected patient material of 81 patients with autoimmune focal pancreatitis (AIP) and 22 patients with pancreatic adenocarcinoma. They used TIC analysis and found 100% sensitivity and specificity by using the peak intensity or the max intensity gain in the suspected pancreatic area. Inflammatory lesions had much higher contrast enhancement than adenocarcinomas [28]. In a similar study from 2013, Gheonea et al. presented a case control study of 19 patients with CP and 32 patients with pancreatic cancer (PC) . Using TIC analysis with Vue-box®, they found a sensitivity of 93.8% and a specificity of 89.5% for diagnosing a malignant lesion correctly. Two false-positive cases were identified in each group [29].

Identification of Malignant and Pre-malignant Pancreatic Cysts

CE-EUS has been used to differentiate cysts with a malignant potential and cysts representing malignant tumors. It may be difficult to differentiate cystic thickened wall or noduli from echogenic debris within a cyst, but CE-EUS is able to show the delineation between vascularized and non-vascularized

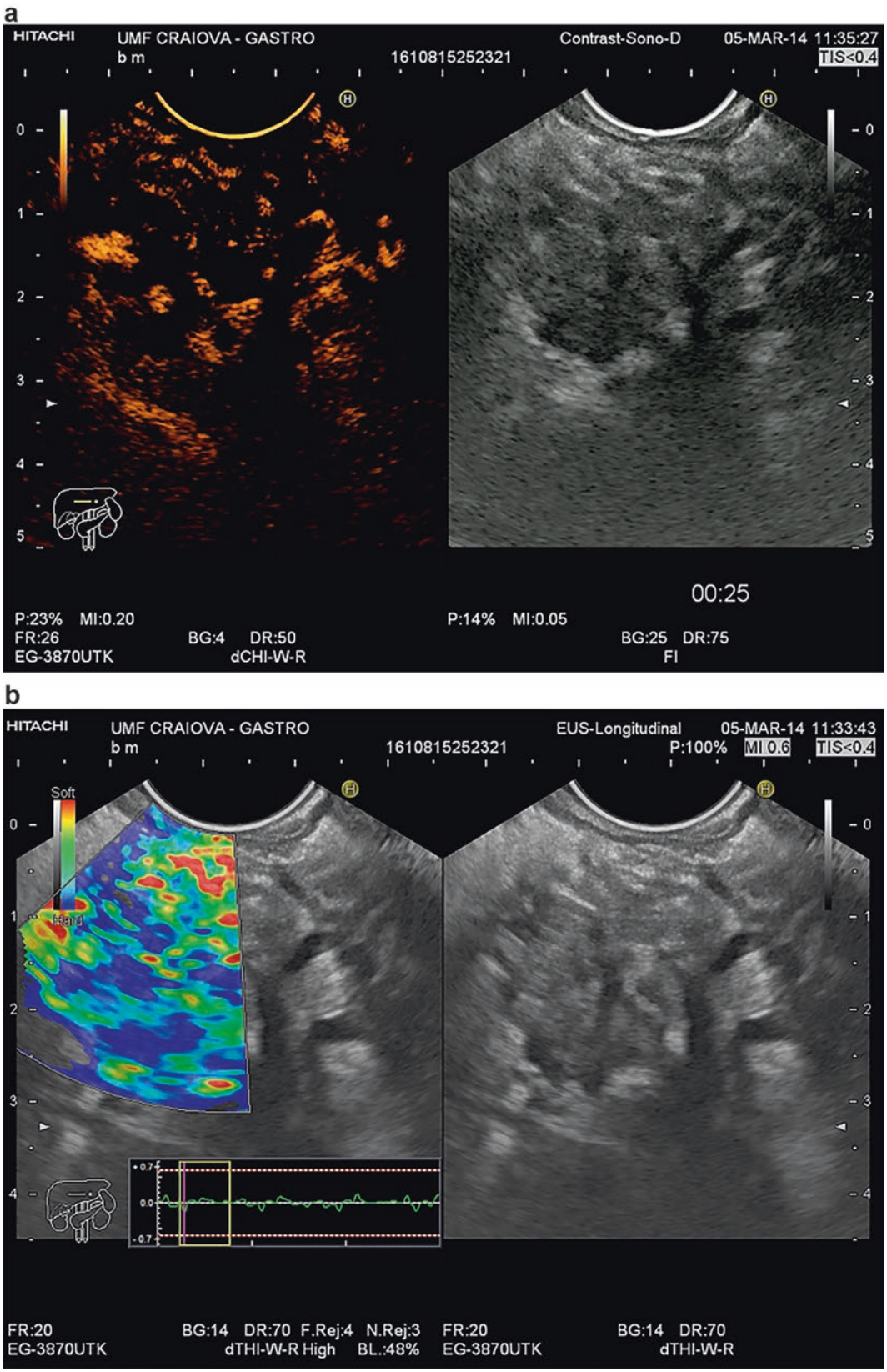

Fig. 36.3 EUS images of a focal pancreatitis. (**a**) CE-EUS in the early phase of Sonovue administration as a bolus (25 s after administration). The signal is scattered in the lesion as well as in the surrounding tissue. Hypoenhancing areas are also seen. (**b**) Elastogram from the same area shows a scattered signal of blue-green and red pattern that does not indicate a focal increase in tissue hardness within the lesion (Images: A. Saftoiu)

tissue. Hocke et al. studied 125 cystic lesions prospectively and found that contrast enhancement in the cyst wall identified the majority of neoplastic cysts (sens: 100%, Spec: 94%). Only 4 of 69 pseudocysts or dysontogenetic cysts showed uptake in the cyst wall. However, all serous cystic adenomas were classified as neoplastic cysts, and only three were actual malignant cysts [30]. Kamata et al. followed prospectively 581 patients with cystic lesions of which 70 underwent surgery. In this group, they found that CE-EUS did not improve differentiation of mucinous from non-mucinous cysts significantly, but malignant neoplastic cysts ($n = 30$) were differentiated significantly from nonmalignant cysts. The specificity was improved from 40% to 75% by adding contrast, and the sensitivity remained at 97% for both modes. Detecting mural nodules was significantly better using contrast than fundamental B-mode EUS (AUC 0.93 vs. 0.84, $p = 0.028$). If mural nodules were ≥4 mm in height, the risk of having a malignant lesion increased with an OR of 56.0 [31].

EUS-FNA Guided by CE-EUS

Contrast enhancement in EUS may be used to guide tissue sampling toward viable tissue and avoid necrotic areas in large tumors, lymph nodes, or in subepithelial tumors such as GISTs. Whether the use of CE-EUS is useful for better yield in EUS-FNA has been investigated in some studies. Kintano et al. found that CE-EUS increased FNA sensitivity from 92.2 to 100% in a prospective study from 2012 [25]. Seicean et al. found an increase in accuracy from 78.4% to 86.5% of CE-EUS-guided FNA in 51 patients with pancreatic lesions compared to EUS-guided FNA. This difference was, however, not significant [32]. A retrospective study by Hou et al. identified 58 patients who had undergone CE-EUS-FNA and 105 who had undergone EUS-FNA of pancreatic lesions in a 3-year period. They found a trend toward higher diagnostic yield in CE-EUS-guided FNA with an increase in accuracy from 80.0% to 87.9%, but the improvement was not statistically significant. They also calculated a favorable cost for CE-EUS-FNA per correct diagnosis compared to EUS-FNA alone, although the cost per procedure was higher and the procedure time was longer [33]. We have experienced a deterioration of the B-mode image quality when switching to "contrast mode" when a dual-screen image is used, and we anticipate this may contribute to decrease the difference in diagnostic accuracy.

Contraindications to CE-EUS

Although very rare, having a previous allergic reaction to intravenous US contrast agents is an absolute contraindication for using it a second time. With Sonazoid, allergies to hen eggs may potentially cross-react with constituents of the contrast agent (phosphatidyl sodium from eggs are used), and this should be addressed before injecting the contrast agent.

If the patient is known with multiple allergies including drug-related allergies, caution should be taken. A set containing an epinephrine auto-injector, a bag-valve mask, and oxygen should always be available in the room where US contrast is used, in case of anaphylactic reactions. A monitoring system including arterial BP, pulse oximetry, and ECG should be available in the department.

Possible Future Usage of Contrast Agents

The UCAs consist of small gas bubbles covered by phospholipids. By connecting antibodies to known protein receptors or endothelial cell expressed receptors, a "homing" of contrast agents in the capillaries to inflammatory or neoplastic tissue can be obtained [34]. By attaching, e.g., specific antibodies to endothelial proteins expressed in inflammatory and neoplastic tissues (E-selectin, P-selectin, ICAM-1, integrin αVβ3, or VGFR-2) on the surfaces of the bubbles, it has been possible to concentrate the adhesion of UCAs in capillaries of inflammatory and neoplastic vessels to localize and quantify inflammation or neoplastic growth and even to evaluate the response to anti-angiogenic therapy in animal models [35, 36]. Methods for separating bound from unbound microbubbles are under investigation [37].

The UCAs can be controlled by US and possibly be used as carriers of drugs. If US can be used to deposit the drugs or even increase the cell permeability locally, targeted contrast agents may also come to serve a role in targeted therapy, possibly enabling high local concentrations of otherwise toxic drugs. This may become an important principle for drug delivery in treatment of several cancers and chronic inflammatory diseases.

In a pilot study in mice with pancreatic tumors, the combination of Gemcitabine and an UCA improved survival compared to gemcitabine alone and sham treatment [38]. A small pilot study in humans with inoperable pancreatic cancer subsequently showed increased survival in patients who got the combination of UCA and Gemcitabine [39].

The previously mentioned sonoporation is a phenomenon where the oscillation of UCAs near cell surfaces induces transient pores in these. The mechanisms behind this are under investigation, and several mechanisms may work in concert depending on the acoustic energy used [5, 40].

Conclusion

Ultrasound contrast agents are sub-cell-sized gas bubbles injected into veins, and they emit a nonlinear acoustic signal when exposed to US. They can be used to visualize perfusion

in live tissues, while temporal differences in perfusion show typical patterns for different diagnoses. Early washout from focal lesions or hypoenhancement in all phases of bolus tracking is a feature of pancreatic adenocarcinomas. UCAs are established in transcutaneous US of the liver and can also increase accuracy in several EUS applications. In future applications, homing of contrast bubbles to diseased tissue may be achieved by covering their surface with specific proteins or receptors. Having a hydrophilic outside layer and a hydrophobic inside layer, UCAs may also become carriers of drugs, nanoparticles, or genes to specific sites.

References

1. Papadopoulou V, Tang MX, Balestra C, Eckersley RJ, Karapantsios TD. Circulatory bubble dynamics: from physical to biological aspects. Adv Colloid Interf Sci. 2014;206:239–49.
2. Ltd. DP. SonoVue 8 microlitres/ml, powder and solvent for dispersion for injection. medicines.org.uk; 2015.
3. Sontum PC. Physicochemical characteristics of Sonazoid, a new contrast agent for ultrasound imaging. Ultrasound Med Biol. 2008;34(5):824–33.
4. Wang B, Zang WJ, Wang M, Ai H, Wang YW, Li YP, et al. Prolonging the ultrasound signal enhancement from thrombi using targeted microbubbles based on sulfur-hexafluoride-filled gas. Acad Radiol. 2006;13(4):428–33.
5. Karshafian R, Bevan PD, Williams R, Samac S, Burns PN. Sonoporation by ultrasound-activated microbubble contrast agents: effect of acoustic exposure parameters on cell membrane permeability and cell viability. Ultrasound Med Biol. 2009;35(5):847–60.
6. Piscaglia F, Bolondi L, Italian Society for Ultrasound in M, Biology Study Group on Ultrasound Contrast A. The safety of Sonovue in abdominal applications: retrospective analysis of 23188 investigations. Ultrasound Med Biol. 2006;32(9):1369–75.
7. Aggeli C, Giannopoulos G, Roussakis G, Christoforatou E, Marinos G, Toli C, et al. Safety of myocardial flash-contrast echocardiography in combination with dobutamine stress testing for the detection of ischaemia in 5250 studies. Heart. 2008;94(12):1571–7.
8. Sonazoid, GE Healthcare [Internet]. Felleskatalogen A/S. 2016 [cited 15.03.2016]. Available from: http://www.daiichisankyo.com/media_investors/media_relations/press_releases/detail/005564.html.
9. Landmark KE, Johansen PW, Johnson JA, Johansen B, Uran S, Skotland T. Pharmacokinetics of perfluorobutane following intravenous bolus injection and continuous infusion of sonazoid in healthy volunteers and in patients with reduced pulmonary diffusing capacity. Ultrasound Med Biol. 2008;34(3):494–501.
10. Hauben M, Hung EY, Hanretta KC, Bangalore S, Snow V. Safety of perflutren ultrasound contrast agents: a disproportionality analysis of the US FAERS database. Drug Saf. 2015;38(11):1127–39.
11. Postema M, Gilja OH. Ultrasound-directed drug delivery. Curr Pharm Biotechnol. 2007;8(6):355–61.
12. Postema M, Gilja OH. Contrast-enhanced and targeted ultrasound. World J Gastroenterol. 2011;17(1):28–41.
13. Yu M, Liu Q, Song HP, Han ZH, Su HL, He GB, et al. Clinical application of contrast-enhanced ultrasonography in diagnosis of superficial lymphadenopathy. J Ultrasound Med. 2010;29(5):735–40.
14. Kanamori A, Hirooka Y, Itoh A, Hashimoto S, Kawashima H, Hara K, et al. Usefulness of contrast-enhanced endoscopic ultrasonography in the differentiation between malignant and benign lymphadenopathy. Am J Gastroenterol. 2006;101(1):45–51.
15. Hocke M, Menges M, Topalidis T, Dietrich CF, Stallmach A. Contrast-enhanced endoscopic ultrasound in discrimination between benign and malignant mediastinal and abdominal lymph nodes. J Cancer Res Clin Oncol. 2008;134(4):473–80.
16. Vitali F, Hansen T, Kiesslich R, Heinrich S, Kumar A, Mildenberger P, et al. Frequency and characterization of benign lesions in patients undergoing surgery for the suspicion of solid pancreatic neoplasm. Pancreas. 2014;43(8):1329–33.
17. Dudekula A, Munigala S, Zureikat AH, Yadav D. Operative trends for pancreatic diseases in the USA: analysis of the nationwide inpatient sample from 1998-2011. J Gastrointest Surg:2016.
18. Gillen S, Schuster T, Meyer Zum Buschenfelde C, Friess H, Kleeff J. Preoperative/neoadjuvant therapy in pancreatic cancer: a systematic review and meta-analysis of response and resection percentages. PLoS Med. 2010;7(4):e1000267.
19. Iordache S, Costache MI, Popescu CF, Streba CT, Cazacu S, Saftoiu A. Clinical impact of EUS elastography followed by contrast-enhanced EUS in patients with focal pancreatic masses and negative EUS-guided FNA. Med Ultrason. 2016;18(1):18–24.
20. Choi JH, Seo DW. The expanding role of contrast-enhanced endoscopic ultrasound in pancreatobiliary disease. Gut Liver. 2015;9(6):707–13.
21. Gong TT, Hu DM, Zhu Q. Contrast-enhanced EUS for differential diagnosis of pancreatic mass lesions: a meta-analysis. Gastrointest Endosc. 2012;76(2):301–9.
22. Saftoiu A, Vilmann P, Dietrich CF, Iglesias-Garcia J, Hocke M, Seicean A, et al. Quantitative contrast-enhanced harmonic EUS in differential diagnosis of focal pancreatic masses (with videos). Gastrointest Endosc. 2015;82(1):59–69.
23. Ishikawa T, Itoh A, Kawashima H, Ohno E, Matsubara H, Itoh Y, et al. Usefulness of EUS combined with contrast-enhancement in the differential diagnosis of malignant versus benign and preoperative localization of pancreatic endocrine tumors. Gastrointest Endosc. 2010;71(6):951–9.
24. Yamashita Y, Kato J, Ueda K, Nakamura Y, Kawaji Y, Abe H, et al. Contrast-enhanced endoscopic ultrasonography for pancreatic tumors. Biomed Res Int. 2015;2015:491782.
25. Kitano M, Kudo M, Yamao K, Takagi T, Sakamoto H, Komaki T, et al. Characterization of small solid tumors in the pancreas: the value of contrast-enhanced harmonic endoscopic ultrasonography. Am J Gastroenterol. 2012;107(2):303–10.
26. Havre RF, Odegaard S, Gilja OH, Nesje LB. Characterization of solid focal pancreatic lesions using endoscopic ultrasonography with real-time elastography. Scand J Gastroenterol. 2014;49(6):742–51.
27. Duell EJ, Lucenteforte E, Olson SH, Bracci PM, Li D, Risch HA, et al. Pancreatitis and pancreatic cancer risk: a pooled analysis in the International Pancreatic Cancer Case-Control Consortium (PanC4). Ann Oncol. 2012;23(11):2964–70.
28. Imazu H, Kanazawa K, Mori N, Ikeda K, Kakutani H, Sumiyama K, et al. Novel quantitative perfusion analysis with contrast-enhanced harmonic EUS for differentiation of autoimmune pancreatitis from pancreatic carcinoma. Scand J Gastroenterol. 2012;47(7):853–60.
29. Gheonea DI, Streba CT, Ciurea T, Saftoiu A. Quantitative low mechanical index contrast-enhanced endoscopic ultrasound for the differential diagnosis of chronic pseudotumoral pancreatitis and pancreatic cancer. BMC Gastroenterol. 2013;13:2.
30. Hocke M, Cui XW, Domagk D, Ignee A, Dietrich CF. Pancreatic cystic lesions: the value of contrast-enhanced endoscopic ultrasound to influence the clinical pathway. Endosc Ultrasound. 2014;3(2):123–30.
31. Kamata K, Kitano M, Omoto S, Kadosaka K, Miyata T, Yamao K, et al. Contrast-enhanced harmonic endoscopic ultrasonography for

differential diagnosis of pancreatic cysts. Endoscopy. 2016;48(1): 35–41.
32. Seicean A, Badea R, Moldovan-Pop A, Vultur S, Botan EC, Zaharie T, et al. Harmonic contrast-enhanced endoscopic ultrasonography for the guidance of fine-needle aspiration in solid pancreatic masses. Ultraschall Med. 2015;
33. Hou X, Jin Z, Xu C, Zhang M, Zhu J, Jiang F, et al. Contrast-enhanced harmonic endoscopic ultrasound-guided fine-needle aspiration in the diagnosis of solid pancreatic lesions: a retrospective study. PLoS One. 2015;10(3):e0121236.
34. Dayton PA, Pearson D, Clark J, Simon S, Schumann PA, Zutshi R, et al. Ultrasonic analysis of peptide- and antibody-targeted microbubble contrast agents for molecular imaging of alphavbeta3-expressing cells. Mol Imaging. 2004;3(2):125–34.
35. Pysz MA, Foygel K, Rosenberg J, Gambhir SS, Schneider M, Willmann JK. Antiangiogenic cancer therapy: monitoring with molecular US and a clinically translatable contrast agent (BR55). Radiology. 2010;256(2):519–27.
36. Bettinger T, Bussat P, Tardy I, Pochon S, Hyvelin JM, Emmel P, et al. Ultrasound molecular imaging contrast agent binding to both E- and P-selectin in different species. Investig Radiol. 2012;47(9):516–23.
37. Daeichin V, Akkus Z, Skachkov I, Kooiman K, Needles A, Sluimer J, et al. Quantification of bound microbubbles in ultrasound molecular imaging. IEEE Trans Ultrason Ferroelectr Freq Control. 2015;62(6):1190–200.
38. Kotopoulis S, Delalande A, Popa M, Mamaeva V, Dimcevski G, Gilja OH, et al. Sonoporation-enhanced chemotherapy significantly reduces primary tumour burden in an orthotopic pancreatic cancer xenograft. Mol Imaging Biol. 2014;16(1):53–62.
39. Kotopoulis S, Dimcevski G, Gilja OH, Hoem D, Postema M. Treatment of human pancreatic cancer using combined ultrasound, microbubbles, and gemcitabine: a clinical case study. Med Phys. 2013;40(7):072902.
40. Delalande A, Kotopoulis S, Postema M, Midoux P, Pichon C. Sonoporation: mechanistic insights and ongoing challenges for gene transfer. Gene. 2013;525(2):191–9.

Technique of Endoscopic Ultrasound-Guided Fine Needle Aspiration (EUS-FNA)

37

Subbaramiah Sridhar and Pornchai Leelasinjaroen

Introduction

The advent of endoscopic ultrasound (EUS) and guided fine needle aspiration (FNA) has significantly altered the management of benign and malignant gastrointestinal, biliary-pancreatic, and mediastinal disorders. Over the past two decades, EUS has evolved from being a diagnostic imaging modality to an interventional modality. Several evolving therapeutic applications are paving the way to previously unimaginable procedures such as transluminal endosurgery [10]. The technique of EUS-guided fine needle aspiration (EUS-FNA) forms the basis for all of the more invasive applications such as EUS-guided celiac ganglion neurolysis, pseudocyst drainage, pancreatic necrosectomy, periluminal abscess drainages, transgastric or transduodenal biliary-pancreatic drainage procedures, etc. [9, 10].

The advantages of EUS-FNA are:

1. Tissue diagnosis for intramural or periluminal lesions in relation to the GI tract.
2. Detection and aspiration of even small sub-centimeter lymph nodes in posterior mediastinal, para-celiac, and periportal regions for staging of malignancies.
3. Access to anatomically difficult locations like aortopulmonary window.
4. FNA of smaller lesions in pancreas.
5. In seriously ill patients such as severe necrotizing pancreatitis with fluid collections, EUS-guided procedures are preferable due to relatively less invasive nature of the procedure.
6. EUS-guided procedures are possible even bedside in intensive care situations due to the mobility of equipment.
7. Provides a needle access to the periluminal structures.

Indications

Diagnostic indications for EUS-FNA include evaluation of mediastinal and intra-abdominal lymph nodes, staging of lung cancer by evaluation of contralateral lymph nodes, staging of esophageal cancer by evaluation of para-celiac nodes, staging of biliary-pancreatic cancers by evaluation of periportal/para-celiac lymph nodes, and staging of anorectal cancers by evaluation of perirectal nodes. In addition, periluminal fluid collections such as small pleural effusions can be sampled, when malignancy is suspected (not accessible by US/CT-guided thoracentesis), minimal ascites, when malignancy is suspected (not otherwise detected nor accessible by US/CT-guided thoracentesis), peripancreatic fluid collection when infected pancreatic necrosis is suspected, postsurgical periluminal collections (anastomotic leaks as in peri-esophagogastric, perirectal, gall bladder fossa), and pseudocyst drainage, especially in the absence of a transluminal bulge or in the presence of periluminal blood vessels.

Sampling of focal lesions excludes malignancy such as focal pancreatic lesions, suspicious biliary strictures, sus-

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pected adrenal metastases, suspected hepatic/splenic lesions, and suspicious submucosal lesions.

Therapeutic indications include drainage of pseudocysts, celiac ganglion neurolysis/block, EUS-guided biliary-pancreatic drainage, drainage of abscesses (mediastinal/intra-abdominal/perirectal), and fine needle injection.

Contraindications

Absolute contraindications include suspected bowel perforation and severe uncorrected coagulopathy (advanced liver disease, DIC). Relative contraindications include combative, difficult-to-sedate patient (suspect excessive alcohol use, delirium tremens, or narcotic over use; preferable to proceed under general anesthesia), ongoing use of anticoagulant or antiplatelet agents, and luminal narrowing.

Pre-evaluation

It is preferable to pre-evaluate patients well in advance when consultation or referral was made for the procedure or definitely immediately prior to the procedure. Such evaluations include review of the indication; review of the available investigations, particularly any imaging (US, CT, MR) to determine the region of interest; nature of the suspected lesion and its approximate location and size; and its relationship vis-à-vis standard anatomical structures, if available. This greatly facilitates the rapid detection and evaluation of the lesion by EUS and potentially reduces the procedure time, and review of potential risks for sedation, and safe intubation of the echoendoscope.

Practical Considerations

- Absolute contraindications for an EUS procedure include suspected bowel perforation and severe uncorrected coagulopathy.
- Pre-procedure evaluations should include a thorough review of the indication, results of the available investigations including imaging (US, CT, MR) to determine the region of interest, nature of the suspected lesion and its approximate location and size, and its relationship to standard anatomical structures.
- Consider pre-procedural antibiotics while accessing periluminal fluid collections, duplication cysts, cystic lesions or pseudocyst drainage, EUS-guided drainage of obstructed biliary-pancreatic system, and transrectal FNA or interventions.

Preparation

Proper preparation is critical to optimize the safety of the procedure. Preparations should include overnight, or at least 6 h, fasting; correction of bleeding tendency; discussion and counseling of the patient regarding the details of procedure, including the need for avoiding abrupt movements during lighter planes of conscious sedation; pre-procedural antibiotics while accessing periluminal fluid collections, duplication cysts, cystic lesions or pseudocyst drainage, EUS-guided drainage of obstructed biliary-pancreatic system, and transrectal FNA or interventions; and pre-procedural benzocaine spray of posterior pharyngeal wall.

Position

The left lateral position of the patient is generally suitable for most indications. The left lateral semi-prone position may be useful for difficult to access lesions in the head-uncinate region of pancreas. Nondependent gastric antral and perirectal lesions can be accessed in supine position. Occasionally, we have used the sitting position with a 75° backrest for mediastinal lesions in patients with severe COPD and respiratory failure or in the presence of superior vena cava syndrome.

Equipment

The Echoendoscope

Curved linear array echoendoscopes are available from Pentax, Olympus, and Toshiba-Fujinon (Table 37.1). While most experience is with the instruments from the former two manufacturers, for routine indication for EUS-FNA, the choice of instrument should not matter. There are differences among these instruments in terms of the length of the bending section of the echoendoscope, size and resolution of the transducer, length of the working channel, available diameters of the working channel, etc. [14, 23]. Although these differences are not enormous, it helps to be familiar with the equipment if different instruments are used routinely.

The most important difference between the Olympus and the Pentax instruments that have practical implications is that in the Pentax scope, the transducer and the bending section are longer, and, hence, caution is warranted while maneuvering the scope around the posterior pharyngeal curve and while intubating the duodenal bulb to enter the second part of duodenum. In this chapter, photographs of the Olympus curvilinear and radial echoendoscopes are provided (Fig. 37.1). Olympus introduced another echoendoscope with a forward

Table 37.1 Curvilinear echoendoscopes (CLE) for EUS-FNA

Instrument	Electronic/mechanical	Working channel (mm)	Working length (cm)	Scope-balloon suction
Olympus				
GF-UMD140P	M	2.8	124.4	Dual level
GF-UC30P	E	2.8	126	Dual level
GF-UC140(P)-AL5	E	3.7 (2.8)	125	Dual level
GF-UC160(P)-OL5	E	3.7 (2.8)	125	Dual level
GF-UCT180	E	3.7	125	Dual level
TGF-UC180J	E	3.7	124.5	Dual level
Pentax				
EG-3630UT	E	2.4	125	Separate
EG-3870UTK	E	3.8	125	Separate
Fujifilm				
EG-530UT2	E	3.8	125	N/A

view combined with a sector scanning transducer that allows fine needle aspiration and other interventions (Fig. 37.2).

Prior Radial EUS

Although in expert hands radial EUS is not necessary when EUS-FNA is planned, in general, it is a good practice to perform a quick radial EUS before proceeding for tissue diagnosis (Fig. 37.2b). Recent trends favor the use of linear scopes with the idea of tissue acquisition [16]. However, in the early phase of learning and while performing the procedure for cancer staging, it is preferable to do an initial diagnostic radial EUS to delineate the anatomy, location, and echomorphology. This would greatly help with the orientation when CLE is used for EUS-FNA and also helps in developing a plan for the puncture of the target lesions. In the presence of a suspected metastasis, it is often helpful to sample the metastatic lesion before puncturing the primary tumor for tissue diagnosis to avoid using separate set of needles. If suspected metastatic lesions are present in more than one location, the farthest lesion should be sampled first, since the implications or positivity would be different in terms of staging of the lesion (such as the presence of para-celiac and periportal lymph nodes in a patient with a focal pancreatic lesion in the head-uncinate region).

Fig. 37.1 Curvilinear and radial echoendoscopes from Olympus

The Needle

Various needles are available across the world (Table 37.2) [1, 12, 20]. GIP/Medi-Globe needles are relatively more popular in Europe, while Wilson-Cook needles are more widely used in the USA. The Cook needle systems are disposable and are available in 25 G, 22 G, and 19 G sizes besides a disposable Tru-Cut biopsy needle. Olympus makes a reusable handle and outer sheath with a disposable needle stylet in 22 G and 25 G and a spring-loaded biopsy needle as well. Both these needle systems have adjustable lengths of the sheath, and the needle has separate screws to maintain the selected position for use with various echoendoscopes (Fig. 37.4). It is important to check every time to ensure that the sheath of the needle system used is adequately exiting the working channel of the echoendoscope and its tip is visible endoscopically to avoid expensive damage to the instrument.

In general, 22 G needles are easier to handle, and the tissue sample is adequate for interpretation. The quality and quantum of the aspirate is better with 19 G, and at times it is possible to obtain tissue cores adequate for histology. However, the 19 G needle is sturdier and more difficult to maneuver while using for transduodenal indications. The main advantage of the 19 G needle is in EUS-guided interventions such as pseudocyst drainage or transgastric or transduodenal biliary-pancreatic interventions where a 0.035″ guide wire can be deployed through the needle, whereas the 22 G needle allows only a thin 0.018″ guide wire which is difficult to maintain position and exchange accessories for further interventions. Recent studies demonstrated the non-inferiority of using 25 G needles, which may even prove to be useful in puncturing difficult pancreatic head lesions [18, 24].

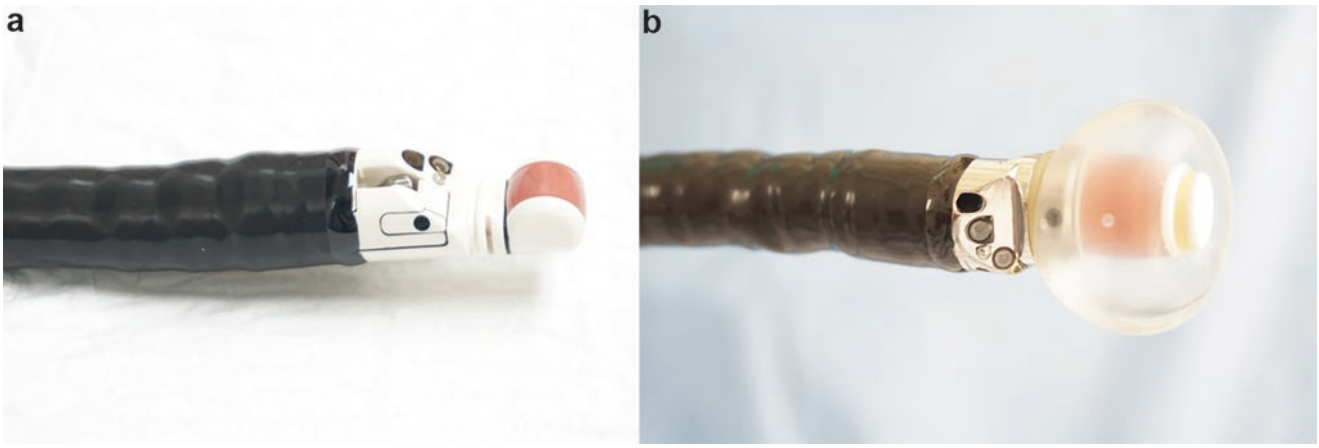

Fig. 37.2 (**a**) Curvilinear echoendoscope from Olympus. (**b**) Radial echoendoscope with balloon from Olympus

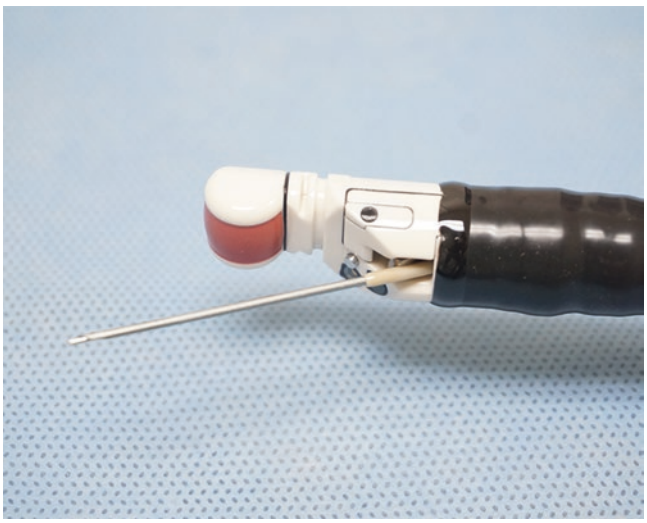

Fig. 37.3 Linear echoendoscope with FNA needle from Olympus

The nature of the stylet used with the needle has an important bearing on the outcomes. Rounded tip stylets are safer in terms of avoiding accidental scope damage. But, they have to be withdrawn by a centimeter into the needle just before puncturing the luminal wall to allow the beveled tip of the needle to come into contact with the tissue (Fig. 37.5). On the other hand, while using the beveled tip stylets, one has to be obsessive to ensure that the needle is well within the channel, using the tightening screw on the handle (Fig. 37.4).

Suction Syringes

While most syringes use low-volume suction while performing the EUS-FNA, one could sample soft, fleshy lesions that do not offer much resistance to the needle without suction, to avoid excessively bloody specimens. Some authors have demonstrated that 5–10 mL suction is better than 20 mL and that continuous is better than intermittent suction. Unless the initial pass yields a bloody specimen, the quality of the aspirate is, in general, better by using suction [17, 18, 21, 22]. Using the special suction syringes provided with the needles is preferable. Occasionally, one could improvise using a regular 10 mL syringe to apply suction by an assistant with a three-way lock to maintain it. Having a three-way attachment routinely between the suction syringe and the needle is useful to keep the syringe prepared with the suction and the three-way in closed position. Once the needle is within the target, the nurse assistant could connect the three-way suction syringe after removing the stylet to apply suction (Fig. 37.6). After 5–10 back and forth movements of the needle, depending on operator preference, the assistant or the operator releases the suction slowly while the needle tip is still within the lesion (Fig. 37.7). While gradually releasing the suction prior to withdrawing the needle ensures loss of aspirated material into the suction syringe, the use of the three-way attachment avoids the need to release the suction within the needle. However, one has to remember to discon-

Practical Considerations

- The choice of the echoendoscope depends on the indications for the procedure.
- The choice of the FNA needle depends on the indications and the endosonographer. In general, 22 G needles are easier to handle and the tissue sample is adequate for interpretation. The quality and quantum of the aspirate is better with 19 G, and at times it is possible to obtain tissue cores adequate for histology. It is important to remember that the 19 G needle is sturdier and difficult to maneuver while using for transduodenal indications.

Table 37.2 Commonly used EUS-FNA needles

Device name	Sheath diameter (mm or F)	Needle size (gauge)	Unique characteristics
Boston Scientific			
Expect	1.52 mm (25G) 1.65 mm (22G) 1.83 mm (19G)	19, 22, 25	Cobalt-chromium needle,echogenic pattern to needle tip
Expect Flex	1.73 mm	19	Nitinol needle has increased flexibility
Expect Slimline	1.52 mm (25G) 1.65 mm (22G) 1.83 mm (19G)	19, 22, 25	Smaller diameter handle forergonomic purposes
Expect Slimline Flex	1.73 mm	19	19G nitinol needle with smaller diameter handle
CONMED			
ClearView	1.8 mm (22G, 25G) 2.1 (19G)	19, 22, 25	Twist locks aid in one-handed use, laser etching of needle tip over 2 cm length
ClearView Sheath Stabilizer	2.7 mm	22, 25	Larger diameter sheath to increase needle stability
ClearView Extended Bevel	1.8 mm 2.7 mm (sheath stabilizer)	22	Extended stylet bevel to assist with puncture
Cook Medical			
Echotip Ultra	5.2F	19, 22, 25	Ergonomic handle, integratedsheath adjustor
Echotip Ultra Coil Sheath	5.2F	22	Coil sheath with increased flexibility
Echotip Ultra HD access	5.2F	19	Sharp stylet tip with smooth needle tip to prevent sheering during guide wire passage
Medtronic			
Beacon EUS delivery system with BNX FNA preloaded needle	2.5 mm	19, 22, 25	Needle is combined with a universal delivery sheath. The needle may be removed/exchanged while leaving the sheath in place. A safety sheath covers the needle tip when removed from the delivery sheath
BNX FNA needle(without sheath)		19, 22, 25	19G is a nitinol needle
Olympus			
EZ Shot 2	1.85 mm	19, 22, 25	Echogenic dimpled needle tip
EZ Shot 2 side port	1.85 mm	22	Side port hole near needle tip to improve tissue acquisition
EZ Shot 3 Plus with or without side port	2.2 mm (22G)2.6 mm (19G)	19, 22	Nitinol, Menghini tip design
Medi-Globe			
SonoTip Pro Control	1.8 mm (25G) 1.8 mm (22G) 1.8 mm (19G)	19,22,25G	Twist-lock technology
SonoTip Pro Control with tip stabilizer	2.7 mm (25G) 2.7 mm (22G)	22,25G	Twist-lock technology,tip stabilizer to accommodate large working channels (e.g., 3.2 mm, 3.7 mm, 3.8 mm)

nect the three-way lock to reinsert the stylet for extracting the aspirated material from the hollow core of the needle and not try to release the three-way lock.

Technique

The basic technique of EUS-guided fine needle aspiration is similar across the GI tract, with certain variations according to the site [4, 5, 7, 8, 18, 20, 22].

The steps of the procedure are identification of the target lesion, maneuvering the echoendoscope to align the lesion in the projected path of the needle, stabilizing the transducer in the chosen position, opposing the transducer close against the GI wall, color doppler evaluation of the projected path of the needle to insure a safe path devoid of vessels, advancing the needle out of the channel to puncture the GI wall and the lesion, sampling the targeted lesion with or without suction, withdrawal of the needle out of the lesion and removal from the scope, and transfer of the sampled tissue or fluid for cytopathology.

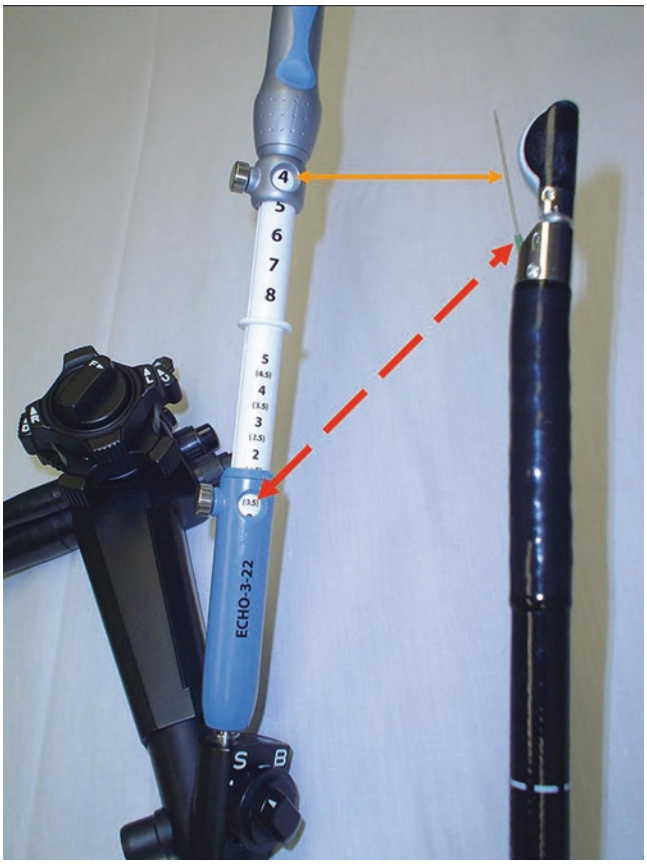

Fig. 37.4 Positioning the sheath and needle. The length of the sheath can be adjusted to keep it extended just beyond the bridge or elevator of the echoendoscope with a dedicated screw (*arrow with solid lines*). This can vary depending on the instrument used. The length of the needle can be separately adjusted as desired (*arrow with broken lines*)

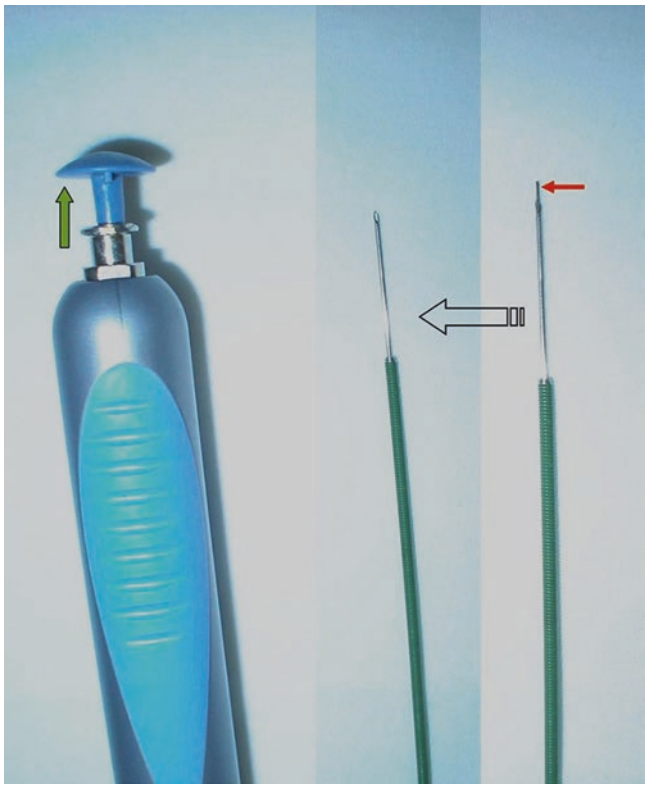

Fig. 37.5 Positioning the stylet. A rounded tip stylet avoids accidental scope damage, but it has to be withdrawn by a centimeter into the needle just before puncturing the luminal wall

Identification/Selection of the Target Lesion

Most often, the target lesion is obvious from the pre-procedural workup. It is important to review the available imaging such as CT scans for the primary lesion, for the presence of enlarged regional or distant lymph nodes, and for any metastatic lesions such as liver metastases or ascites. It is also important to assess the potential impact of the proposed procedure. Sampling of the para-celiac nodes is important in case of distal esophageal malignancies as well as lesions in head and uncinate region of pancreas or bile duct tumors. Sampling of pleural effusion or ascites is important if minimal amounts are detected when otherwise not suspected on prior imaging. This could potentially indicate advanced stage and inoperability, if positive for malignancy. Nodal metastases could help determining the need for adjuvant chemoradiotherapy in esophageal and rectal cancers.

Alignment of the Lesion in the Projected Path of the Needle

The side from which the needle exits on the screen is marked by a white dot outside the image indicating the oral-caudal orientation. Most Europeans orient the image with this dot on the left side, while American endosonologists use the opposite orientation. Once the needle is extended out of the channel, it is visualized as a bright linear structure. Drawing an imaginary path of the needle, the scope is maneuvered in such a way as to bring the lesion into A, B, C, or D positions, as depicted in Fig. 37.7a, b, by gently advancing the scope further, all the while maintaining the lesion within range of imaging. Further maneuvering to align the needle with the lesion can be achieved by the use of an elevator or turning the big wheel upward to change the angle of exit of the needle.

Stabilizing the Transducer

After the target lesion is aligned, the position of the transducer has to be maintained while the operator is trying to adjust the parameters on the ultrasound console or switching on the color Doppler or performing the needle aspiration. The options available are "fixing" the scope position by the use of "F-knob" on the big wheel (controlling the up-down movement), maintaining the direction and hand-body position of the operator (controlling the left-right movement and torque), and having a reliable assistant to hold the scope position at the bite guard. A combination of these maneuvers offers the best possibility to maintain the stable position of the transducer.

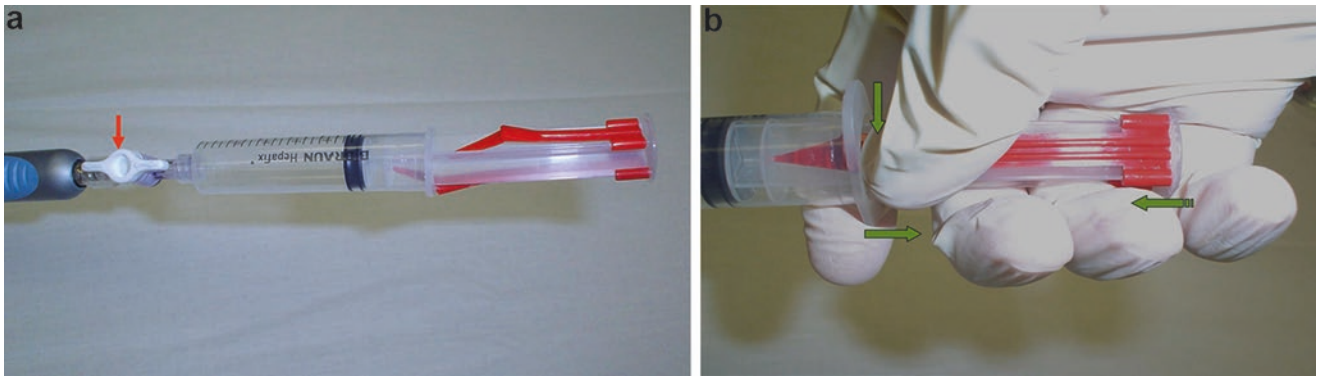

Fig. 37.6 (**a**) Positioning the suction syringe. When the needle is within the target and the stylet is removed, the three-way suction syringe could be attached to the needle and the three-way knob could be twisted to be in line with the needle to allow suction. (**b**) Tissue sampling. Once the lesion is sampled, while the needle tip is still within the lesion, the suction could be slowly released pressing the red stopper on the syringe with the thumb and holding the piston between the thumb and index fingers to let it slowly slide toward the syringe carefully, avoiding sudden release of suction

Apposition of the Transducer

To ensure that there is no gap between the transducer and the wall to be punctured, the position of the transducer is stabilized as described above. Gentle suction and decompression of the bowel lumen helps by removing any interfering air artifacts. At times, inflating the balloon on the transducer with water also helps achieving the best apposition and acoustic coupling to facilitate the needle puncture. If balloon inflation is used, it is advisable to extend the needle out of the channel by about 1 cm and then inflate the balloon in order to avoid puncturing the balloon.

Color Doppler Evaluation

Use of color Doppler imaging to evaluate the projected path of the needle ensures a passage devoid of large vessels. Even with Doppler scanning, most significant vessels can be detected by the appearance of anechoic linear structures that could be traced by following their course by EUS. In the event of suspicious vascular structures in the path of the needle, these can be avoided by changing the position of the transducer and the projected needle path by gently adjusting the transducer. Maintaining the hand-scope position, rotation of the scope tip by mild left or right rotation of the body of the operator can change the angle. Rarely, minimal torque on the scope by an assistant is useful to complete the procedure. When using color Doppler, it is important to adjust the noise level on the console to avoid artifacts. Microvessels within the tumor due to hypervascularity need not preclude EUS-FNA (Fig. 37.8). In such lesions, some amount of bloody aspirate is expected and cannot be avoided. But, this can be minimized by using less or no suction while sampling such lesions or smaller caliber needles.

Needle Puncture

Once the target is chosen, the transducer is positioned, the needle path is determined, and measuring the distance from the center of the lesion to the site of exit of the needle provides an approximate idea of the length of needle to be extended. Accordingly, the screw on the handle of the needle is adjusted to the limit of the extended depth of penetration of the needle (Fig. 37.4). It is useful to allow an additional 1–2 cm to compensate for yield of the tissues or movement of the GI wall away from the transducer during puncture. Alternately, while puncturing critical areas like the aortopulmonary window, one could start with a shorter needle length and adjust as appropriate as the needle is advanced.

While 19 G needles come with a round-tipped stylet that extends about 1 cm beyond the beveled tip, 22 G needles have an option of a beveled stylet that is flush with the bevel of the needle or a round-tipped stylet that extends beyond the bevel. While using the needles with round-tipped stylets, the stylet has to be withdrawn by 1 cm to allow the beveled needle tip to come in contact with the mucosal surface to enable puncture. Some prefer to remove the stylet altogether before the puncture. However, it is important to be aware that in the absence of the stylet, the cellular material from the tissues traversed while reaching the target lesion will be admixed with the aspirate. This could become an issue when dealing with well-differentiated malignancies [13].

The degree of difficulty of EUS-FNA varies with location (Table 37.3) increasing from transesophageal to transduodenal to transgastric lesions by site. It is obvious that the EUS-guided therapeutic interventions are more complicated than the EUS-FNA. But, the common requirement for any advanced EUS-guided interventions is mastery of the technique of EUS-FNA. Sampling of large mediastinal masses or enlarged mediastinal lymph nodes are the easiest and should

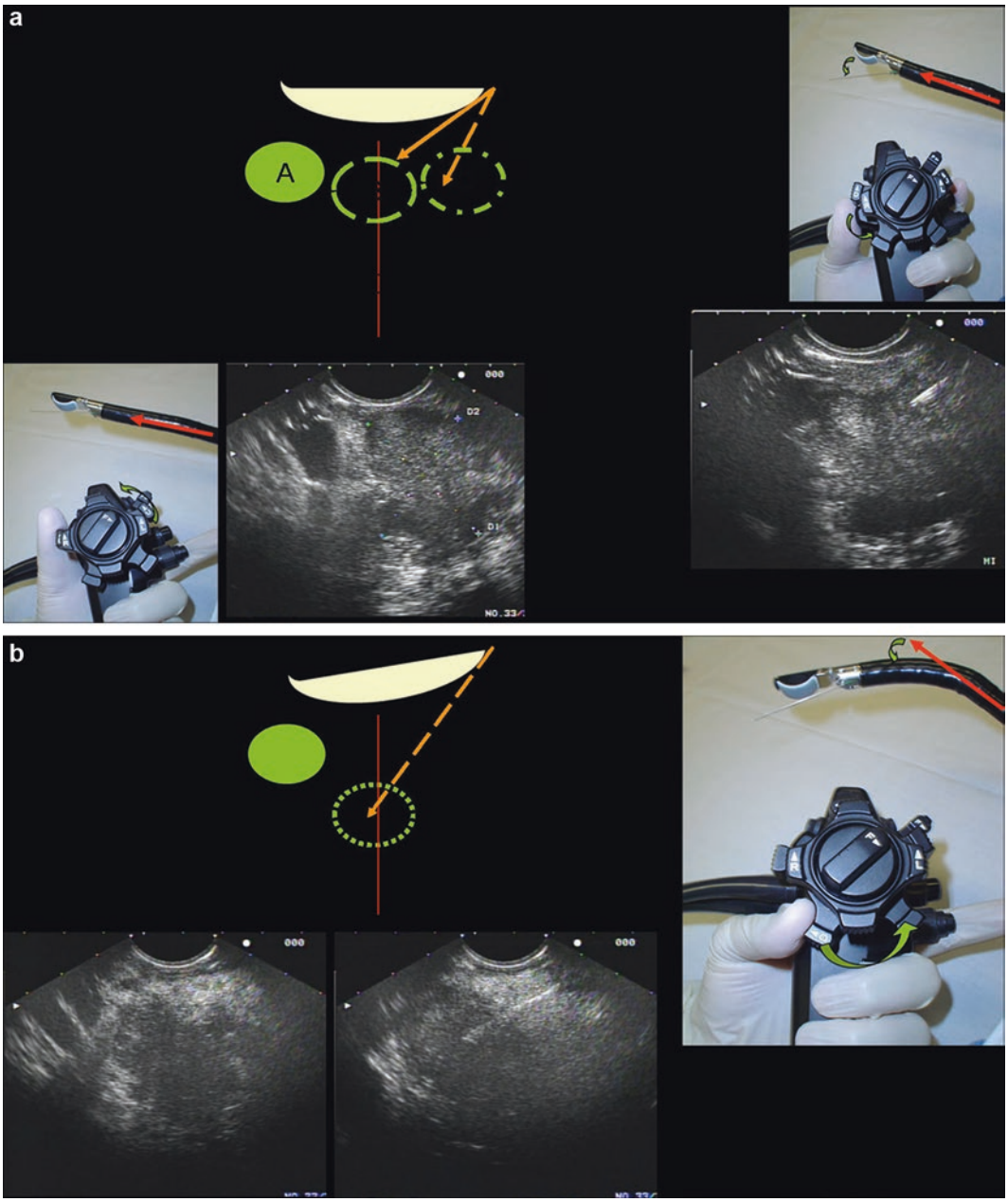

Fig. 37.7 (**a**) Approach to the lesion. Drawing an imaginary path of the needle, the scope is maneuvered in such way as to bring the lesion in to A, B, or C positions by either gently advancing the scope further, while maintaining the lesion within range of imaging, or by the use of elevator as demonstrated in a pancreatic head mass. (**b**) Aiming the needle. Further maneuvering to align the needle and the lesion could also be achieved by turning the big wheel upward to change the angle of exit of the needle without straining the elevator as demonstrated in the same case as above

be the first lesions to start with. Puncturing these lesions in a relatively closed space is relatively easy with the fixed structures offering counter resistance to advancement of the needle (Figs. 37.9 and 37.10).

The difficulty with the pancreatic head lesions is mostly due to the issues with positioning of the transducer and the curvature of the bending section of the scope making it difficult to advance needle. The other issues are inherent to the nature of the lesions as in presence of chronic pancreatitis due to fibrosis. Whereas puncturing the lesions adjacent to or within the gastric wall are difficult due to the tremendous yield of the tissues with no counter resistance offered to allow the puncture. In such situations, it is often useful to have an extended needle length made available. Initially, the advancement of the needle results in "tenting" of the GI wall layers. At this time, a quick jab of the needle tip (spearing) rather than gentle advancement facilitates the successful puncture. It is important to develop a "feel" for the different lesions being punctured.

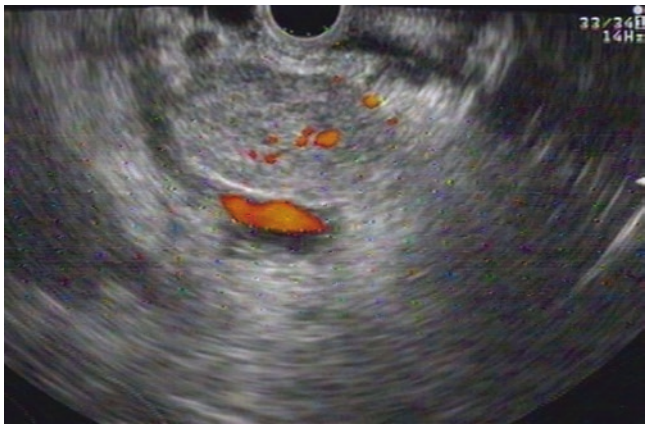

Fig. 37.8 Color Doppler evaluation. This is useful to avoid significant vessels in the projected path of the needle. Microvessels due to hypervascularity of the tumor need not preclude EUS-FNA

Sampling the Targeted Lesion With or Without Suction

Once the needle is within the lesion, the stylet is removed completely and a self-sustaining suction syringe is attached. Due to the longer length of the stylet, as it is being removed, the assistant has to carefully wind it in larger circles avoiding kinks. Some operators prefer not to use suction, while some use low-volume suction. In general, the use of moderate suction with a 10 mL syringe provides better quality of the aspirate. However, in hypervascular lesions, excessive suction might reduce the quality of the sample due to the presence of bloody aspirate. Maintaining the suction, the needle is moved back and forth approximately 5–10 times within the lesion to disrupt the tissue and collect the cellular material.

During sampling, the material stays within the hollow needle and except while aspirating cystic lesions or fluid collection, aspirate will not be seen coming into the syringe due to the length of the needle. Detection of bloody aspirate at the level of syringe indicates puncture of a vessel. In this event, one should stop further suction and manipulation, but observe the image to determine whether there is any hypo/anechoic structure in the path of the needle. It is important to close the suction by turning the three-way valve to the off position and withdraw the needle. If excess bleeding is noted, there is usually a change of echomorphology around the area of puncture indicating a local hematoma. Although most such events resolve spontaneously, one should use clinical judgment as to whether to continue with the procedure in such an occurrence.

Withdrawal of the Needle

Once the sample is collected within the needle, as described above, suction is released slowly in a controlled manner prior to withdrawal while the tip of the needle is still within the lesion (Fig. 37.6). Then, the elevator is released, the needle is drawn back into the channel, and the screw is fastened to avoid damage to the scope by extending the needle out of the channel during withdrawal. The whole needle assembly is detached and withdrawn from the scope. Then, the transducer is moved away from the bowel wall to visualize the puncture site.

Transfer of the Sampled Tissue or Fluid for Cytopathology

Extending the tip of the needle from the channel, the stylet is reinserted slowly holding the tip of the needle over a couple of glass slides delivering a drop of the aspirate on each slide. The rest of the material is delivered into *cytolyte* solution for subsequent processing in the laboratory. The material on the glass slide is spread thin using another glass slide as shown in Fig. 37.11. Then, the smear is air-dried and stained to examine for adequacy by an on-site cytopathologist.

Alternately, the adequacy of specimen can be assessed by smearing the aspirate to prepare as many smears as possible by transferring material onto various glass slides and examining the smears for tiny particulate matter on the slides. If a good amount of particulate material is seen on at least three or four slides, the sampling will be usually adequate. Bloody specimens do not necessarily contain representative material. However, if excess blood is seen in the specimen, clots can be separated and sent to pathology in formalin solution for clot histology, which can sometimes increase the yield of the specimen. There are several studies now available highlighting the limitation of visual interpretation of endosonographer or even a technician regarding on-site evaluation of stained smears by a cytopathologist. Rapid on-site cytopathology reduces the number of passes, ensures specimen adequacy, provides definitive diagnosis, and should be used whenever available [15].

Once the material is collected from the needle, the stylet is reinserted and the needle assembly is prepared for another pass. The stylets of the 22 G and 25 G needles are very thin and easily kink unless extreme care is taken while handling them. Generally, it takes one or two passes for mediastinal lesions to obtain an adequate specimen, while pancreatic lesions would require 3–4 passes. The material obtained from different passes can be processed and reported together. However, when more than one lesion is punctured, it is important to use different needles and to label the specimen for interpretation, separately. While labeling the specimens, it is important to indicate if the sampling is transesophageal, transgastric, transduodenal, etc. This will help the cytopathologist to differentiate the material obtained from the lesion versus contamination from the cells of the bowel wall.

Whenever lymphoma is in the differential diagnosis of a lesion being aspirated, it is very important to send the aspi-

Table 37.3 Level of difficulty in various EUS-guided procedures

Level	Location	Lesions	Unique features and tricks
I	Mediastinum	Large tumors	Transesophageal sampling from lesions closely apposing the esophageal wall is the easiest to puncture (Fig. 37.9)
		Lymph nodes	Subcarinal and lower para-esophageal are relatively easy to access (Fig. 37.10)
			Having an assistant hold the position of the scope helps while aspirating nodes proximally located in the paratracheal and aortopulmonary window
II	GE junction	Fundal masses	Almost similar to lower mediastinal lesions
			Apposing the transducer to the lesion or the GI wall is the key
			Diaphragm and adjacent structures offer counter resistance facilitating puncture
	Liver	Metastases	Accessible lesions in this large organ offer a relatively easier target
	Structures in relation to posterior gastric wall	Para-celiac lymph nodes	Initial evaluation with radial EUS helps in orientation of the structures in relation to the vessels, pancreas, and distance from the GE junction
		Tumors of pancreatic body-tail	
		Peripancreatic lymph nodes	Identifying the aorta, celiac, and superior mesenteric vessels with the CLE and then correlating with the findings of initial radial EUS help in localizing the smaller lesions
		Left adrenal metastases	Position of the transducer to bring the target lesions in the imaginary path of the needle and have an assistant hold the scope orientation and position at the mouthpiece
		Fluid collections	
			To compensate for the yield of tissues, it is useful to allow about 1 cm longer length of needle than the estimated distance of the lesion from the scope
			Softer or easily displaced lesions are accessible by initial transgastric puncture until the lesion and subtle adjustment of position to keep the target directly in line with the tip of the needle and use a quick "jab" movement to enter the lesion
	Perirectal	Lymph nodes	Access to the lower perirectal lesions is like periesophageal lesions
			The technique for the rectosigmoid lesions is similar to that described above

(continued)

Table 37.3 (continued)

Level	Location	Lesions	Unique features and tricks
III	Transduodenal	Lymph nodes in relation to pancreatic head, hepatic hilum	19 G needles are difficult to maneuver for transduodenal sampling due to multiple levels of bending of the scope
		Pancreatic head-uncinate tumors	
		Biliary strictures	Short scope position is most suitable for EUS-FNA; hence, the time taken to proper positioning of the scope in relation to the lesion is well spent.
			Using the big wheel to alter the direction or orientation of the needle is preferable to the use of the elevator while accessing the lesions in head and uncinate region of pancreas
			Lesions in the head-genu region are accessible through the duodenal bulb
			Distal biliary strictures are more accessible in short route along the medial duodenal wall
			Proximal biliary strictures are accessible from the duodenal bulb using torsion on the scope to change the orientation toward the superior fornix of the duodenal bulb
			Presence of biliary stent serves as an identifiable structure to trace sonologically, either proximally or distally to detect and target the lesion
	Gastric body (anterior wall, greater curve), antrum	Intramural lesions	Most difficult lesions to access due to the mobility of the stomach lacking any adjacent structures to offer a firm counter resistance
			The lesions get displaced as the needle is advanced and are best punctured by a two-step method
			Initial step is to puncture the gastric wall advancing the needle tip closer to the lesion aligning it, and the next step is a quick jab-like movement(like spear fishing)
			Part of the difficulty of sampling these lesions is also because of the nondependent position of the antrum making it difficult to obtain a proper acoustic coupling in left lateral position. At times, changing the patient to supine helps
IV	EUS-guided interventions	Celiac ganglion neurolysis	
		Pseudocyst drainage	
		Biloma drainage	
		Pancreatic cyst ablation	
		Biliary-pancreatic ductal access	

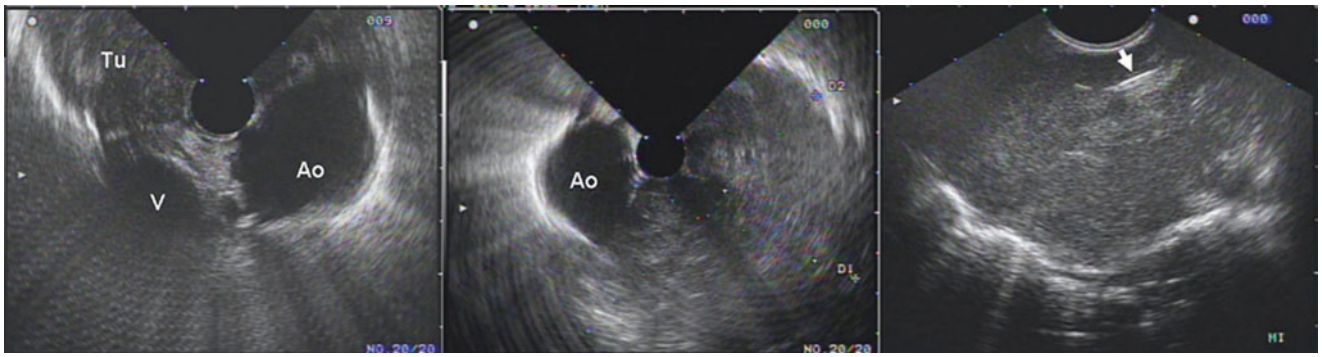

Fig. 37.9 Lung cancer. Large periesophageal tumor (*Tu*), predominantly in anterior location as seen on initial radial EUS (Pentax EG-3630UR) with the vertebra (*V*) at 6 o'clock and the aorta (*Ao*) at 5 o'clock positions (*left image*). Rotating the scope by 180° brings almost the entire tumor into view (*middle image*). 19 G fine needle (*arrow*) aspiration using Pentax EG-3630 U revealed squamous cell lung cancer

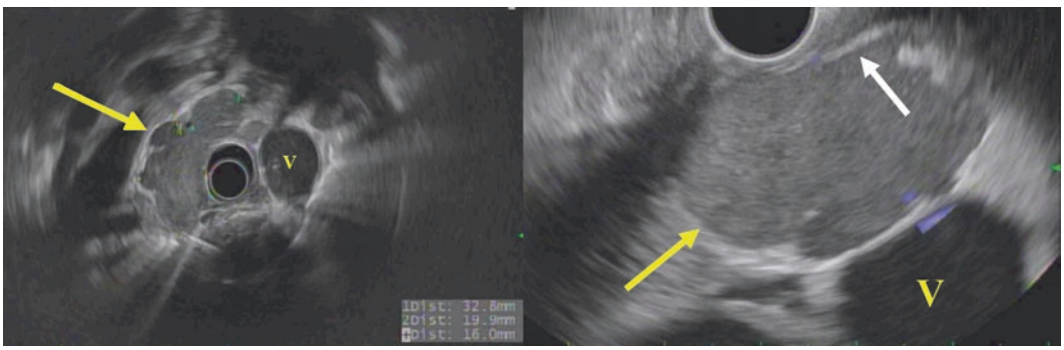

Fig. 37.10 Lymph nodes. Enlarged mediastinal lymph nodes in relation to vascular structures (V) using the Olympus GF-UC140P-AL5 (*left*). Advancing the scope aligns the target lesion with the needle (*arrow*) away from the vessel enabling safe puncture

rate for flow cytometry. For this purpose, every facility performing EUS-FNA should also have *RPMI* solution that preserves cellular material in the aspirate to enable flow cytometry.

When aspirating cystic lesions of the pancreas, 1–2 mL of fluid should be sent for estimation of CEA levels besides routine analysis, including cell count, amylase, and lipase. Some laboratories offer cyst fluid DNA analysis in equivocal cases for excluding malignant mucinous tumors. Although routinely not available, the use of molecular methods on the EUS-FNA aspirate is increasing to aid in the diagnosis of malignancy in solid tumors as well.

Examples of actual cases diagnosed by EUS-FNA are shown in Figs. 37.11, 37.12, 37.13, 37.14, 37.15, 37.16, 37.17, 37.18, 37.19, and 37.20.

Complications

Complications are uncommon with EUS as well as EUS-FNA, but are possible and have been reported. Besides sedation-related events that can occur in any endoscopic procedure, EUS is associated with two important complications,

Practical Considerations

- The side from which the FNA needle exits on the screen is marked by a white dot outside the image indicating the oral-caudal orientation. Most Europeans orient the image with this dot on the left side, while American endosonologists use the opposite orientation.
- After the target lesion is aligned, the position of the transducer has to be maintained while the operator is trying to adjust the parameters on the ultrasound console. This can be achieved by "fixing" the scope position by the use of "F-knob" on the big wheel (controlling the up-down movement), maintaining the direction and hand-body position of the operator (controlling the left-right movement and torque), and having an assistant to hold the scope position at the bite-guard.
- Maintain no gap between the transducer and the wall to be punctured.
- Use color Doppler imaging to evaluate the projected path of the needle to ensure a passage to avoid large vessels.

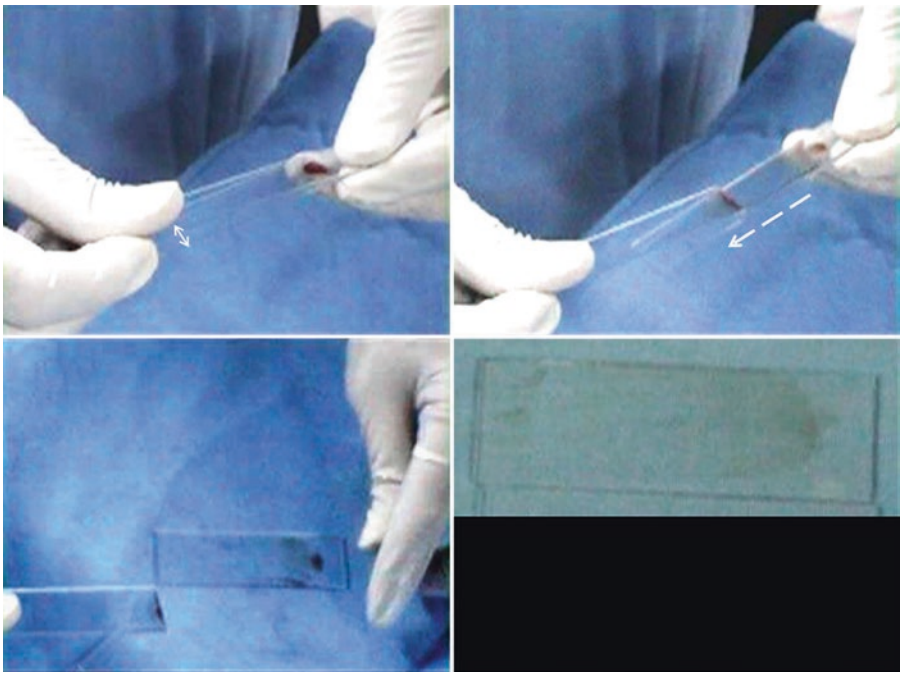

Fig. 37.11 A drop of the aspirate is gently expelled on to a glass slide and is smeared with the help of another glass slide placed at 10–15° angle (*top left*) and drawn down its length (*top right*), spreading the material into a thin layer (*bottom left*) that could either be air-dried (*bottom right*) or stained immediately

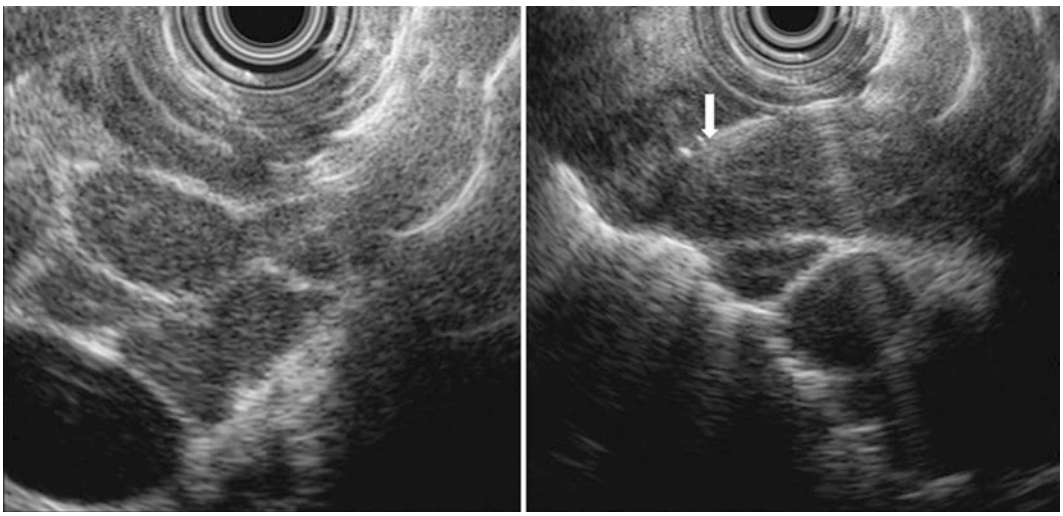

Fig. 37.12 Sarcoid. A 28-year-old male with dyspnea and dry cough without fever, night sweats, or weight loss. Mediastinal widening was seen on chest x-ray and prominent mediastinal lymph nodes on thoracic CT. PPD negative. EUS (*left*) showed multiple paraesophageal and subcarinal enlarged coalescing lymph nodes. EUS-FNA (*right*) using a 22 G needle (*arrow*) demonstrated granulomatous inflammation without caseation or acid-fast bacilli suggesting sarcoidosis

perforation and pancreatitis. In addition, EUS-FNA is also associated with bleeding and infection [2, 3, 6, 19].

Perforation

Although the rate of perforation for EUS-FNA is comparable to that of EGD, it is important to note the differences in conventional gastroscopes and the echoendoscopes to appreciate the higher potential for problems. Due to the presence of the transducer at the tip of the echoendoscope, there is a variable length (depending on the manufacturer and the type of transducer) of a rigid segment before the bending section that makes maneuvering a little difficult during intubation across the pharyngoesophageal junction and while negotiating the duodenal bulb into the second part of duodenum. Visual guidance and repositioning the head-neck region (the neck bent forward with a backward head tilt) helps intubation

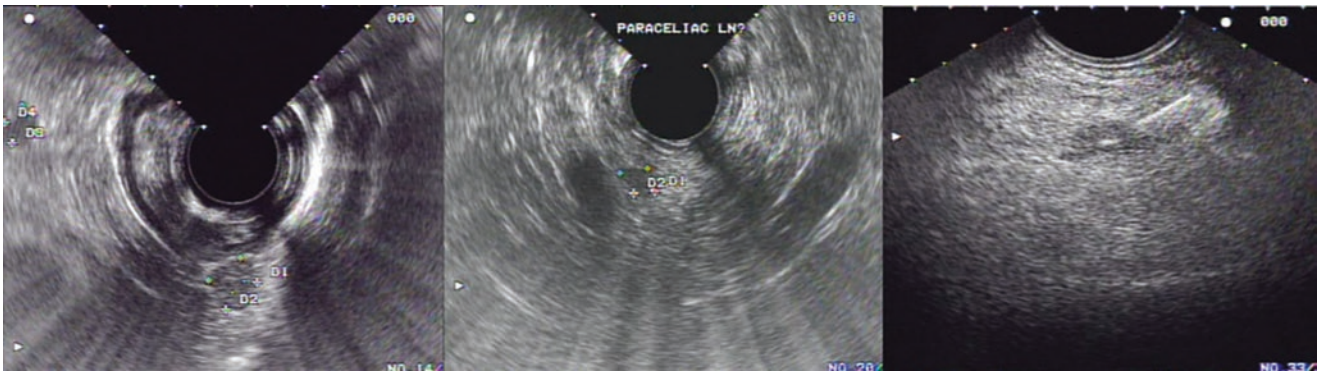

Fig. 37.13 Esophageal cancer. A 54-year-old male with iron deficiency anemia and no esophageal symptoms had a distal esophageal adenocarcinoma on EGD (*left*) that was staged as T2 N1 (*middle*). But a 6 mm non-regional para-celiac lymph node showed metastatic disease on EUS-FNA (*right*)

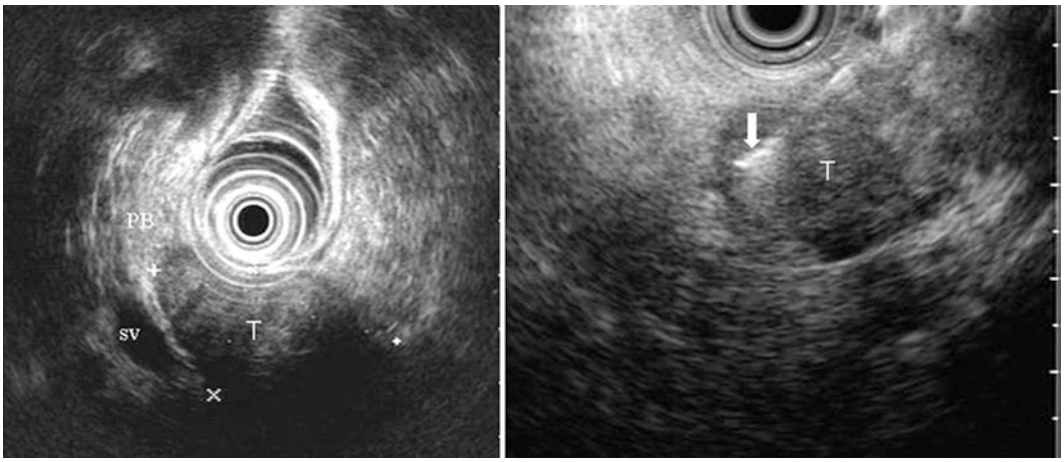

Fig. 37.14 Pancreatic cancer. A 62-year-old male with severe left upper quadrant pain and unexplained weight loss. Abdominal US was normal, but contrast CT showed bulky pancreatic tail. EUS showed a 3 × 2.5 cm hypoechoic mass (*left*) which was confirmed to be adenocarcinoma on EUS-FNA (*right*) using a 22 G needle (*arrow*) leading to a successful distal pancreatectomy. (*SV* splenic vein, *T* tumor)

across the hypopharynx. In case of intubation difficulty across the hypopharynx or when maneuvering across the duodenal bulb into the second part of duodenum, keeping the balloon around the transducer partially inflated helps to gently glide the rigid part of the echoendoscope. Another important cause of bowel wall injury is the use of radial EUS to complete the endoscopic part of the examination, especially visualizing the proximal stomach and fundus in retroflexion. In general, it is important to keep in mind that the echoendoscopes are relatively stiffer than the conventional endoscopes. It is helpful to complete this part of the examination prior to sonological evaluation by inflating the stomach adequately for a safe retroflexion. Once this is completed, the stomach can be decompressed completely and instilled with water for completing the EUS.

The rigid segment of the CLE scope is longer than the radial EUS scope and, among the two commonly used instruments, the Pentax system has a longer rigid segment. It is also important to note that the optics in the CLE is like that of a duodenoscope, and that the transducer extends up to an inch beyond the lens. Likewise, the Olympus radial instruments are oblique viewing. Hence, the axis of the tip of the echoendoscope is different from the visual axis, and it is important to make the corresponding adjustments in maneuvering the big wheel to align the instrument appropriately.

Acute Pancreatitis

Acute pancreatitis has been reported with even radial EUS without FNA. This could possibly be related to the lengthy procedure during biliary-pancreatic evaluation, with repeated back and forth movements of the transducer with inflated balloon along the medial aspect of the duodenum (massaging the pan-

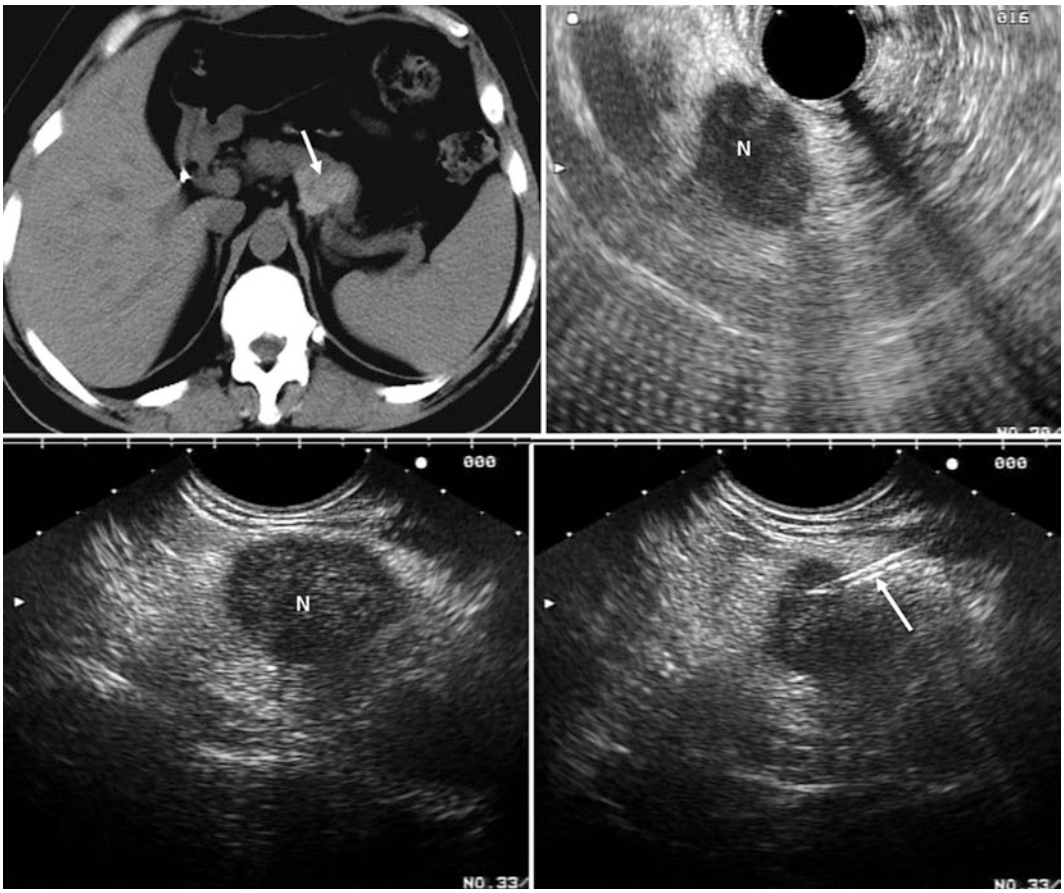

Fig. 37.15 Pancreatic lymphoma. Follow-up abdominal CT in a patient with large B-cell lymphoma showed a pancreatic body lesion (*arrow, top left*). He completed chemotherapy recently with excellent clinical response. CA 19-9 levels were normal. EUS was suggestive of residual peripancreatic lymph nodes (N) rather than pancreatic body mass (radial imaging: *top right*; linear imaging: *bottom left*). EUS-FNA using a 19 G needle (*arrow, bottom right*) showed necrotic tissue excluding residual tumor

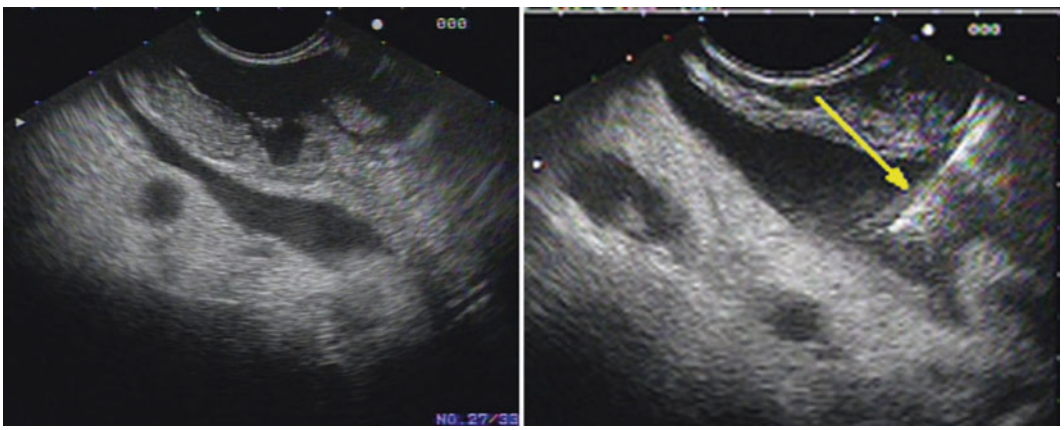

Fig. 37.16 Ascites in gastric cancer. A 55-year-old male with adenocarcinoma of GE junction underwent EUS for staging that showed T3 N1 lesion involving the GE junction transmurally. Patient had, in addition, minimal perigastric ascites indicating peritoneal spread (*left*). EUS-guided aspiration of the fluid with 22 G needle (*right*) showed metastatic disease

creatic head and uncinate region of the gland). This is often mild and self-limiting. Occasionally, pancreatitis was reported following EUS-FNA, particularly when multiple passes had been made. In general, acute pancreatitis is not a common complication although one study reported up to 2% of the cases, and there are no predictors identified for prevention.

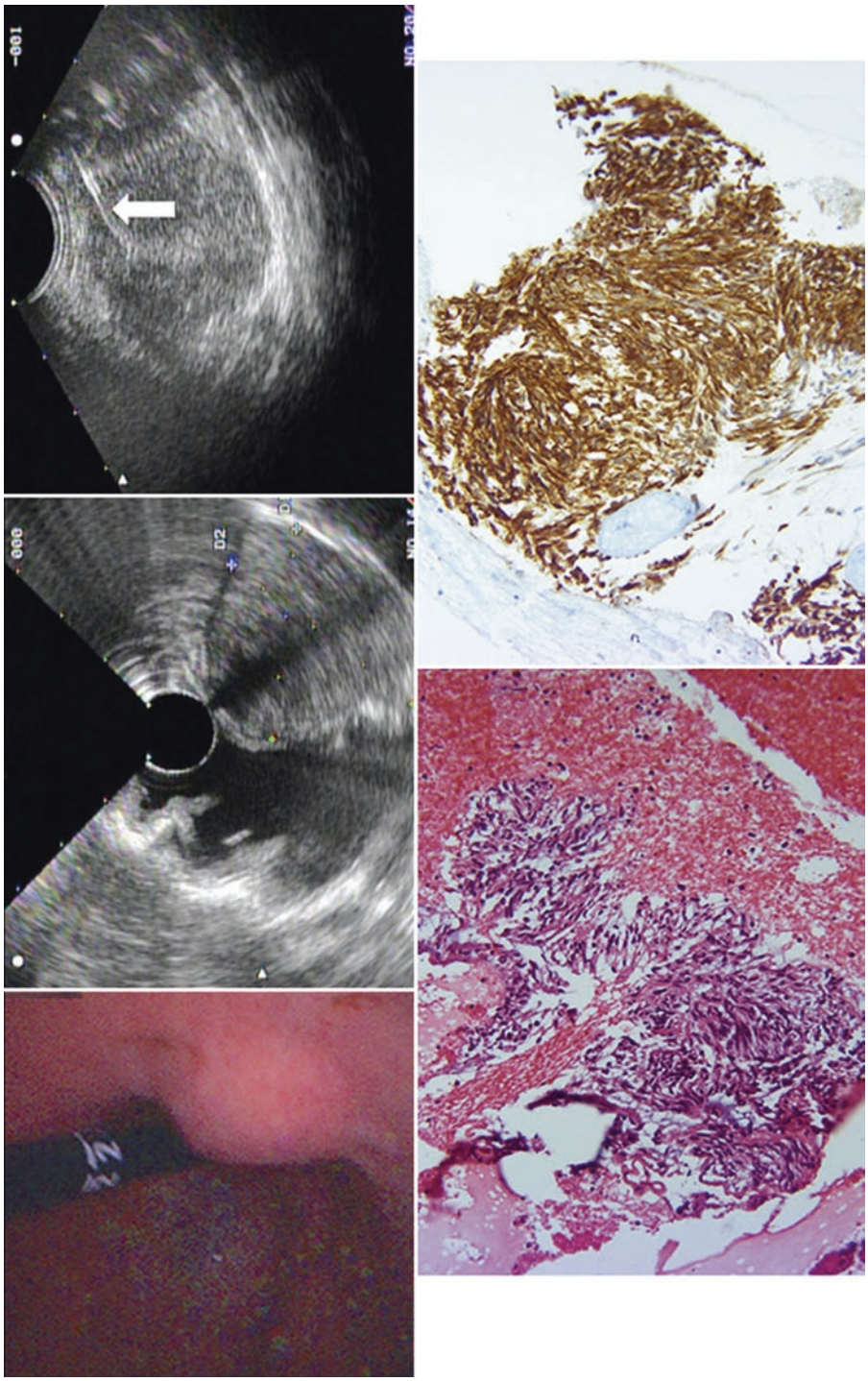

Fig. 37.17 Rectal stromal tumor. A distal rectal submucosal lesion (*arrow*) in retroversion (*left*) and the same on radial EUS with Pentax EG-3630UR (*middle*) suspicious for stromal tumor. EUS-FNA (*right*) using a 19 G needle (*block arrow*) provided biopsy quality material to confirm the diagnosis. Cohesive tissue fragments of the lesion described above comprised of spindle cells with fusiform nuclei on H & E (*left*). Immunohistochemistry for CD117 (c-Kit) was strongly and diffusely positive (*right*) confirming the gastrointestinal stromal tumor (*GIST*)

Bleeding

Unless repeated passes are made with a 19 G needle, mucosal bleeding is not an issue with EUS-FNA. There was an occasional report of mucosal bleeding that responded to endotherapy with epinephrine injection. Delayed bleeding is unusual, and most instances of bleeding can be recognized before the echoendoscope is withdrawn from the patient. Routine use of color Doppler is important to evaluate the vascularity of the lesion and to assess the projected path of the needle. Even when dealing with an obviously safe lesion to puncture, it helps to verify the relative location of any significant vascular structures. After completing the procedure, before the instrument is withdrawn, it is always a good practice to inspect the lesion and the site of puncture, both on EUS and endoscopy for any evidence of bleeding. Local

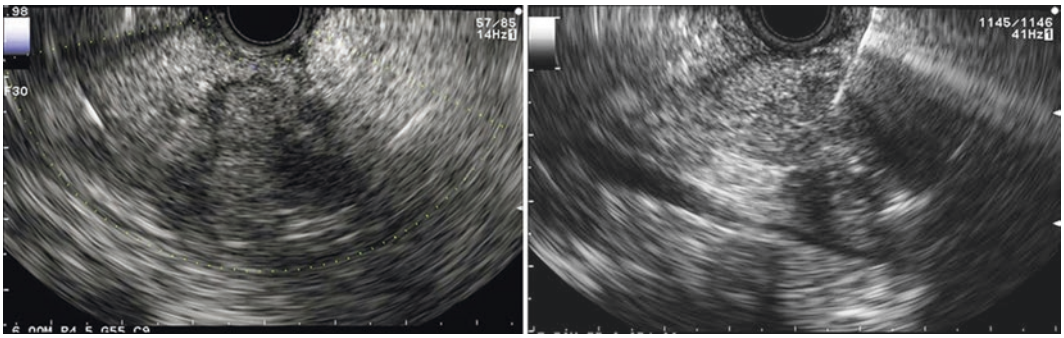

Fig. 37.18 Pancreatic cancer. Pancreatic head mass (*left*) imaged with the Olympus GF-UC140P-AL5. EUS-FNA using a 22 G needle showed adenocarcinoma

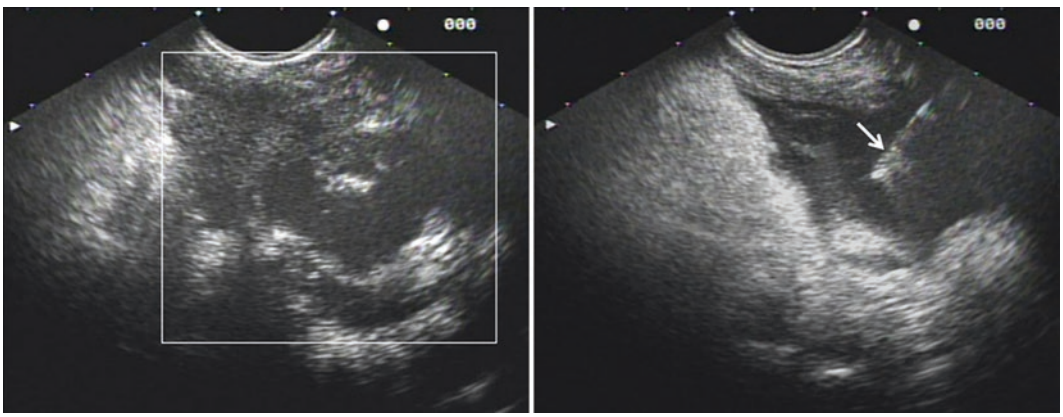

Fig. 37.19 Pancreatic cancer. A 36-year-old male with severe abdominal pain, vomiting, and weight loss of 2 weeks duration was referred with an abdominal CT showing enlarged head of pancreas. Pancreatic enzymes and tumor markers were normal. An MRI of abdomen with contrast showed a lesion in the head of pancreas encasing the SMA (*top left*) suspicious for malignancy

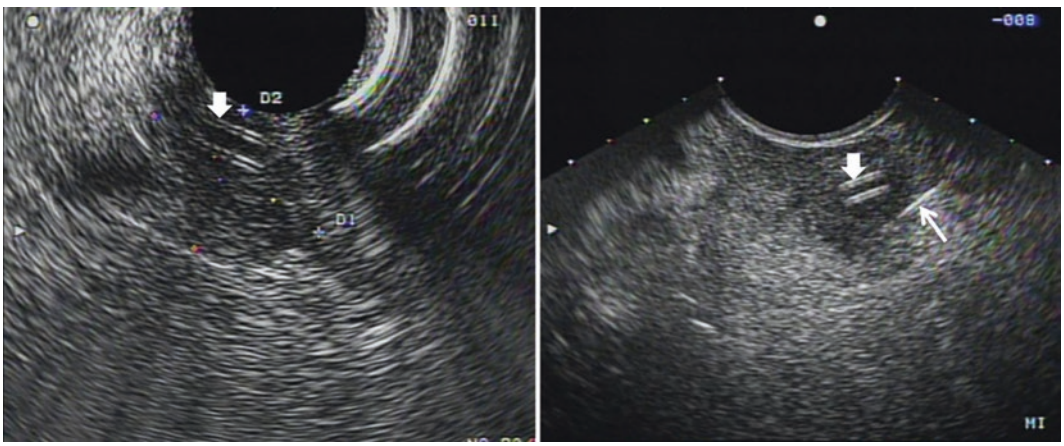

Fig. 37.20 Cholangiocarcinoma. A 52-year-old male admitted with painless progressive jaundice of 4 weeks duration and marked weight loss. Abdominal CT showed diffuse dilation of the intrahepatic and extrahepatic bile ducts with distal narrowing. ERCP, biliary sphincterotomy, and stenting were performed. Biliary brush cytology was inconclusive. EUS (*left*) showed distal biliary stricture seen as a thickening around the stent (*block arrow*), and EUS-FNA (right) using a 22 G needle (*arrow*) established cholangiocarcinoma

bleeding can be suspected if a solid lesion appears to have increased in size or there is excessive debris in a cystic lesion compared to before puncture. A corresponding change in hemodynamics or a drop in hematocrit >2 g/dL connotes significant bleeding and requires further measures. When significant bleeding is suspected, even in the absence of endoluminal bleeding, in-hospital observation with resuscitative measures and transfusion support may be required. It

is extremely unusual to require any interventional radiology techniques for a EUS-FNA-related bleeding.

EUS-FNA is considered a high-risk procedure in the context of anticoagulant use, and it is recommended to withhold antiplatelet agents and anticoagulants 3–5 days prior to procedure, so that it can be done safely. However, in one study, the bleeding risk was not found to be increased in patients on aspirin/NSAIDs compared to controls [11]. However, the use of prophylactic low-molecular-weight heparin was still associated with a higher rate of bleeding.

Infection

Infection is a potential complication when cystic lesions are sampled, such as in mediastinum or pancreas. A routine preprocedural prophylactic antibiotic is mandatory whenever cystic lesions, loculated collections, or necrotic tumors are punctured. In general, solid lesions are less at risk for infection following EUS-FNA, except when puncturing perirectal lesions, where infective complications are high and administration of antibiotics prior to procedure is recommended.

Practical Considerations

- Besides sedation-related events that can occur in any endoscopic procedure, EUS is associated with two important complications, perforation and pancreatitis.

Conclusions

- EUS-FNA is indicated for evaluation of mediastinal and intra-abdominal lymph nodes and staging of lung, esophageal, biliary-pancreatic, and anorectal cancers by evaluation of nodes.
- Periluminal fluid collections can be sampled from small pleural effusions, minimal ascites, peripancreatic fluid, and pseudocysts.
- Focal lesions can be sampled to exclude malignancy.
- EUS is associated with two important complications, perforation and pancreatitis, but pancreatitis and infection can also occur.

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References

1. Adler DG, Conway JD, Coffie JM, Disario JA, Mishkin DS, Shah RJ, et al. EUS accessories. Gastrointest Endosc. 2007;66(6):1076–81.
2. Al-Haddad M, Wallace MB, Woodward TA, Gross SA, Hodgens CM, Toton RD, et al. The safety of fine-needle aspiration guided by endoscopic ultrasound: a prospective study. Endoscopy. 2008;40(3):204–8.
3. Al-Haddad M, Gill KR, Raimondo M, Woodward TA, Krishna M, Crook JE, Skarvinko LN, Jamil LH, Hasan M, Wallace MB. Safety and efficacy of cytology brushings versus standard fine-needle aspiration in evaluating cystic pancreatic lesions: a controlled study. Endoscopy. 2010;42(2):127–32.
4. Binmoeller KF, Rathod VD. Difficult pancreatic mass FNA: tips for success. Gastrointest Endosc. 2002;56(4 Suppl):S86–91.
5. Erickson RA. EUS-guided FNA. Gastrointest Endosc. 2004;60(2):267–79.
6. Fisher L, Segarajasingam DS, Stewart C, Deboer WB, Yusoff IF. Endoscopic ultrasound guided fine needle aspiration of solid pancreatic lesions: performance and outcomes. J Gastroenterol Hepatol. 2009;24(1):90–6.
7. Fritscher-Ravens A, Brand B, Bohnacker S, Sriram P, Soehendra N. Technique of endoscopic ultrasonography-guided fine-needle aspiration of the lymph nodes. Tech Gastrointest Endosc. 2000b;2(3):142–8.
8. Fritscher-Ravens A, Broering DC, Sriram PV, Topalidis T, Jaeckle S, Thonke F, et al. EUS-guided fine-needle aspiration cytodiagnosis of hilar cholangiocarcinoma: a case series. Gastrointest Endosc. 2000a;52(4):534–40.
9. Fritscher-ravns A. EUS-experimental and evolving techniques. Endoscopy. 2006;38(S1):S1–4.
10. Giovannini M. Ultrasound-guided endoscopic surgery. Best Pract Res Clin Gastroenterol. 2004;18:183–200.
11. Kien-Fong Vu C, Chang F, Doig L, Meenan J. A prospective control study of the safety and cellular yield of EUS-guided FNA or Trucut biopsy in patients taking aspirin, nonsteroidal anti-inflammatory drugs, or prophylactic low molecular weight heparin. Gastrointest Endosc. 2006;63(6):808–13.
12. Hwang JH, Aslanian HR, Thosani N, Goodman A, Manfredi M, Navaneethan U, Pannala R, Parsi MA, Smith ZL, Sullivan SA, Banerjee S. Devices for use with EUS. VideoGIE. 2017;2(3):35–45.
13. Mitsuhashi T, Ghafari S, Chang CY, Gu M. Endoscopic ultrasound-guided fine needle aspiration of the pancreas: cytomorphological evaluation with emphasis on adequacy assessment, diagnostic criteria and contamination from the gastrointestinal tract. Cytopathology. 2006;17(1):34–41.
14. Murad FM, Komanduri S, Abu Dayyeh BK, Chauhan SS, Enestvedt BK, Fujii-Lau LL, Konda V, Maple JT, Pannala R, Thosani NC, Banerjee S. Echoendoscopes. Gastrointest Endosc. 2015;82(2):189–202.
15. Nguyen YP, Maple JT, Zhang Q, Ylagan LR, Zhai J, Kohlmeier C, et al. Reliability of gross visual assessment of specimen adequacy during EUS-guided FNA of pancreatic masses. Gastrointest Endosc. 2009;69(7):1264–70.
16. Noh KW, Woodward TA, Raimondo M, Savoy AD, Pungpapong S, Hardee JD, et al. Changing trends in endosonography: linear imaging and tissue are increasingly the issue. Dig Dis Sci. 2007;52(4):1014–8.
17. Puri R, Vilmann P, Săftoiu A, Skov BG, Linnemann D, Hassan H, et al. Randomized controlled trial of endoscopic ultrasound-guided fine-needle sampling with or without suction for better cytological diagnosis. Scand J Gastroenterol. 2009;44(4):499–504.
18. Savides TJ. Tricks for improving EUS-FNA accuracy and maximizing cellular yield. Gastrointest Endosc. 2009;69(2 Suppl):S130–3.

19. Shah JN, Muthusamy VR. Minimizing complications of endoscopic ultrasound and EUS-guided fine needle aspiration. Gastrointest Endosc Clin N Am. 2007;17(1):129–43. vii–viii
20. Vilmann P, Săftoiu A. Endoscopic ultrasound-guided fine needle aspiration biopsy: equipment and technique. J Gastroenterol Hepatol. 2006;21(11):1646–55.
21. Wani S, Muthusamy VR, Komanduri S. EUS-guided tissue acquisition: an evidence-based approach (with videos). Gastrointest Endosc. 2014;80:939–59.e7.
22. Yamao K, Mizuno N, Takagi T, Hara K. How I do it and when I use (and do not use) EUS-FNA. Gastrointest Endosc. 2009;69(2 Suppl):S134–7.
23. Yusuf TE, Tsutaki S, Wagh MS, Waxman I, Brugge WR. The EUS hardware store: state of the art technical review of instruments and equipment (with videos). Gastrointest Endosc. 2007;66(1):131–43.
24. Yusuf TE, Ho S, Pavey DA, Michael H, Gress FG. Retrospective analysis of the utility of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) in pancreatic masses, using a 22-gauge or 25-gauge needle system: a multicenter experience. Endoscopy. 2009;41(5):445–8.

Endoscopic Ultrasound-Guided Biliary Access and Drainage

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Vinay Dhir, Irfan Sandozi, and Amit Maydeo

Introduction

Drainage of an obstructed biliary tree is an integral part of management of patients who have obstructive jaundice with itching or cholangitis. In addition to providing relief from the jaundice and infection, a randomized controlled trial found that endoscopic biliary drainage is associated with an improved quality of life [1]. These patients usually are managed with endoscopic retrograde cholangiopancreatography (ERCP), where the success rate of biliary cannulation is over 90% [2]. In a small minority of patients, there is failure to achieve the intended drainage by ERCP [3]. These are patients in whom cannulation of the bile ducts fails during ERCP or there is inadequate biliary drainage even after successful cannulation with stent placement during ERCP. Then there are some patients who pose a challenge for ERCP due to an altered anatomy of the gastrointestinal (GI) tract either from past surgeries, radiation exposure, acquired or congenital deformities, or tumor involvement. In these patients, alternative methods are chosen to achieve biliary drainage. Traditionally, these approaches have been percutaneous transhepatic biliary drainage (PTBD) or surgery. Compared to endoscopic drainage, surgery has a lower rate of recurrent biliary obstruction (relative risk 0.14; 95% confidence interval, 0.03–0.63) but associated with prolonged hospitalization [4]. These approaches have the disadvantage of being invasive and involving skin incisions or puncture sites, which can cause pain and prolonged hospitalization. The percutaneous approach requires multiple sessions and frequently involves external drainage, which causes fluid and electrolyte imbalance that needs to be closely monitored and corrected. The extra post-procedure care required after these procedures, especially percutaneous drains, is quite cumbersome for the patient and caregivers [5–7]. This especially becomes an issue of concern as a majority of such patients have advanced malignancies and are debilitated, frequently being limited to palliative care. To circumvent these hurdles, in the last decade, endoscopic ultrasound (EUS) has been utilized to provide guidance to place stents endoscopically and provide biliary drainage internally into the gastrointestinal tract [3]. This is in line with the general trend of EUS transforming from a diagnostic to a therapeutic modality, as more and more techniques are being developed utilizing EUS to provide a road map to perform endoscopic therapy. Thus, EUS-guided biliary drainage (EUS-BD) has evolved as an additional method to provide the necessary relief of biliary obstruction in patients in whom ERCP has failed or is not possible.

Why do we need biliary drainage?	How can we drain the biliary system?
Relief from itching Treat infection (cholangitis) Improve quality of life	ERCP PTBD Surgery EUS-BD

Indications

EUS-guided biliary drainage (EUS-BD) is indicated in the following clinical settings:

- Failed cannulation of the common bile duct (CBD) during ERCP
- No improvement of jaundice despite placement of stent by ERCP

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- ERCP not possible due to surgically altered anatomy, i.e., Roux-en-Y gastrojejunostomy, Bilroth II gastrojejunostomy, Whipple surgery, biliopancreatic diversion, etc. [3]
- ERCP not possible due to tumor infiltration of ampulla, duodenal stenosis or obstruction, and presence of a duodenal stent
- Gastric outlet obstruction due to any cause where there is failure to reach the duodenal papilla

Practical Considerations for EUS-BD

- Dilated CBD or intrahepatic biliary radicals to allow EUS-guided needle puncture and guidewire passage
- Endoscopic proximity of the target biliary duct to allow the EUS-guided puncture and guidewire passage
- No intervening blood vessels in the track of the FNA needle

Contraindications

In addition to the general contraindications where comorbidities make the patient unfit for sedation and endoscopic procedures, the following are specific contraindications for EUS-BD:

- Coagulopathy that is not correctable
- Distance and angulation of biliary radicals from the puncture site making access for needle puncture and guidewire passage not possible
- Varices or blood vessels in the area preventing proper puncture and placement of the stent

Instruments and Accessories

The procedure of EUS-guided biliary drainage can be done with an echoendoscope that has a working channel of at least 3.8 mm needed for insertion of 10F accessories and stents. Among the current scopes available, this would be a curved linear array echoendoscope which allows direct endosonographic visualization of fine needle aspiration (FNA) needle while being used to puncture the enteral wall to gain access to the biliary system.

The accessories needed for all the required and anticipated steps of the procedure are as follows:

1. Fine needle aspiration (FNA) needle of 19 gauge, which can accommodate a 0.035-inch guidewire
2. Hydrophilic tip 0.035-inch guidewire – straight and angled, preferably 400 cm long to allow exchanges of accessories. Shorter wires of 260 cm can be used utilizing exchange technique as described [8]
3. Needle knife or Cystotome
4. Snare or rat tooth forceps
5. Traction sphincterotome
6. Dilating balloon (4 and 6 mm) or 10 French Soehendra dilator
7. Stent – plastic or self-expanding metal stent (SEMS). SEMS should include a choice of uncovered, partially covered, or fully covered
8. Naso-biliary drainage tube

Procedure

As the procedure is anticipated to be usually prolonged, it should be done under deep sedation using monitored anesthesia care (MAC) or general anesthesia. For a successful outcome, it is imperative to complete all the steps of the procedure in a single session. We do not recommend conscious sedation, as it is very important to keep the patient under deep (and safe) sedation for the entire procedure and to reduce the risk of procedure failure due to difficulty with sedation. We prefer the left lateral position for the patient, although the patient can be repositioned if needed during the procedure to the supine or prone position. Patients should be given a broad spectrum antibiotic as prophylaxis before or during the procedure [9–18].

There are several approaches to achieving EUS-BD depending upon the site of puncture and stent placement (Table 38.1). These in turn depend upon the level of biliary obstruction, the indication for the procedure, the accessibil-

Table 38.1 Types of EUS-BD

Approach	EUS-BD stent placement	EUS-BD with ERCP
Transgastric	Hepatico-gastrostomy (HGS)	Rendezvous procedure (RZV)
	Antegrade stent insertion (AG)	
	EUS-guided gallbladder drainage (EUS-GBD)	
Transduodenal	Choledochoduodenostomy (CDS)	Rendezvous procedure (RZV)
	Antegrade stent insertion (AG)	
	EUS-guided gallbladder drainage (EUS-GBD)	

ity of the biliary radicals for puncture and drainage, the anatomy of the patient, and the ability to pass the scope to the desired position. A description of the different approaches is presented below.

Hepatico-gastrostomy (HGS)

In this procedure, as the name implies, the stent is placed in the obstructed biliary radicals inside the liver, and the drainage is from the liver to the stomach. The access point for the endosonographic FNA needle puncture is in the proximal stomach along the lesser curvature, and the target biliary radicals are in the left lobe of the liver (segments II or III, Fig. 38.1). Therefore, the left lobe of the liver is drained into the stomach. This would essentially provide drainage of the entire biliary tree and could be the procedure of choice if there is a distal CBD obstruction and the hilar radicals are freely communicating between the right lobe and the left lobe of the liver. If there is tumor involvement of the bifurcation where the right and left systems do not communicate, then a guidewire can be maneuvered into the right intrahepatic duct across the tumor and an uncovered SEMS placed across the stricture in the bifurcation to create a communication with the left hepatic duct, and then a stent can be placed draining from the left intrahepatic ducts into the stomach as is done for the HGS [16].

Guidelines for the Procedure

The echoendoscope is passed via the mouth and advanced into the esophagus and across the esophagogastric (EG) junction and parked in the desired position – proximal stomach below the EG junction. The dilated bile ducts inside the liver are visualized by endosonography. Care is taken to visualize any intervening blood vessels by using Doppler imaging. The puncture point is determined by the accessibility of the dilated bile duct radical from the stomach wall, which is dependent upon the distance from the endoscopic ultrasound probe to the dilated bile duct radical. Ideally this distance should not be more than a few cm and preferably should be less than 1–2 cm [19]. Using a 19-gauge FNA needle, the stomach wall is punctured, and the needle is advanced into the dilated biliary radicals in the left lobe of

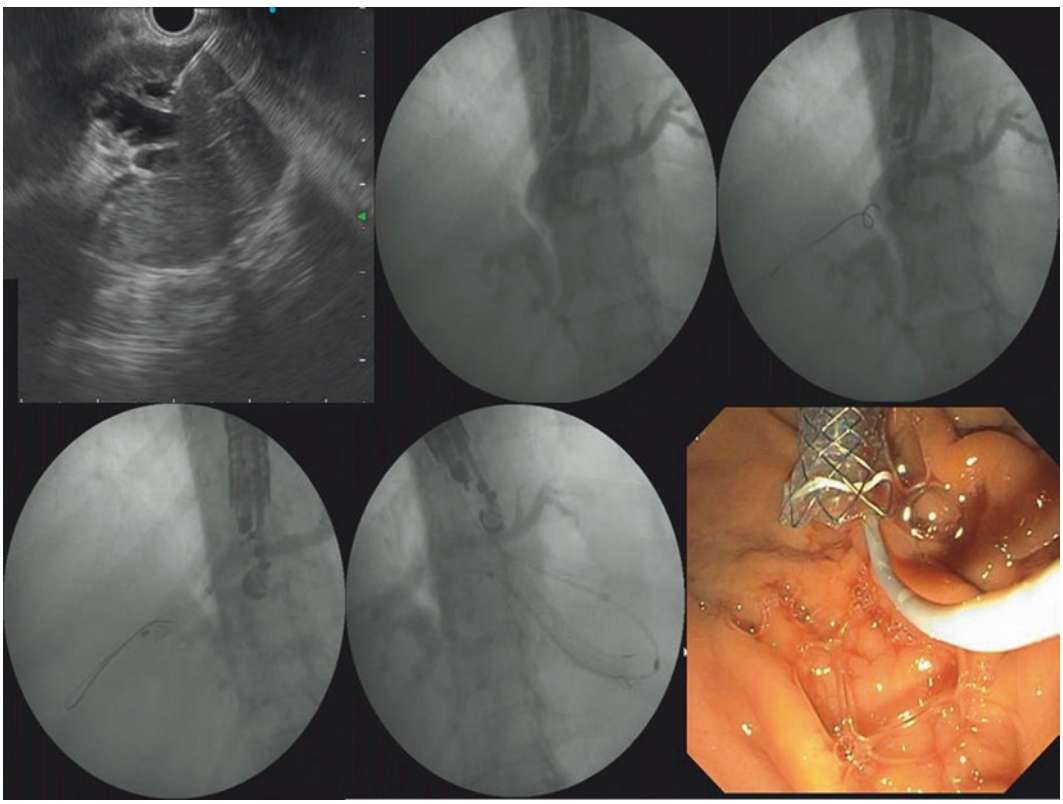

Fig. 38.1 EUS-HGS. *Top left*, EUS image showing puncture of left intrahepatic radical. Note the scope position just beyond gastroesophageal junction. *Top middle*, contrast injection shows a hilar obstruction. *Top right*, a guidewire is passed from left to right. *Bottom left*, stent partially deployed. *Bottom center*, stent fully deployed. Note long intragastric portion of stent. *Bottom right*, endoscopic view of fully deployed stent in the stomach

the liver. Confirmation is done by aspirating bile from the biliary duct and by injecting contrast to do a cholangiogram. Once confirmed, water is injected and a 0.035 inch hydrophilic guidewire is then passed through the FNA needle. Under fluoroscopic guidance, the guidewire is advanced deep into the bile ducts distally to anchor the access tract. The puncture site and access tract is enlarged to a bigger size either with a cystotome. Alternatively, the tract is dilated using a dilating balloon or a 10-F bougie dilator. Dilatation with a dilator can be difficult and usually requires several wire exchanges, and deployment of the stent maybe more difficult through this tract [19]. After the tract is enlarged or dilated, a stent is passed over the wire into the biliary radicals and deployed with the distal end in the hepatic biliary radicals and the proximal end inside the proximal gastric body lumen. The choice of stent can be either a plastic or a fully covered self-expandable metal stent (SEMS).

It is very important to pass the guidewire deep to provide good anchoring for the stent deployment. The manipulation of the guidewire while advancing and pulling back through the needle should be smooth and slow. Frequent advancing and pulling back should be avoided to prevent shearing off the wire tip. If possible, removing the needle and exchanging for a cannula before manipulating the guidewire can avoid the possible shearing of the wire.

If a stent cannot be placed across the right and left bifurcation and there is a need to drain the right sided intrahepatic ducts, then a direct puncture to drain the right lobe of the liver can be done with the echoendoscope parked in the antrum or duodenum bulb [16]. With the echoendoscope rotated in an extreme anticlockwise position, the dilated right-sided intrahepatic ducts are visualized, and the FNA needle is used to puncture from the distal antrum or duodenum bulb into a dilated right intrahepatic biliary radical. A guidewire is advanced into the right intrahepatic ducts and the tract dilated and stent deployed as described above.

Practical Considerations

- In hepatico-gastrostomy the drainage is from the liver to the stomach.
- The access point for the FNA needle puncture is in the proximal stomach along the lesser curvature, and the target biliary radicals should be in the left lobe of the liver.
- The distance from the endoscopic ultrasound probe to the dilated bile duct radical should not be more than 1–2 cm.
- The choice of stent can be either a plastic or a fully covered self- expandable metal stent (SEMS).

Choledochoduodenostomy (CDS)

Here, the extrahepatic bile duct is drained directly into the duodenum. In CDS, following some of the general steps as described above in the HGS procedure, the echoendoscope is advanced to the duodenum, and the puncture is made in the duodenum bulb or second portion of the duodenum to access either the common bile or common hepatic duct. Under fluoroscopic guidance, a guidewire is passed deep into the proximal bile duct and across the hilum into the intrahepatic ducts. The puncture site and tract are enlarged with a cystotome or dilated with a dilating balloon or dilator. A stent is then passed over the wire and deployed to drain the common bile duct/common hepatic duct into the duodenum. Care should be taken to avoid puncturing the cystic duct in CDS. Also, it is important not to puncture across a duodenal fold to avoid creating a longer tract across the duodenal wall for the stent to be advanced [22]. Similarly, cystic duct puncture should be avoided [22].

Practical Considerations

- In choledochoduodenostomy, the extrahepatic bile duct is drained directly into the duodenum.
- The puncture is made in the duodenum bulb or second portion of the duodenum to access either the common bile or common hepatic duct.
- Care should be taken to avoid puncturing the cystic duct in CDS.
- It is important not to puncture across a duodenal fold to avoid creating a longer tract across the duodenal wall.

Antegrade Stent Insertion (AG)

A variation of the above two procedures is to deploy the stent in an antegrade direction across the papilla (or anastomosis) using the HGS or CDS approaches (Fig. 38.2). This is an option especially for failed access into the CBD during ERCP. It has the advantage of avoiding creating a fistulous tract across the gut wall and the biliary system for stent placement, as is done for the other EUS-BD procedures. Briefly, the guidewire is passed into the biliary tree using the HGS or CDS approaches. Under fluoroscopic guidance, the guidewire is directed and advanced antegrade into the lower CBD and across the duodenal papilla (or anastomosis). The puncture site and tract are enlarged or dilated as described above, and over the guidewire, a stent is advanced across the

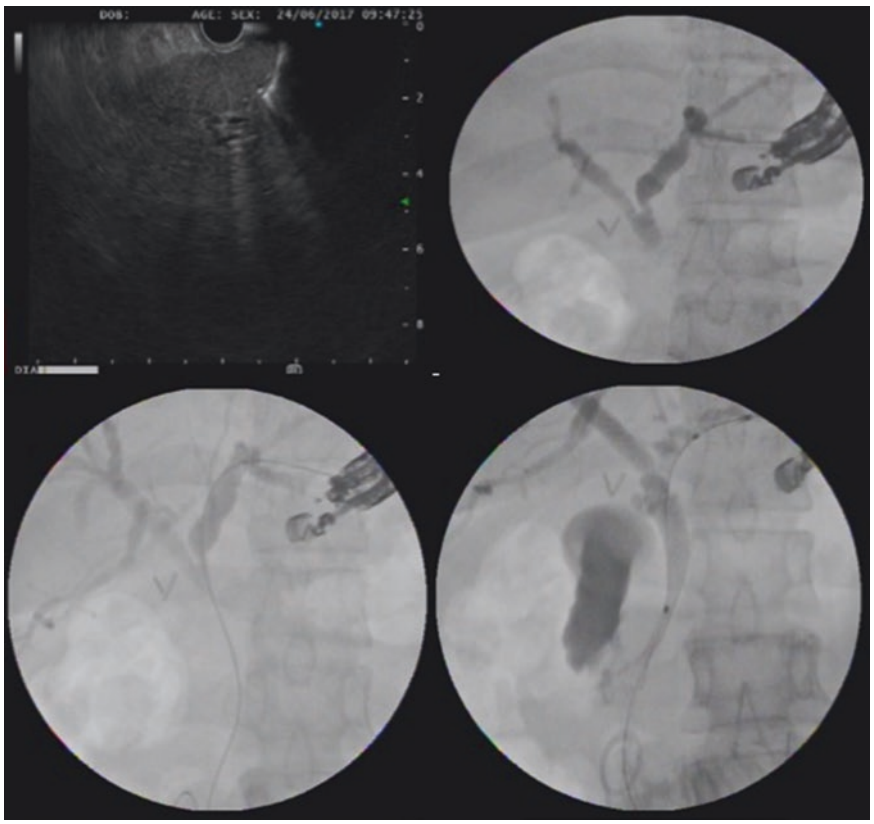

Fig. 38.2 Antegrade procedure. *Tope left,* a 19 gauge needle is used to puncture a left hepatic duct radical. *Top right*, Cholangiogram shows a sub-hilar dilated left duct and Common hepatic duct. *Bottom left*, a guidewire is passed across the hilum and the stricture into the duodenum. *Bottom right*, an expandable stent is placed across the stricture

Practical Considerations

- Antegrade stent insertion is an option especially for failed access into the CBD during ERCP.
- The stent is deployed in the CBD across the duodenal papilla (or anastomosis) into the duodenum.

duodenal papilla (or anastomosis). The sheath of the stent is partially pulled back and contrast injected at the distal end of the stent to confirm the position. When position is confirmed, the stent is deployed in the CBD across the duodenal papilla (or anastomosis) into the duodenum [15].

Rendezvous Procedure (RV)

This procedure is used after failed access into the CBD by ERCP. Thus, an approachable papilla is a prerequisite for this procedure. This is a hybrid procedure requiring EUS for gaining bile duct access and ERCP for final therapy (Fig. 38.3). Using EUS guidance, the bile ducts are accessed with a needle as described above by HGS or CDS. The site of puncture to access the bile duct can be in the stomach cardia or antrum, while in the duodenum it could be the bulb or second portion. Under fluoroscopic guidance, a guidewire is then passed from the bile ducts downstream toward the duodenal papilla and through it into the second duodenum. Passing the guidewire across a stricture can be especially challenging if the approach is through the intrahepatic ducts where the distance traversed by the guidewire is longest, while it is least challenging if the puncture site is in the second duodenum, where the guidewire is passed for a very short distance to pass through the papilla [20]. Once it is passed through the papilla, the guidewire is fed into the jejunum for a distance and the echoendoscope can be removed, leaving the wire in place. A duodenoscope passed to the second part of duodenum alongside the guidewire. The guidewire exiting the papilla is grabbed with a snare or rat tooth forceps and retrieved. Over this guidewire, a sphincterotome is advanced into the CBD and ERCP is carried out. The exchange of the echoendoscope for the duodenoscope bears the risk of losing the guidewire access if the proximal end of

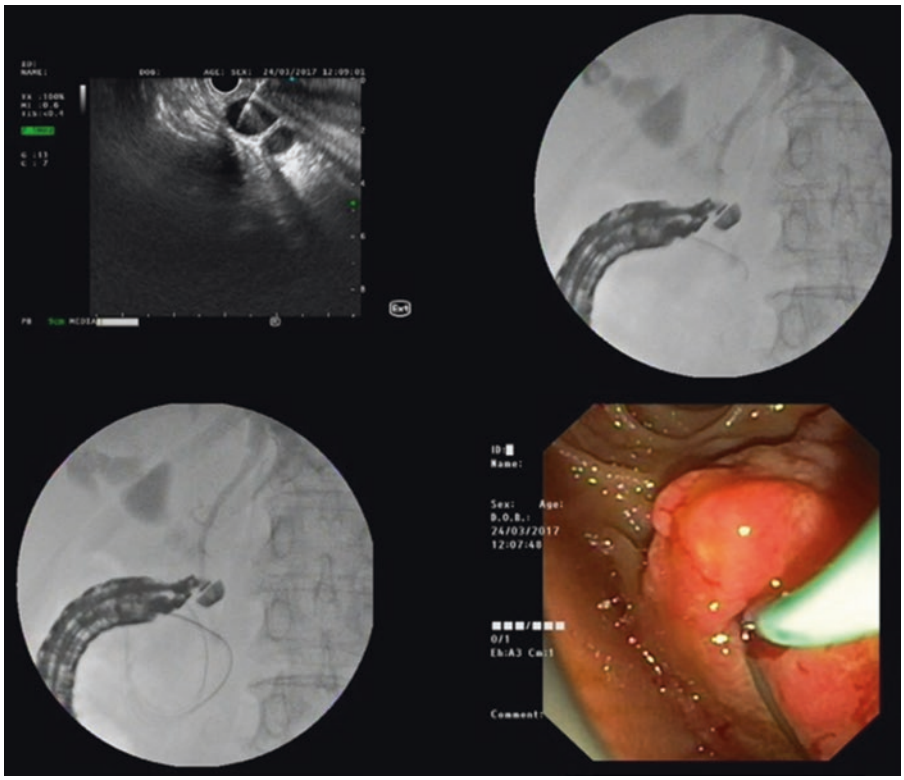

Fig. 38.3 EUS-guided rendezvous. *Top left*, the dilated bile duct is punctured with a 19 gauze needle. *Top right,* a 0.032′ guidewire is passed through the needle in the bile duct. Note the needle position looking towards the papilla. *Bottom left*, the guidewire is negotiated across the papilla and coiled in the duodenum. *Bottom right*, a duodenoscope is positioned at the papilla and cannulation is done by the side of the guidewire exiting through the papilla

the guidewire is pulled back with the echoendoscope. To avoid this from occurring, instead of exchanging the echoendoscope for a duodenoscope, the guidewire exiting out of the papilla is grabbed with a snare or rat tooth forceps and pulled back out of the echoendoscope. The echoendoscope is removed. The guidewire is then back loaded onto a sphincterotome passed through the accessory channel of a duodenoscope and the duodenoscope advanced into the second duodenum over the guidewire. Instead of retrieving the guidewire through the duodenoscope, alternatively, the CBD can be cannulated with a guidewire loaded sphincterotome (or cannula) beside the guidewire exiting from the ampulla, thus avoiding the cumbersome exchange of the scopes over the guidewire. The next steps of placement of a stent (or other maneuvers) are done as per routine ERCPs. If a 260 cm (short) guidewire is used, then the guidewire is not long enough to do the exchange. In this situation, during the exchange of the FNA needle when the proximal end of the wire is fed into the FNA needle, using a 12 cc syringe, water is flushed in while withdrawing the FNA needle to "float the wire" through the exchange maneuver [8, 12]. When the distal wire is being pulled out, then the proximal end of the 260 cm (short) wire can be fed into the mouth by grabbing it with a rat tooth forceps [8]. In RZV, there is no need to dilate the puncture site.

Practical Considerations

- Rendezvous procedure is recommended after failed access into the CBD by ERCP.
- This is a hybrid procedure requiring EUS for gaining bile duct access and ERCP for final therapy.

EUS-Guided Gallbladder Drainage (EUS-GBD)

In cases of acute cholecystitis where the patient is not deemed to be a surgical candidate, the standard of practice has been to drain the gallbladder percutaneously with interventional radiology, by performing a cholecystostomy tube drainage. These patients now have the option of draining the gallbladder by EUS guidance into the duodenum or stomach, which has the advantage of avoiding skin incisions and post-procedure pain. With the EUS scope in the long position, stationed in the duodenum bulb or antrum, a transenteric puncture into the gallbladder is performed with a 19-gauge needle, and bile is aspirated to confirm biliary access. Contrast is injected and the gallbladder position is confirmed fluoroscopically. A guidewire is advanced into the gallbladder and the tract dilated with a dilating balloon or bougie dilator. A stent or naso-biliary drain is placed to provide the necessary drainage

of the gallbladder [23]. The choice of stent can be a plastic double pigtail stent or a fully covered SEMS.

Recently, tissue apposing SEMS, such as Axios Stent, have become available which have a silicone covering and have a 10–15 mm inner diameter and 6–10 mm length [24]. These covered stents prevent bile spillage and tissue in growth and can be removed later endoscopically if necessary.

Practical Considerations

- EUS-GBD is indicated in cases of acute cholecystitis where the patient is not deemed to be a surgical candidate.
- The choice of stent can be a plastic double pigtail stent or a fully covered SEMS

Newer stent deployment systems have also evolved which have a built in thermal system that is used to both puncture and dilate the tract with the tip of the catheter before deploying the stent which can be done by EUS guidance, without the need for any wire-guided exchanges or fluoroscopy.

Success, Complications, and Follow-up

The success rates for all the various EUS-BD procedures have reportedly been higher than 85% in the majority of recent publications [8, 13, 18, 25–28]. For EUS-BD, the technical and clinical success in cases with surgically altered anatomy is 89.18% and 91.07%, whereas the complication rate is 17.5% [3].

The success rates in various studies have been reported as technical success and clinical or functional success. Technical success is referred to the successful completion of the intended procedure, i.e., placement of a stent or drain. Clinical or functional success was defined as decrease in the serum bilirubin by 50% at 2 weeks after the successful completion of the procedure.

So far the success and complication rates are reported almost entirely based on data from retrospective studies. Prospective randomized studies need to be done to get more realistic data and to compare the different methods of biliary drainage (Table 38.2).

Complications of EUS-BD – major	Complications of EUS-BD – minor
Bleeding	Stent migration
Cholangitis	Stent occlusion
Perforation	Sheared wire retention
Bile leak	
Pneumoperitoneum	
Pancreatitis	
Death	

Several complications have been reported for all the procedures for EUS- guided biliary drainage. These range from minor to life-threatening. Due to the learning curve and the wide variation of skills in different centers, the complication rates reported are between 3% and 40%. These are most frequently reported to be are also reported.

Table 38.2 Success, complications, and follow-up of EUS-BD in studies with >50 patients

Study	Number of patients	Technical success	Functional success	Complications	Follow-up
Dhir et al. (India, Brazil, the USA, Spain) [26]	68	65/68 pts. (95.6%)		3/68 (4.4%)	
Khashab et al. 2008–2014 (the USA, Canada, Spain, India, Japan, Korea) [30]	121	112/121 (92.56%)	HGS 82.1% CDS 85.5	HGS 19.67% CDS 13.3%	151 ± 159 days
Kawakubo et al. 2006–2012 (Japan) [25]	64	61/64 (95%)		12/64 (19%)	94 (9–1593) days
Dhir et al. 2009–2011 [8]	58	57/58(98.3%)	57/58(98.3%)	2/58 (3.4%)	>3 months
Vila et al. (Spain) < 2010–2012 [28]	125 106 biliary 19 pancreatic	84 (67.2%) Bil 73(68.9%) Pnc 11(57.9%)	79 (63.2%) Bil 24 (22.6%) Pnc 5(26.3%)	29 (23.2%)	
Dhir et al. (India, Japan, the USA, S. Korea, Hong Kong) 2011–2013 [13]	104	97 (93.26%)	89.42%	8.65%	
Poincloux et al. (France) 2006–2013 [18]	101	98%	92.1%	12 (11.9%)	280 (3–775)
Park et al. (Korea) 2008–2010 [47]	57	55/57 (96.5%)	49/55 (89%)	22/55 (40%)	205 (18–806)
Gupta et al. (the USA, Spain, Brazil, Japan, France) 2000–2010 [27]	240	87%		31%	

Table 38.3 Review of EUS-BD published studies having >25 patients [26]

Author	Access route	Number of patients	Success *n* (%)	Complications *n* (%)
Park do et al. [47]	TD	26	24 (92.3)	5 (19.2)
Dhir et al. [8]	TD	58	57 (98.3)	2 (3.4)
Iwashita et al. [31]	TD	31	25 (80.6)	4 (12.9)
Shah et al. [14]	TD	70	60 (85.7)	6 (8.6)
Vila et al. [28]	TD	26	19 (73.1)	4 (15.4)
Total TD		211	185 (87.7)	21 (9.9)
Maranki et al. [48]	TH	35	29 (82.9)	5 (14.3)
Park do et al. [47]	TH	31	31 (100)	5 (16.1)
Bories et al. [43]	TH	38	36 (94.7)	9 (23.7)
Vila et al. [28]	TH	34	22 (64.7)	11(32.4)
Total TH		138	118 (85.5)	30 (21.7)

P value for total complications = 0.03, *TD* transduodenal, *TH* transhepatic

In a multicenter study, EUS and ERCP have been shown to be equivalent in regard to technical and clinical success to provide short-term relief from malignant biliary obstruction [13].

In a retrospective international multicenter comparative analysis of the various EUS-BD procedures done for malignant obstructive jaundice, complications were significantly higher for the transhepatic route compared to the transduodenal route of biliary drainage (30.5% vs. 9.3%, $P = 0.03$) [26]. There was no significant difference in complication rates among transluminal and trans-papillary stent placement or direct and rendezvous stenting. Logistic regression analysis showed transhepatic access to be the only independent risk factor for complications ($P = 0.031$, $t = 2.2$). There was also no significant difference in the success rates of the various techniques. All three deaths occurred in patients in whom the transhepatic route was used. Complications were higher, though not statistically significant, with AG stent insertion and for proximal obstructions compared with retrograde stent insertion and distal obstruction. The four centers in the study had wide variations in individual choices for access route, direction of stent insertion, and drainage routes. This was in conformation with previous studies.

A review of the publications with studies having more than 25 patients and any access route showed that the reported complication rate is higher with the transhepatic route compared with the transduodenal route (Table 38.3) [26]. Pooled complication rates were 9.9% for the transduodenal approach in five studies (21/211 patients) and 21.7% for transhepatic approach in four studies (30/138 patients). The complications in the transhepatic and transduodenal groups reached statistical significance when the pooled data was compared ($P = 0.03$, Fisher's exact test). Based on this information, it may appear safer to avoid the transhepatic approach if possible; however, we must await judgment until the issue is resolved by prospective studies. In cases where there is no other option, the transhepatic approach should be compared with PTBD in a prospective randomized study. Results for PTBD in recent studies show a success rate of 99%, procedure-related mortality was 2%, and 30-day mortality was 13% [54]. The same study also showed higher stent failure and restenting for distal CBD obstruction. Therefore, for distal CBD obstruction, EUS-BD may be better than PTBD after failed ERCP. If data from the retrospective studies is confirmed in larger multicenter prospective studies that there is no difference between trans-papillary and transluminal stenting and direct and rendezvous stenting, then the procedure of choice for distal CBD obstruction may be EUS-BD.

In the prospective single-operator follow-up study evaluating outcomes of EUS-HGS and EUS-CDS, the use of a needle knife for fistula dilatation compared with graded dilatation was statistically significantly associated with post-procedure adverse events (9/27, 33% vs. 2/28, 7%; $P = 0.02$) [47]. In multivariate analysis, the use of a needle knife was the single risk factor for post-procedure adverse events after EUS-BD ($P = 0.01$; OR 12.4; CI, 1.83–83.5).

There was no significant difference with the type of transluminal stent used for the post-procedure adverse events. However, the larger caliber of the fully covered SEMS created a much larger fistulous tract, making it easier for stent exchanges and revisions compared to the small-caliber fistulous tract of a plastic stent. Among the technical factors, the feasibility of graded dilatation in EUS-HGS was superior to that of EUS-CDS (74%, 23/31 vs. 21%, 5/24; $P < 0.000$). The location of fistula dilatation (gastric body for EUS-HGS vs. duodenal bulb for EUS-CDS) is the predictive factor for successful graded dilatation in multivariate analysis ($P < 0.000$; odds ratio (OR) 0.062; confidence interval (CI), 0.015–0.260).

Although there was no statistically significant difference in the outcomes of EUS-BD for benign versus malignant group (50%, 3/6 vs. 16%, 8/49; $P = 0.087$), it may be more prudent to hold off on performing the EUS-BD procedure for benign disease because of the higher rate of adverse events. We should await further studies to formulate an indication for this group of patients (Table 38.4).

In the single-center study comparing precut papillotomy with EUS-guided rendezvous techniques, treatment success was significantly higher (57/58 patients) for the EUS-guided rendezvous than the precut papillotomy techniques (130/144 patients) (98.3% vs. 90.3%; $P = 0.03$) [8]. There was no significant difference in the rate of procedural complications between the EUS-guided rendezvous and the precut papillotomy techniques (3.4% vs. 6.9%; $P = 0.27$).

Table 38.4 Technical success rate, adverse event rate, and outcomes for PTBD, surgical bypass, and EUS-BD [47]

Study	Number of patients	Alternatives	Technical success (%)	Post-procedure adverse events (%)	Late adverse events (%)	Procedure-related mortality (%)	Stent patency or median survival (*d*)
Doctor et al. [49]	54	PTBD	89	24	18	11	90[a]
Beissert et al. [50]	71	PTBD	100	33	NA	15	166[b]
Kuhn et al. [51]	71	PTBD	97	9	NA	2	NA
Bornman et al. [52]	25	Surgical bypass	76	32	NA	20	450[a]
Park et al. [47]	57	EUS-BD	96.5	20	7	0	133[b]

PTBD Percutaneous transhepatic biliary drainage, *NA* not available, *EUS-BD* EUS-guided biliary drainage with transmural stenting
[a]Median survival day
[b]Median stent patency day

Conclusion

Relieving biliary obstruction in patients with obstructive jaundice has been established as an essential part of management of patients, as the immediate biliary drainage not only improves the quality of life, but it also is cost saving. It becomes imperative in patients with incessant itching and/or cholangitis. The procedure of choice to attain this objective is ERCP with stent placement. Other alternatives such as PTBD or surgery are utilized in cases where ERCP fails or cannot be done to provide the necessary biliary drainage. Recently, EUS-BD procedure has become a serious contender in the armamentarium of procedure choices when ERCP fails or is not an option to provide the needed biliary drainage. There are many advantages of EUS-BD. It can be done as a single-session procedure when ERCP is not successful or possible [4]. Also, the procedure can be done safely as the surrounding blood vessels and organs can be avoided while performing it. When compared to other methods that provide biliary drainage (ERCP, PTBD, and surgery), EUS-BD has a major advantage in that it provides multiple potential access points to drain the biliary tree. The site of access can be tailored to the particular patient depending upon the level of biliary obstruction and the prevalent anatomy of the GI tract. Since the stent can be placed upstream of a malignant obstruction, the problems of stent occlusion from tumor in growth can be avoided. Due to the relatively fewer number of patients requiring this procedure, so far, the available data on EUS-BD is gleaned from retrospective and multicenter studies. There is also no good comparative data available about which procedure is best for providing the needed biliary drainage. Prospective, randomized, controlled trials are needed to provide a lot of answers to several burning questions regarding what is the procedure of choice for a particular clinical situation.

Advantages of EUS-BD	Single-session drainage
	Avoid injury to blood vessels
	Multiple potential sites of drainage
	Avoid tumor ingrowth in stent when draining proximally

In conclusion, EUS-BD is an effective method of draining an obstructed biliary tree. The technique has a high success rate and is relatively safe. It requires skill in advanced endoscopic procedures based on the principles of ERCP and EUS. There is a learning curve as is usual for any newer procedure, but this can be surmounted by performing more number of cases over a shorter period of time. Since the numbers of patients who undergo this procedure are currently small as they are based on failed ERCPs or clinical situations where ERCP is not possible, gastroenterologists should consider EUS-BD as an option early on in the course of treatment of obstructive jaundice. Prospective, randomized controlled clinical trials should be designed to compare the safety and efficacy of EUS-BD with PTBD and surgery and to identify the safest approach and technique for EUS-BD among all the different variations of the procedure.

References

1. Barkay O, Mosler P, Schmitt CM, Lehman GA, Frakes JT, Johanson JF, et al. Effect of endoscopic stenting of malignant bile duct obstruction on quality of life. J Clin Gastroenterol. 2013;47(6):526–31.
2. Adler DG, Lieb JG, Cohen J, Pike IM, Park WG, Rizk MK, et al. Quality indicators for ERCP. Am J Gastroenterol. 2015;81(1):54–66.
3. Glazer ES, Hornbrook MC, Krouse RS. A meta-analysis of randomized trials: immediate stent placement vs. surgical bypass in the palliative management of malignant biliary obstruction. J Pain Symptom Manag. 2014;47(2):307–14.
4. Siripun, A., Sripongpun, P., & Ovartlarnporn, B. Endoscopic ultrasound-guided biliary intervention in patients with surgically altered anatomy. World J Gastrointest Endosc. 2015;7(3):283–289. https://doi.org/10.4253/wjge.v7.i3.283
5. Kahaleh M, Artifon EL, Perez-Miranda M, Gupta K, Itoi T, Binmoeller KF, Giovannini M. Endoscopic ultrasonography guided

biliary drainage: summary of consortium meeting, May 7th, 2011, Chicago. World J Gastroenterol. 2013;19(9):1372–9.
6. Saad WE, Wallace MJ, Wojak JC, Kundu S, Cardella JF. Quality improvement guidelines for percutaneous transhepatic cholangiography, biliary drainage, and percutaneous cholecystostomy. J Vasc Interv Radiol. 2010;21(6):789–95.
7. Umeda J, Itoi T, Tsuchiya T, Sofuni A, Itokawa F, Ishii K, et al. A newly designed plastic stent for EUS-guided hepaticogastrostomy: a prospective preliminary feasibility study (with videos). Gastrointest Endosc. 2015;82(2):390–6.
8. Dhir V, Bhandari S, Bapat M, Maydeo A. Comparison of EUS-guided rendezvous and precut papillotomy techniques for biliary access (with videos). Gastrointest Endosc. 2012;75(2):354–9.
9. Kawakubo K, Isayama H, Sasahira N, Nakai Y, Kogure H, Hamada T, et al. Clinical utility of an endoscopic ultrasound-guided rendezvous technique via various approach routes. Surg Endosc. 2013;27(9):3437–43.
10. Dhir V, Bhandari S, Bapat M, Joshi N, Vivekanandarajah S, Maydeo A. Comparison of transhepatic and extrahepatic routes for EUS-guided rendezvous procedure for distal CBD obstruction. United European Gastroenterol J. 2013;1(2):103–8.
11. Khashab MA, Valeshabad AK, Afghani E, Singh VK, Kumbhari V, Messallam A, et al. A comparative evaluation of EUS-guided biliary drainage and percutaneous drainage in patients with distal malignant biliary obstruction and failed ERCP. Dig Dis Sci. 2015;60(2):557–65.
12. Dhir V, Kwek BEA, Bhandari S, Bapat M, Maydeo A. EUS-guided biliary rendezvous using a short hydrophilic guidewire. J Interv Gastroenterol. 2011;1(4):153.
13. Dhir V, Itoi T, Khashab MA, Park DH, Teoh AYB, Attam R, et al. Multicenter comparative evaluation of endoscopic placement of expandable metal stents for malignant distal common bile duct obstruction by ERCP or EUS-guided approach. Gastrointest Endosc. 2015;81(4):913–23.
14. Shah JN, Marson F, Weilert F, Bhat YM, Nguyen-Tang T, Shaw RE, Binmoeller KF. Single-operator, single-session EUS-guided anterograde cholangiopancreatography in failed ERCP or inaccessible papilla. Gastrointest Endosc. 2012;75(1):56–64.
15. Park DH, Jeong SU, Lee BU, Lee SS, Seo DW, Lee SK, Kim MH. Prospective evaluation of a treatment algorithm with enhanced guidewire manipulation protocol for EUS-guided biliary drainage after failed ERCP (with video). Gastrointest Endosc. 2013;78(1):91–101.
16. Ogura T, Sano T, Onda S, Imoto A, Masuda D, Yamamoto K, et al. Endoscopic ultrasound-guided biliary drainage for right hepatic bile duct obstruction: novel technical tips. Endoscopy. 2015;47(1):72–5.
17. Artifon EL, Marson FP, Gaidhane M, Kahaleh M, Otoch JP. Hepaticogastrostomy or choledochoduodenostomy for distal malignant biliary obstruction after failed ERCP: is there any difference? Gastrointest Endosc. 2015;81(4):950–9.
18. Poincloux L, Rouquette O, Buc E, Privat J, Pezet D, Dapoigny M, et al. Endoscopic ultrasound-guided biliary drainage after failed ERCP: cumulative experience of 101 procedures at a single center. Endoscopy. 2015;47(9):794–801.
19. Prachayakul V, Aswakul P. Endoscopic ultrasound-guided biliary drainage as an alternative to percutaneous drainage and surgical bypass. World J Gastrointest Endosc. 2015;7(1):37–44.
20. Iwashita T, Yasuda I, Mukai T, Iwata K, Ando N, Doi S, et al. EUS-guided rendezvous for difficult biliary cannulation using a standardized algorithm: a multicenter prospective pilot study (with videos). Gastrointest Endosc. 2016;83(2):394–400.
21. Kim YS, Gupta K, Mallery S, Li R, Kinney T, Freeman ML. Endoscopic ultrasound rendezvous for bile duct access using a transduodenal approach: cumulative experience at a single center. A case series. Endoscopy. 2010;*42*(6):496.
22. Ogura T, Higuchi K. Technical tips of endoscopic ultrasound-guided choledochoduodenostomy. World J Gastroenterol: WJG. 2015;21(3):820–8.
23. Tsuyuguchi T, Itoi T, Takada T, Strasberg SM, Pitt HA, Kim MH, et al. TG13 indications and techniques for gallbladder drainage in acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci. 2013;20(1):81–8.
24. de la Serna-Higuera C, Pérez-Miranda M, Gil-Simón P, Ruiz-Zorrilla R, Diez-Redondo P, Alcaide N, et al. EUS-guided transenteric gallbladder drainage with a new fistula-forming, lumen-apposing metal stent. Gastrointest Endosc. 2013;77(2):303–8.
25. Kawakubo K, Isayama H, Kato H, Itoi T, Kawakami H, Hanada K, et al. Multicenter retrospective study of endoscopic ultrasound-guided biliary drainage for malignant biliary obstruction in Japan. J Hepatobiliary Pancreat Sci. 2014;21(5):328–34.
26. Dhir V, Artifon EL, Gupta K, Vila JJ, Maselli R, Frazao M, Maydeo A. Multicenter study on endoscopic ultrasound-guided expandable biliary metal stent placement: choice of access route, direction of stent insertion, and drainage route. Dig Endosc. 2014;26(3):430–5.
27. Gupta K, Perez-Miranda M, Kahaleh M, Artifon EL, Itoi T, Freeman ML, et al. Endoscopic ultrasound-assisted bile duct access and drainage: multicenter, long-term analysis of approach, outcomes, and complications of a technique in evolution. J Clin Gastroenterol. 2014;48(1):80–7.
28. Vila JJ, Pérez-Miranda M, Vazquez-Sequeiros E, Abadia MAS, Pérez-Millán A, González-Huix F, et al. Initial experience with EUS-guided cholangiopancreatography for biliary and pancreatic duct drainage: a Spanish national survey. Gastrointest Endosc. 2012;76(6):1133–41.
29. Itoi T, Sofuni A, Itokawa F, Tsuchiya T, Kurihara T, Ishii K, et al. Endoscopic ultrasonography-guided biliary drainage. J Hepatobiliary Pancreat Sci. 2010;17(5):611–6.
30. Khashab MA, DeWitt J. Treatment and prevention of wire shearing during EUS-guided biliary drainage. Gastrointest Endosc. 2012;76(4):921–3.
31. Iwashita T, Lee JG, Shinoura S, Nakai Y, Park DH, Muthusamy VR, Chang KJ. Endoscopic ultrasound-guided rendezvous for biliary access after failed cannulation. Endoscopy. 2012;44(1):60–5.
32. Iwashita T, Doi S, Yasuda I. Endoscopic ultrasound-guided biliary drainage: a review. Clin J Gastroenterol. 2014;7(2):94–102.
33. Paik WH, Park DH, Choi CJ, Choi JH, Lee SS, Seo DW, Lee SK, et al. Simplified fistula dilation technique and modified stent deployment maneuver for EUS-guided hepaticogastrostomy. World J Gastroenterol. 2014;20(17):5051–9.
34. Itoi T, Binmoeller KF. EUS-guided choledochoduodenostomy by using a biflanged lumen-apposing metal stent. Gastrointest Endosc. 2014;79(5):715.
35. Perez-Miranda M, De la Serna Higuera C, Gil-Simon P, Hernandez V, Diez-Redondo P, Fernandez-Salazar L. EUS-guided choledochoduodenostomy with lumen-apposing metal stent after failed rendezvous in synchronous malignant biliary and gastric outlet obstruction (with video). Gastrointest Endosc. 2014;80(2):342–4.
36. Brückner S, Arlt A, Hampe J. Endoscopic ultrasound-guided biliary drainage using a lumen-apposing self-expanding metal stent: a case series. Endoscopy. 2015;47(9):858–61.
37. Maluf-Filho F, Retes FA, Neves CZ, Sato CFM, Kawaguti FS, Jureidini R, et al. Transduodenal endosonography-guided biliary drainage and duodenal stenting for palliation of malignant obstructive jaundice and duodenal obstruction. JOP J Pancreas. 2012;13(2):210–4.
38. Hara K, Yamao K, Niwa Y, Sawaki A, Mizuno N, Hijioka S, et al. Prospective clinical study of EUS-guided choledochoduodenostomy for malignant lower biliary tract obstruction. Am J Gastroenterol. 2011;106(7):1239–45.

39. Ogura T, Kurisu Y, Masuda D, Imoto A, Hayashi M, Malak M, et al. Novel method of endoscopic ultrasound-guided hepaticogastrostomy to prevent stent dysfunction. J Gastroenterol Hepatol. 2014;29(10):1815–21.
40. Song TJ, Lee SS, Park DH, Seo DW, Lee SK, Kim MH. Preliminary report on a new hybrid metal stent for EUS-guided biliary drainage (with videos). Gastrointest Endosc. 2014;80(4):707–11.
41. Artifon EL, Aparicio D, Paione JB, Lo SK, Bordini A, Rabello C, et al. Biliary drainage in patients with unresectable, malignant obstruction where ERCP fails: endoscopic ultrasonography-guided choledochoduodenostomy versus percutaneous drainage. J Clin Gastroenterol. 2012;46(9):768–74.
42. Bapaye A, Dubale N, Aher A. Comparison of endosonography-guided vs. percutaneous biliary stenting when papilla is inaccessible for ERCP. United European Gastroenterol J. 2013;1(4):285–93.
43. Tapping CR, Byass OR, Cast JEI. Percutaneous transhepatic biliary drainage (PTBD) with or without stenting—complications, re-stent rate and a new risk stratification score. Eur Radiol. 2011;21(9):1948–55.
44. Yoon WJ, Brugge WR. EUS-guided biliary rendezvous: EUS to the rescue. Gastrointest Endosc. 2012;75(2):360–1.
45. Hara K, Yamao K, Hijioka S, Mizuno N, Imaoka H, Tajika M, et al. Prospective clinical study of endoscopic ultrasound-guided choledochoduodenostomy with direct metallic stent placement using a forward-viewing echoendoscope. Endoscopy. 2012;45(5):392–6.
46. Park DH, Jang JW, Lee SS, Seo DW, Lee SK, Kim MH. EUS-guided biliary drainage with transluminal stenting after failed ERCP: predictors of adverse events and long-term results. Gastrointest Endosc. 2011;74(6):1276–84.
47. Maranki J, Hernandez AJ, Arslan B, Jaffan AA, Angle JF, Shami VM, Kahaleh M. Interventional endoscopic ultrasound-guided cholangiography: long-term experience of an emerging alternative to percutaneous transhepatic cholangiography. Endoscopy. 2009;41(6):532–8.
48. Bories E, Pesenti C, Caillol F, Giovannini M. Endoscopic ultrasound-guided biliary procedures: report of 38 cases. Endoscopy. 2008;40(Suppl 1):A55.
49. Doctor N, Dick R, Rai R, Dafnios N, Salamat A, Whiteway H, et al. Results of percutaneous plastic stents for malignant distal biliary obstruction following failed endoscopic stent insertion and comparison with current literature on expandable metallic stents. Eur J Gastroenterol Hepatol. 1999;11(7):775–80.
50. Beissert M, Wittenberg G, Sandstede J, Beer M, Tschammler A, Burghardt W, et al. Metallic stents and plastic endoprostheses in percutaneous treatment of biliary obstruction. Z Gastroenterol. 2002;40(7):503–10.
51. Kühn JP, Busemann A, Lerch MM, Heidecke CD, Hosten N, Puls R. Percutaneous biliary drainage in patients with nondilated intrahepatic bile ducts compared with patients with dilated intrahepatic bile ducts. Am J Roentgenol. 2010;195(4):851–7.
52. Bornman P, Tobias R, Harries-Jones EP, Stiegmann G, Terblanche J. Prospective controlled trial of transhepatic biliary endoprosthesis versus bypass surgery for incurable carcinoma of head of pancreas. Lancet. 1986;327(8472):69–71.

EUS-Guided Drainage of Pelvic Abscesses

39

Ji Young Bang and Shyam Varadarajulu

Introduction

Deciding how to treat pelvic abscesses can pose a clinical dilemma. They usually occur after surgery or in patients with medical conditions such as Crohn's disease, diverticulitis, ischemic colitis, sexually transmitted diseases, or septic emboli from endocarditis. However, the anatomical challenges are what make this a clinical obstacle, with navigation needed around the bony pelvis, bladder, bowel, reproductive organs in females, prostate in men, rectum, and other neurovascular structures. Historically, pelvic abscesses necessitated surgery and ultrasound-guided transrectal or transvaginal intervention or were percutaneously drained under computed tomography (CT) guidance. In recent times, there have been advances in the field of interventional endosonography that have opened a new avenue for drainage. This chapter will review the different treatment options for draining pelvic abscesses, with a focus on the technique of endoscopic ultrasound (EUS).

Transvaginal/Transrectal Ultrasound-Guided Drainage

Ultrasound guidance has typically been performed using a transvaginal or transrectal approach [4, 5, 9, 10, 15]. Passage through a transvaginal route was utilized because of the close proximity of the vaginal fornices to the pelvic fluid collection. In order to access the fluid collection, a catheter is attached to an endoluminal ultrasound probe which allows the passage of a needle for direct drainage. Only abscesses within the reach of the ultrasound probe can be drained using this technique. Other disadvantages with this procedure include the limitations of true sterility. Therefore, the transvaginal approach is generally limited to biopsy of solid lesions or for complete aspiration of cystic lesions [12]. Also, the procedure is associated with significant pain necessitating local anesthesia with lidocaine. Attempts at transrectal drainage were evaluated in a study of 15 patients who had failed intravenous antibiotic therapy and had collections not suitable for drainage via colpotomy, transvaginal, or transabdominal routes [6]. Out of the 15 women, 14 had return of purulent material and were successfully treated. However, some patients required an indwelling catheter for a prolonged period of time. Transrectal and transvaginal ultrasound-guided drainage therefore remains limited by (1) the distance of the abscess from the ultrasound probe, (2) the inability to deploy stents for continued drainage, and (3) patient discomfort.

CT-Guided Drainage

Percutaneous abscess drainage was first introduced in the 1980s [2]. CT-guided drainage of pelvic abscesses utilizes a transgluteal approach if the abscess is posterior, and a transabdominal approach if located anteriorly [4]. The initial step in this procedure, regardless of the drainage route, is needle aspiration to determine the nature of the collection and establish a differential diagnosis [2]. For collections smaller than 3 cm, simple aspiration usually suffices and percutaneous drainage is not necessary. Transabdominal anterior approach is the most preferred route due to technical ease. However, this is not always practical due to overlying bowel. If the fluid collection cannot be accessed via the anterior or lateral transabdominal approach, transgluteal approach through the greater sciatic foramen can be attempted, while the patient is in the prone or lateral decubitus position [2]. Success rates range from 27% to 93%, depending on various clinical characteristics, abscess location and morphology, and presence or absence of a fistula [2]. This procedure is

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associated with pain at the procedural site in up to 20% of patients, and can result in limitations in ambulation and bed rest due to a catheter which protrudes through the buttocks [3]. Additional limitations include (1) possible injury to the inferior gluteal artery which may lead to hemorrhage or formation of a pseudoaneurysm in 2% of patients and (2) an adequate window may not be identifiable at CT for placement of a drainage catheter [11, 13].

Surgical Drainage

Pelvic and abdominal fluid collections can arise as a result of postsurgical adverse events. Therefore, the optimal treatment approach chosen should be the least invasive option. In one study of 500 patients with perirectal abscesses undergoing surgical drainage [7], 9.6% required reinterventions with four of these patients requiring a second reintervention after initial drainage. The most common reasons for reintervention included initial inadequate drainage because of inadequate incision or premature closure. Consequently, initial surgical exploration and drainage should be limited to those patients who are clinically unstable with life-threatening infections.

Practical Considerations

- The transvaginal approach is generally limited to biopsy of solid lesions or for complete aspiration of cystic lesions.
- Transrectal and transvaginal ultrasound-guided drainage remain limited by the distance of the abscess from the ultrasound probe, the inability to deploy stents for continued drainage, and patient discomfort.
- The CT-guided aspiration is not always practical due to overlying bowel.
- The initial surgical exploration and drainage should be limited to patients who are clinically unstable with life-threatening infections.

Endoscopic Ultrasound (EUS) Drainage

Why EUS Drainage?

The ability to visualize fluid collections that are extrinsic to the rectum extending up to the splenic flexure and intervene in real-time under sonographic guidance via the transrectal or transcolonic route makes EUS an ideal treatment modality for management of pelvic abscesses [1, 11–13].

Pre-procedure

All patients should undergo a dedicated CT or MRI of the pelvis to define the anatomy and location of the abscess to ascertain if the fluid collection is amenable to transrectal EUS-guided drainage. Patients should receive prophylactic antibiotics (amoxicillin plus clavulanic acid, 2 g) and continue with antibiotics for 3 days. Prior to the procedure, patients should undergo local preparation with an enema to assist with optimal visualization and minimize contamination. Also, patients should either void prior to the procedure or have an indwelling Foley catheter to ensure that a distended bladder will not impair visualization of a small fluid collection or that the bladder is not mistaken for an abscess.

Instruments and Accessories

- Endoscopy unit equipped with fluoroscopy
- A curvilinear array echoendoscope
- 19 gauge fine needle aspiration (FNA) needle
- 0.035 inch guidewire
- 4.5 Fr ERCP cannula for tract dilation
- 8–10 mm over-the-wire biliary balloon dilator
- 7 Fr 4 cm plastic double pigtail stents
- 10 Fr 80 cm single pigtail drain
- Normal saline for flushing the pigtail drain
- Syringes for aspiration and irrigation of pelvic abscess contents

Procedural Techniques

1. The curvilinear array echoendoscope is inserted into the rectum or distal colon to identify the pelvic fluid collection.
2. Once located, intervening vasculature is excluded using color Doppler.
3. Under EUS guidance, a 19 gauge FNA needle is used to puncture the abscess cavity. The stylet is removed and the needle is flushed with saline and aspirated to remove as much pus as possible. At this time, a sample of fluid can be collected for gram stain and culture.
4. With the needle in place, a 0.035 inch guidewire is passed through the needle into the fluid collection and coiled several times into the collection (Fig. 39.1).
5. The needle is exchanged over the guidewire for a 4.5 Fr ERCP cannula to dilate the tract between the rectum and the abscess cavity. The tract is then further dilated using an 8 mm over the wire biliary balloon dilator (Fig. 39.2).
6. Once the tract is dilated, one or two 7 Fr 4 cm double pigtail transmural stents are deployed (Fig. 39.3). The decision for one or two stents is dependent on the

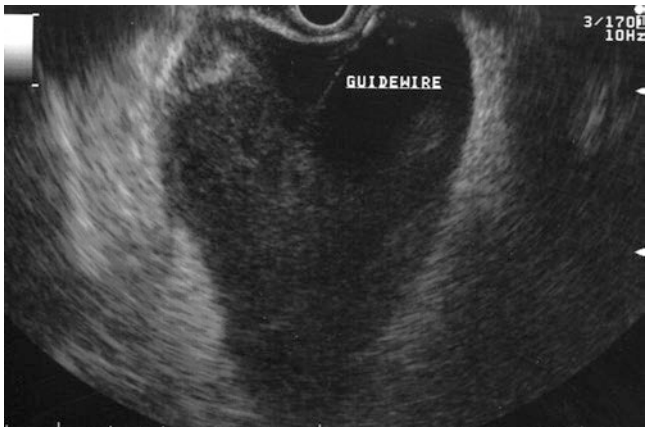

Fig. 39.1 A FNA needle is passed into the pelvic abscess under EUS guidance, and a guidewire is coiled within the abscess cavity

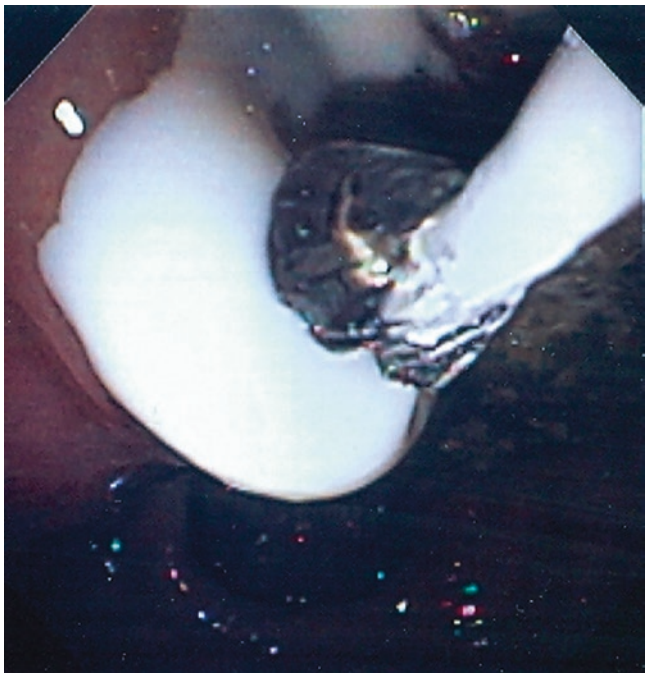

Fig. 39.2 The transmural tract is dilated to 8 mm with extrusion of pus

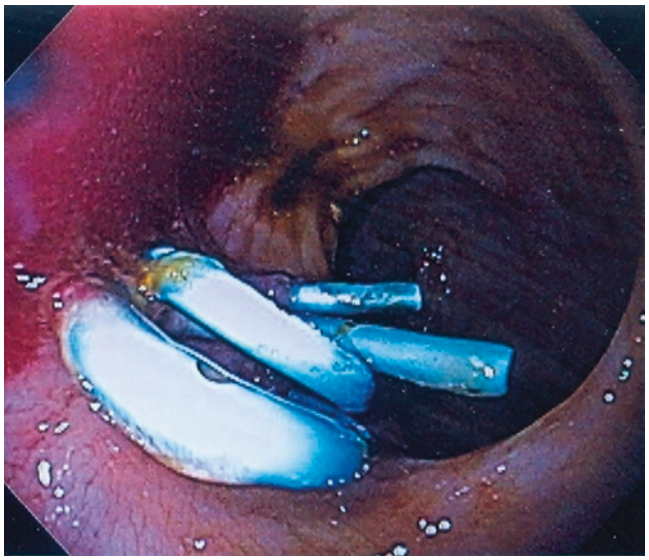

Fig. 39.3 Two double pigtail transrectal stents are deployed within the abscess cavity

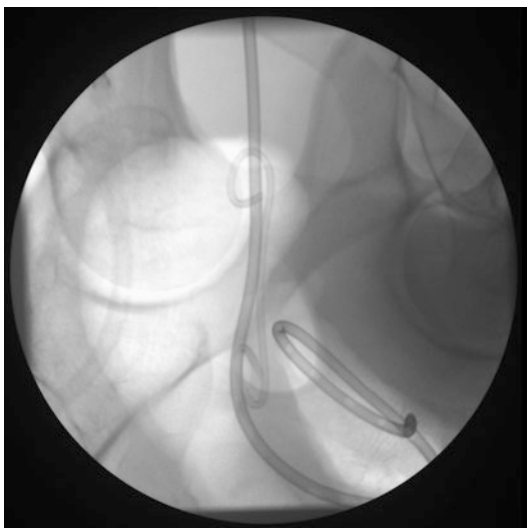

Fig. 39.4 A transrectal drainage catheter is seen within the pelvic abscess by fluoroscopy

viscosity of the abscess contents: one is used if the fluid flows out smoothly and two if the contents are viscous.

7. After the stents are deployed, the cavity is again accessed with a 5 Fr ERCP cannula to pass another 0.035 inch guidewire into the fluid cavity. A 10 Fr 80 cm single pigtail drain is then deployed inside the fluid collection to aid drainage (Fig. 39.4). This drain will exit the anus and remain secured to the patient's gluteal region using tape. This drain is flushed with 30–50 cc of normal saline every 4 h until the aspirate is clear.

Post-procedure

1. A follow-up CT is obtained at 36–48 h post-drainage to ensure that the fluid collection has decreased in size. If there is greater than a 50% reduction in size of the abscess cavity, the drainage catheter can be removed and the patient discharged home.
2. A second follow-up CT is performed at 2 weeks post-procedure. If repeat imaging shows complete resolution of the fluid collection, the remaining stents are removed at this time during sigmoidoscopy.

Practical Considerations

- All patients should undergo a dedicated CT or MRI of the pelvis to define the anatomy and location of the abscess before the planned transrectal EUS-guided drainage.
- Patients should receive prophylactic and continue with antibiotics for 3 days following the procedure.
- Patients should undergo an enema to assist with optimal visualization and minimize contamination.
- Insertion of a Foley catheter prior to the procedure.
- A follow-up CT is obtained at 36–48 h post-drainage and again at 2 weeks.

Clinical Outcomes

Several studies (Table 39.1) have evaluated the outcomes of EUS-guided drainage for the management of pelvic abscesses [1, 11, 13]. The first from Europe evaluated 12 patients using EUS-guided transrectal stents [1]. In this study, transrectal stents were deployed with a successful clinical outcome in 8 of 12 patients (75%). The difficulty with transrectal stents is the high potential to clog easily, particularly by fecal matter or pus, and when left long-term can cause perirectal pain or migrate spontaneously. In the second study, this limitation was overcome by placement of transrectal drainage catheters in four patients [13]. Although the technical and treatment outcomes were excellent, there was the potential for accidental dislodgement of the drainage catheter. Additionally, the need for periodic flushing and aspiration of the drainage catheter mandated a prolonged inpatient hospital stay for most patients. Therefore, a combined approach which included EUS-guided placement of a transrectal drainage catheter and transmural stents for drainage of the pelvic abscess was later adopted [11, 14]. Following complete resolution of pelvic fluid collections in all four patients in a small study [11], in a larger study of 25 patients, the additional short-term placement (36–48 h) of a drainage catheter provided access for rapid initial drainage of large fluid collections >8 cm in size, while the 2-week transmural stent placement facilitated maintenance of a patent tract for complete abscess resolution over a prolonged period of time. This combined therapy resulted in clinical success rate of 96% with no recurrence at mean follow-up of 189 days.

In addition, although pelvic fluid collections can be drained from both the rectum and the sigmoid/descending colon (depending on the location of the fluid collection), transcolonic drainage is considered to pose a higher technical challenge, owing to the thinner colonic wall and anatomic location. However, in one comparative study of 38 patients that compared treatment outcomes between transrectal and transcolonic routes in patients undergoing EUS-guided pelvic abscess drainage [8], there was no significant difference in treatment success rates with transrectal drainage at 96.3 vs. 70% for the transcolonic route (0 = 0.052). Furthermore, fluid recurrence was not observed in any patient experiencing treatment success with initial endoscopic drainage, regardless of the drainage route.

Table 39.1 EUS-guided drainage of pelvic abscess

Author	Pts (*n*)	Mean abscess size (mm)	Drainage mode	Treatment success rate (%)
Giovannini et al. [1]	12	48.9 × 43.4	Stents only	75
Varadarajulu and Drelichman [13]	4	68 × 72	Drainage catheter only	100
Trevino et al. [11]	4	93 × 61	Stents + drainage catheter	100
Varadarajulu and Drelichman [14]	25	68.5 × 52.4	Stents + drainage catheter	96

Limitations of EUS-Guided Drainage

The main limitations of EUS-guided pelvic abscess drainage are:

1. Fluid collections greater than 20 mm distant from the gastrointestinal lumen preclude successful drainage.
2. Accessing fluid collections which are located more proximal are not feasible due to the current limited maneuverability of echoendoscopes.
3. Multiple fluid collections are usually not amenable to EUS-guided drainage.

Conclusion

Current evidence shows that EUS-guided drainage is a minimally invasive, safe, and effective technique for management of patients with pelvic abscesses. EUS-guided drainage can be effective in patients with pelvic fluid collections that are not amenable to US or CT-guided drainage or have previously failed radiologically guided drainage procedures. Larger studies are required to definitively evaluate the technical and treatment outcomes of EUS-guided drainage and to determine its cost-effectiveness when compared with other modalities such as CT and US for drainage of pelvic abscesses.

References

1. Giovannini M, Bories E, Moutardier V, et al. Drainage of deep pelvic abscesses using therapeutic echo endoscopy. Endoscopy. 2003;35:511–4.
2. Golfieri R, Cappelli A. Computed tomography-guided percutaneous abscess drainage in coloproctology: review of the literature. Tech Coloproctol. 2007;11(3):197–208.
3. Harisinghani MG, Gervais DA, Maher MM, et al. Transgluteal approach for percutaneous drainage of deep pelvic abscesses: 154 cases. Radiology. 2003;228:701–5.
4. Jaffe TA, Nelson RC, Delong DM, et al. Practice patterns in percutaneous image-guided intraabdominal abscess drainage: survey of academic and private practice centers. Radiology. 2004;233:750–6.
5. Kuligowska E, Keller E, Ferrucci JT. Treatment of pelvic abscesses: value of one-step sonographically guided transrectal needle aspiration and lavage. AJR Am J Roentgenol. 1995;164:201–6.
6. Nelson AL, Sinow RM, Olaik D. Transrectal ultrasonographically guided drainage of gynecologic pelvic abscesses. Am J Obstet Gynecol. 2000;6:1382–8.
7. Onaca N, Hirshberg A, Adar R. Early reoperation for perirectal abscess. Dis Colon Rectum. 2001;44:1469–73.
8. Ramesh J, Bang JY, Trevino J, Varadarajulu S. Comparison of outcomes between endoscopic ultrasound-guided transcolonic and transrectal drainage of abdominopelvic abscesses. J Gastroenterol Hepatol. 2013;28:620–5.
9. Ryan RS, McGrath FP, Haslam PJ, et al. Ultrasound-guided endocavitary drainage of pelvic abscesses: technique, results and complications. Clin Radiol. 2003;58:75–9.
10. Sudakoff GS, Lundeen SJ, Otterson MF. Transrectal and Transvaginal sonographic intervention of infected pelvic fluid collections. Ultrasound Q. 2005;21:175–85.
11. Trevino J, Drelichman ER, Varadarajulu S. Modified technique for EUS-guided drainage of pelvic abscess. Gastrointest Endosc. 2008;68:1215–9.
12. Varadarajulu S. EUS-guided drainage of pelvic abscess. Tech Gastrointest Endosc. 2007;9:51–4.
13. Varadarajulu S, Drelichman ER. EUS-guided drainage of pelvic abscess. Gastrointest Endosc. 2007;66:372–6.
14. Varadarajulu S, Drelichman ER. Effectiveness of EUS in drainage of pelvic abscesses in 25 consecutive patients (with video). Gastrointest Endosc. 2009;70:1121–7.
15. Wroblicka JT, Kuligowska E. One-step needle aspiration and lavage for the treatment of abdominal and pelvic abscesses. AJR Am J Roentgenol. 1998;170:1197–203.

Endoscopic Ultrasound-Guided Celiac Plexus Block and Celiac Plexus Neurolysis

40

Amit H. Sachdev, Ali S. Khan, and Frank G. Gress

Introduction

Pain is one of the most common and difficult to control symptoms in patients with chronic pancreatitis (Fig. 40.1) and pancreatic cancer (Fig. 40.2) [1, 2]. Endoscopic ultrasound (EUS)-guided celiac block (CPB) and celiac plexus neurolysis (CPN) are novel non-pharmacological techniques that have been proven to effectively alleviate chronic abdominal pain associated with chronic pancreatitis and pancreatic cancer, respectively [3–5]. Celiac plexus block (CPB), a temporizing treatment, most commonly refers to the injection of a steroid and a long-acting local anesthetic into the celiac plexus to control pain associated with chronic pancreatitis. In contrast, celiac plexus neurolysis (CPN) generally refers to injection of alcohol or phenol, agents with more permanent effect, into the celiac axis area and can be used to treat pancreatic cancer (Table 40.1) [6].These modalities offer many benefits over nonnarcotic therapy, which provides inadequate pain relief, and opioids, which are associated with numerous side effects [7]. Nearly all patients treated with opioids will continue opioid therapy even after these procedures are completed.

The initial technique for performing celiac plexus neurolysis was described in 1914 by Kappis et al. [8]. The initial technique for performing EUS-guided CPB/CPN in pancreatic cancer was described in 1996 by Wiersema et al. [6, 9]. The initial technique for performing EUS-guided CPB in patients with pain related to chronic pancreatitis was described in 1999 by Gress et al. [10]. Since then, numerous medium-sized retrospective and prospective studies have been performed and have shown that CPB/CPN is beneficial in alleviating pain. The benefit of CPN is more pronounced in alleviating pain secondary to pancreatic malignancy, with less relief of abdominal pain in patients with chronic pancreatitis. The reason for the variation is unclear but may include different mechanisms of pain causation, transmission, and characteristics of the patient population. Therefore, CPN is more frequently used in patients with pancreatic cancer; however, it is not used as frequently in patients with chronic pancreatitis. The timing of celiac plexus block relative to the onset of pain is also important, and it appears that pain response is better when CPB and CPN are performed early in the onset of pain symptoms as opposed to later on [11]. The 2-month mark has been suggested in the context of malignancy for CPN [11], although no time frame has been agreed upon for chronic pancreatitis. More recently, it has been shown that direct injection into the celiac ganglia is also beneficial in providing long-term pain relief [12].

Practical Consideration

- Often times patients treated with CPB and CPN will continue opioid therapy even after these procedures are completed.
- The timing of celiac plexus block relative to the onset of pain is important, and studies have shown that pain response is better when CPB and CPN are performed early in the onset of pain symptoms as opposed to later on.

Anatomy

In order to better understand celiac plexus block and neurolysis, one must understand the anatomical location of the pancreas, the splanchnic nerve, and celiac plexus. The pancreas is a retroperitoneal exocrine, endocrine, and paracrine gland.

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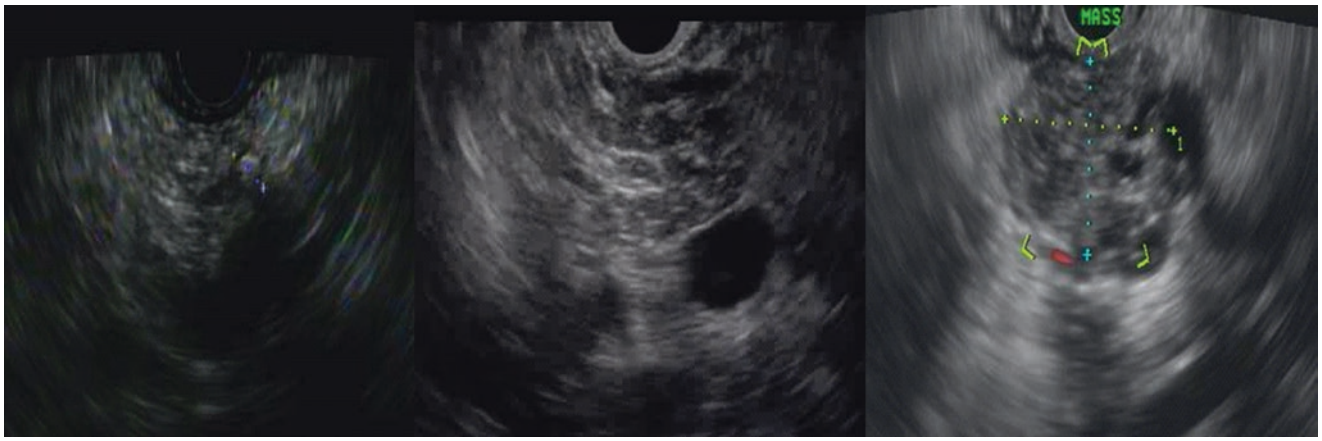

Fig. 40.1 *Left*: EUS demonstration of lobularity, one of the major criteria to help diagnose chronic pancreatitis by endoscopic ultrasonography. CPB is effective in treating pain associated with chronic pancreatitis. *Middle*: EUS demonstration of a pancreatic duct stone, another major criteria often seen in chronic pancreatitis. *Right*: Hypoechoic pancreatic mass as seen by endoscopic ultrasonography. CPN is effective in treating pain associated with pancreatic cancer

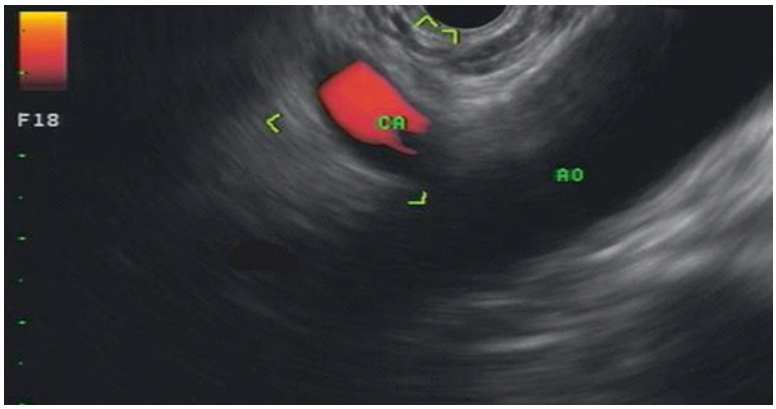

Fig. 40.2 Doppler evaluation of the celiac artery. The descending aorta is usually located 35 cm from the incisors. The celiac artery takeoff or trunk is usually located 40–50 cm from the incisors

The head of the pancreas is located at the L2 vertebra, and the tail is located at the L1 vertebra. Visceral pain associated with the pancreas is epigastric and typically radiates to the back. The splanchnic nerves and celiac plexus are independent anatomically distinct entities separated by the diaphragm [11, 13, 14]. The splanchnic nerve is located above and posterior to the diaphragm and anterior to the T12 vertebra. The celiac plexus is located below and anterior to the diaphragm near the aorta at the level of the celiac artery between the T12 and L2 regions (Fig. 40.3) [13]. The celiac plexus transmits pain stimulus from the pancreas via visceral afferent neurons before synapsing with the spinal cord. It is the largest plexus of the sympathetic nervous system, as it innervates the upper abdominal organs including the pancreas, diaphragm, liver, spleen, adrenal glands, kidneys, abdominal aorta, mesentery, stomach, small bowel, ascending colon, and the proximal portion of the transverse colon. The left celiac plexus is typically located more caudally than its counterpart on the right. The preganglionic sympathetic fibers of the celiac plexus are grouped into the greater (T5–10), lesser (T10–11), and the least (T12) splanchnic nerves, and the plexus also receives parasympathetic fibers from the celiac branch of the right vagus nerve. It was initially believed that the celiac plexus could not be identified as a discrete structure and targeted directly, and one needed to find it based on its location to the celiac trunk; however, it is now believed that the celiac plexus can be recognized directly [15].

Celiac blockage or neurolysis may target either the plexus or the celiac ganglia, and blocking or destroying the plexus or ganglia can mitigate the pain associated with chronic pancreatitis or pancreatic cancer.

Practical Consideration

- Direct visualization of the celiac ganglia may be challenging; the celiac trunk should be used as a landmark to help locate the celiac ganglia.

Table 40.1 Comparison of EUS-guided celiac plexus block and EUS-guided celiac plexus neurolysis

	EUS-guided celiac plexus block	EUS-guided celiac plexus neurolysis
Indications	Chronic pancreatitis pain (refractory to medications)	Pancreatic cancer pain (refractory to medications)
		Chronic pancreatitis pain (refractory to medications) on a case-by-case basis
Contraindications	*Absolute*	*Absolute*
	Lack of patient cooperation	Lack of patient cooperation
	Platelet count <50,000	Platelet count <50,000
	Coagulopathy	Coagulopathy
	Relative	*Relative*
	Altered anatomy from prior surgery congenital abnormalities	Altered anatomy from prior surgery
		Congenital abnormalities
Type of needle used	22 gauge needle	22 gauge needle
Chemical agent injected	20 mL of 0.25% bupivacaine, followed by 40 mg of triamcinolone for injection on each side in the bilateral approach or 80 mg in the unilateral approach	20 mL of 0.25% bupivacaine for nerve block and 98% dehydrated ethyl alcohol for injection
Prophylactic antibiotics necessary	Recommended	May not be necessary due to bactericidal properties of ethyl alcohol
Most common complications	Transient diarrhea, hypotension, and abdominal pain	Transient diarrhea, hypotension, and abdominal pain
Most common procedural setting	Outpatient	Outpatient
Follow-up post-procedure	2 h – Monitor vital signs for orthostatic hypotension	2 h – Monitor vital signs for orthostatic hypotension
Average long-term effect	3 months, 60% response rate to initial treatment	3 months

Indications for Endoscopic Ultrasound-Guided Celiac Plexus Block and Celiac Plexus Neurolysis

EUS-CPB is most commonly used for chronic pancreatitis. The NCCN guidelines recommend that EUS-CPN be used for treatment of severe pancreatic tumor-associated pain. CPB and CPN are especially useful when patients have intolerable side effects to opioid therapy including delirium, constipation, and drowsiness or when maximal amounts of opioids are used. One must also watch for addiction, which is frequently associated with narcotic medications, and therefore many patients may prefer these procedures if they are concerned about the addictive properties of narcotics.

	EUS-guided celiac plexus block	EUS-guided celiac plexus neurolysis
Indications	Chronic pancreatitis pain (refractory to medications)	Pancreatic cancer pain (refractory to medications)
		Chronic pancreatitis pain (refractory to medications) on a case-by-case basis

Contraindications for Endoscopic Ultrasound-Guided Celiac Plexus Block and Celiac Plexus Neurolysis

Absolute contraindications for CPB and CPN are lack of patient cooperation, platelet count <50,000, or coagulopathy. Relative contraindications for CPB and CPN are altered anatomy from prior surgery or congenital abnormalities [16].

The lack of response or partial response with the first celiac block should not prevent a repeat attempt if the patient understands these risks and benefits, as subsequent blocks may be beneficial. In patients with pancreatic cancer, studies have shown that although repeat celiac blocks are not as effective as initial celiac blocks, they are effective if there isn't significant progression of disease [17].

	EUS-guided celiac plexus block	EUS-guided celiac plexus neurolysis
Contraindications	*Absolute*	*Absolute*
	Lack of patient cooperation Platelet count <50,000 Coagulopathy	Lack of patient cooperation Platelet count <50,000 Coagulopathy

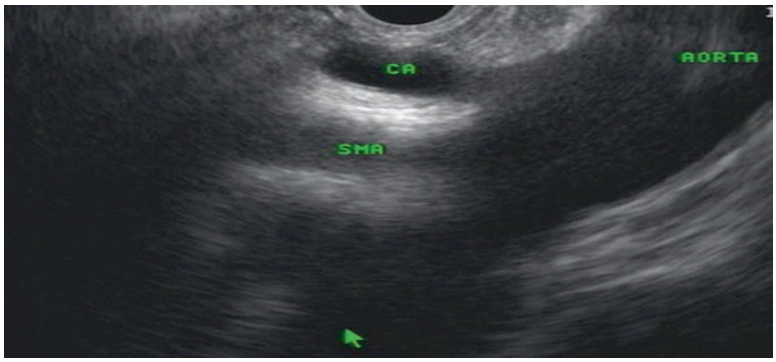

Fig. 40.3 Linear-array EUS imaging of the aorta, celiac artery (*CA*), and superior mesenteric artery (*SMA*) takeoff

Instruments and Accessories

Instruments and Accessories

- Curved linear-array endoscope
- Twenty-two gauge EUS-guided fine needle aspiration "spray" needle
- *Celiac plexus block*: 20 mL of 0.25% bupivacaine followed by 40 mg of triamcinolone for injection on each side of the celiac plexus in the bilateral approach or 80 mg on one side in the unilateral approach
- *Celiac plexus neurolysis*: 20 mL of 0.25% bupivacaine followed by 98% dehydrated ethyl alcohol for injection into the celiac plexus
- General anesthesia or deep IV sedation

The Procedure: The Technique for Performing Endoscopic Ultrasound-Guided Celiac Plexus Block and Celiac Plexus Neurolysis

CPB and CPN are performed under EUS guidance as an outpatient procedure. EUS-guided CPB/CPN is performed using a linear echoendoscope via a trans-gastric approach from the proximal stomach. EUS is beneficial because it can help diagnose and treat disease, and views are not limited by gastrointestinal gas and abdominal fat.

Prior to performing the procedure, informed consent must be obtained, and the risks and benefits of the procedure must be discussed with the patient. Given the potential risks from the procedure, it is advisable to discuss the patients' expectations and outcomes in terms of symptom control one office visit prior to the procedure (as opposed to open access scheduling in which a patient is scheduled for the procedure directly). A thorough history and physical exam should be obtained, and patients should be asked about allergies and

Technique

- Discuss planned procedure at least one office visit prior to the procedure (as opposed to open access scheduling).
- Obtain informed consent on the day of the procedure.
- Obtain a thorough history and physical exam; patients should be asked about allergies and the use of anticoagulants.
- Check a complete blood count and coagulation profile prior to the procedure.
- Patients should be fasting post-midnight prior to the procedure.
- Pre-procedural hydration with 500–1000 mL of normal saline should be started.
- Place the patient in the left lateral position under general anesthesia or deep IV sedation.
- Consider the use of antibiotics for celiac plexus block.
- During the procedure monitor the blood pressure, pulse, and blood oxygen saturation level.
- Perform per oral insertion of the curved linear echoendoscope.
- Advance the echoendoscope to the esophagogastric junction and posterior lesser curvature of the gastric fundus.
- Assess the vessel-gut relationship with color Doppler.
- Identify landmarks – the descending aorta: 35 cm from the incisors: the celiac artery: 40–50 cm from the incisors.
- Rotate the echoendoscope clockwise or anticlockwise so that the celiac artery takeoff is not visible.

Color Doppler is used to rule out major vessels between the transducer and the periaortic space in this position.
- Connect a 20 gauge EUS "spray" FNA needle to a 10 cc syringe.
- Load the needle through the biopsy channel of the echoendoscope.
- Perform an aspiration test by pulling the plunger of the syringe. If no blood return is seen in the syringe, the plunger is pushed forward expelling a few cc of saline to clear the needle of any tissue material.
- Determine if you will take the bilateral or unilateral approach.
- Inject 20 mL of 0.25% bupivacaine followed by 40 mg of triamcinolone for injection on both sides in the bilateral approach or 80 mg in the unilateral approach for celiac plexus block or 98% dehydrated ethyl alcohol in celiac plexus neurolysis.
- Before withdrawing the needle, the needle should be flushed with 3 mL normal saline to prevent seeding of the needle track with alcohol, which may produce transient severe post-procedure pain in CPN.
- Withdraw the needle from the periaortic space into its outer sheath.
- Transport the patient to the patient recovery room and monitor vital signs for 2 h post-procedure.

the use of anticoagulants. It is advisable to check a complete blood count and coagulation profile prior to the procedure paying attention the platelet count and looking for evidence of coagulopathy.

Patients should be fasting post-midnight prior to the procedure. Usually patients will require pre-procedural hydration with 500–1000 mL of normal saline, followed by CPB/CPN performed while the patient is in the left lateral position under general anesthesia or deep IV sedation. Some endosonographers give antibiotic prophylaxis to prevent retroperitoneal abscess formation in EUS-guided CPB. Cases have been reported in which patients developed an infectious complication (peripancreatic abscess) after a EUS-guided CPB that resolved with a 2-week course of antibiotics. In the first case, the authors concluded that the patient might have had a predisposition to infection owing to gastroduodenal colonization with bacteria because the patient was taking a proton pump inhibitor. They suggested that prophylactic antibiotics should be considered in patients who are receiving acid suppression and undergoing EUS-CPB [10]. Given the bactericidal properties of absolute alcohol [18], the use of prophylactic antibiotics for EUS-CPN is probably not needed. During the procedure blood pressure, pulse, and blood oxygen saturation level should be monitored.

After oral intubation, the echoendoscope is slowly advanced down the esophagus into the esophagogastric junction and posterior lesser curve of the gastric fundus. Color Doppler is used to assess the vessel-gut relationship, and a therapeutic linear-array echoendoscope is used and the puncture site is chosen. The landmark that is used is the descending aorta, which is easily identified as a long anechoic tubular structure located at 35 cm from the incisors. The celiac artery is then located which is the first major branch off the descending aorta below the diaphragm, which is usually located at 40–50 cm from the incisors. Prior to performing the EUS-CPB or CPN, it is recommended that a complete endosonographic examination is performed to visualize the remaining organs and structures to confirm the diagnosis of chronic pancreatitis or in the case of pancreatic cancer to determine the extent of the disease. A Doppler assessment of the area of interest must also be performed.

Usually 19-G or 22-G needles are used, and special needles designed for EUS-CPN can also be used. The advantage of the EUS needle is that it is a "spray" needle with multiple side holes available, which facilitates spread of the injected material.

Two different injection techniques have been described. If a central injection approach is chosen, the needle is advanced above the celiac trunk, in the space between the aorta and the origin of the celiac axis (Fig. 40.4). If bilateral injection is

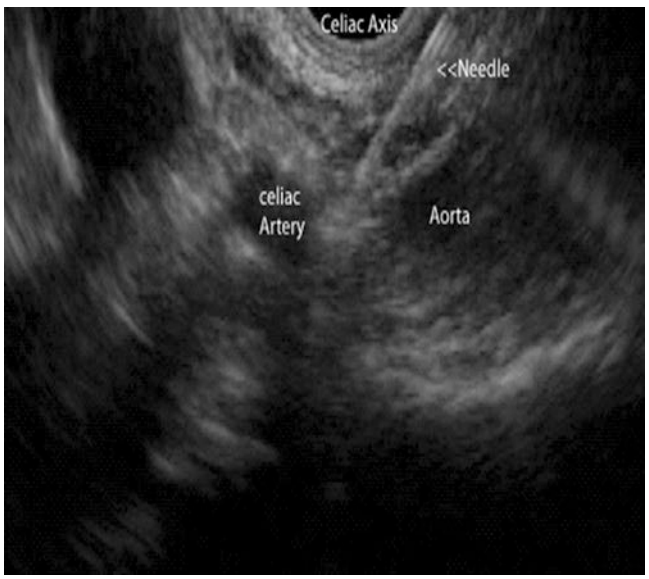

Fig. 40.4 Endoscopic ultrasound image showing the position of the needle above the celiac plexus. The origin of the celiac axis just above the celiac artery from the aorta is seen

chosen, the echoendoscope, situated above the celiac axis, is rotated to one side until the origin of the celiac axis is no longer seen, and half of the entire solution is injected; the procedure is then repeated on the opposite side [19]. The type of technique used for obtaining the best response is still controversial. One randomized trial comparing the central vs. bilateral technique showed no difference in duration of pain relief, complete pain relief, or reduction in pain medications [20].

The difference between CPN and CPB techniques is in terms of the chemical agent injected. Bupivacaine (0.25%) is used for both as an initial local anesthetic, whereas it is followed by either ethyl alcohol (98%) [21] for CPN or triamcinolone (40 mg) for CPB, respectively [10, 15]. The alcohol, which produces an echogenic cloud, may lead to discomfort despite sedation. Before withdrawing the needle, the needle should be flushed with 3 mL normal saline to prevent seeding of the needle track with alcohol, which may produce transient severe post-procedure pain and in some cases tissue necrosis. It is important to make sure that alcohol is not injected near the diaphragm as this may cause pain as the alcohol is spread. A local analgesic is often used to prevent transient pain, while the neurolytic agent is used. Aspiration should be performed prior to injecting the neurolytic agent to ensure that vascular puncture has not occurred. Each time a new syringe is exchanged, it should be aspirated prior to injection to confirm proper positioning. Inadvertent injection of these agents, especially bupivacaine, into a blood vessel can be lethal.

The reason for using steroids instead of alcohol for the CPB in patients with chronic pancreatitis is based on the fact that this is a chronic rather than a terminal condition and absolute alcohol injection would in theory destroy the plexus causing permanent damage [22].

Recently, entire ganglia have been targeted in what is termed celiac plexus ganglialysis (CPG) [15]. Alcohol injection into the ganglia appears to be safe and effective in both patients with pancreatic cancer and chronic pancreatitis. Ganglia can be identified in as many as 95% of patients in some studies, suggesting that this is a promising approach [12]. In CPG, the echoendoscope is rotated clockwise, and celiac ganglia are found above the celiac trunk, alongside the trunk, and below the trunk, just above the superior mesenteric artery takeoff [23]. Most frequently, the celiac ganglia are seen to the left of the celiac artery, between the aorta and the left adrenal gland, at the level between the celiac artery and the left renal artery. As many ganglia as possible should be injected starting in the central part and continual injection while withdrawing the needle.

Practical Consideration

- Antibiotics should be given prior to CPB and are not necessary prior to CPN.
- Prior to performing CPB or CPN, a Doppler assessment of the area should be performed.
- The central injection technique and the bilateral technique are two alternatives that should be used for CPB and CPN and which is the best technique remains controversial.
- Bupivacaine (0.25%) is used as the initial local anesthetic for both CPB and CPN, whereas it is followed by either ethyl alcohol (98%) for CPN or triamcinolone (40 mg) for CPB, respectively.
- It is extremely important to perform aspiration prior to injecting the neurolytic agent to ensure that vascular puncture has not occurred.

Complications

Common side effects reported in the literature for celiac plexus block and celiac plexus neurolysis include transient hypotension, transient diarrhea, and transient increase in abdominal pain [9, 18, 24, 25].

More common	Less common
Transient hypotension [21]	Retroperitoneal bleed [26]
Transient diarrhea [21]	Retroperitoneal abscess [27]
Transient increase in abdominal pain [21]	Ischemia [28] Ejaculatory failure [29] Brain abscess [30] Spinal cord infarction [31] Gastric necrosis/death [32]

Transient diarrhea and hypotension are a result of sympathetic blockade and unopposed parasympathetic activity which may occur in up to 38–44% of patients [25]. When minor side effects such as diarrhea and hypotension occur, they actually provide a sign that the block has been administered at the optimal location and that the proper area has been effectively blocked. This is important, because patients' anatomies vary, and though the celiac plexus is generally in the same area, the exact location can differ and therefore be

missed. Diarrhea and hypotension usually resolve within 48 h [33]. The diarrhea responds well to loperamide [34]. Hypotension in these patients responds rapidly to IV fluids [12, 27]. Transient pain can also occur, which can also last up to 48 h post-procedure and can be relieved by an increase in narcotics in some patients [3, 24, 35].

In addition, other less common complications that have been reported in the literature include hepatic bowel infarction, gastric necrosis, brain abscess, pneumothorax, retroperitoneal bleeding, and paraplegia. Paraplegia occurs in about 1% of patients undergoing percutaneous radiology-guided celiac plexus neurolysis through a posterior approach [36]. This is a theoretical risk in patients undergoing EUS-guided CPN and has been reported once in the literature [37]. Cephalic spread of the neurolytic agent can also result in involvement of the cardiac nerves and plexus affecting the heart and thoracic structures [38].

It is important to note that there is little evidence to suggest that celiac plexus block or celiac plexus neurolysis has any effect on subsequent surgical intervention. Neurolysis can result in histologically increased hyalinized fibrotic tissue [22] which may effect surgery, and the issue of interference should be discussed with surgical colleagues at high-volume centers although it is not believed that this will effect surgical outcomes. Animal models have also confirmed that although the overall adhesion score was higher in the celiac plexus neurolysis group vs. the celiac block group, there was no interference with surgery (or vascular plane involvement) overall [39].

Technical challenges can also arise in some patients where the anatomic landmarks cannot be well visualized or in patients who are cachectic and have very little fat around the aorta. In this case, the celiac plexus region may not be able to be reached with the needle, and alternative methods for celiac plexus destruction need to be employed [40].

Practical Consideration

- When minor side effects such as diarrhea and hypotension occur, they actually provide a sign that the block has been administered at the optimal location.

Follow-Up

After the procedure, the patient's vital signs should be monitored (temperature, blood pressure, and heart rate) for at least 2 h. Individual institutions should consider formulating protocols for pre-procedure, post-procedure observation, and follow-up. Referral to higher-volume centers should be considered if institutional experience is limited.

Practical Consideration

- Monitor vital signs (temperature, blood pressure, and heart rate) for at least 2 h post-procedure.

Conclusion: Efficacy of Endoscopic Ultrasound-Guided Celiac Plexus Block and Celiac Plexus Neurolysis

While CPB and CPN are considered safe procedures, the long-term efficacy of CPB and CPN has been limited in terms of its duration of pain relief, and the effects on quality of life are controversial depending on the study [41, 42]. Most studies evaluating percutaneous CPB for controlling pain from chronic pancreatitis have been small retrospective case series and have reported marginal benefit [10, 27, 43]. A meta-analysis of EUS-guided celiac plexus blocks and neurolysis reported response rates of 59% in chronic pancreatitis and 80% in pancreatic cancer; however, most of these patients continued to take analgesic medications [44]. The average length of relief for patients with CPB is approximately 3 months in most studies, and CPB is therefore seen as a temporizing measure. It is important to note that 60% of patients with CPB report relief of pain after EUS-CPB, meaning 40% do not respond [45]. In one study, younger patients and patients with prior pancreatic surgery were less likely to respond. The reasons for this are unclear. Studies have shown however that repeated EUS-CPB in a single patient can be safe and that response to the first EUS-CPB is associated with response to subsequent blocks [46]. In fact, in this study patients had up to 10 blocks with pain relief and without serious adverse events although the majority of patients in this study received 4 blocks total.

In a large meta-analysis of 1145 patients undergoing CPN for palliation of cancer pain (63% of which had pancreatic cancer), good or excellent pain relief was noted in 70–90% of patients 3 months after the procedure [25]. One randomized control trial comparing central versus bilateral technique for CPN showed no difference in duration of pain relief or reduction in pain medications [20]. The type of technique showing the best response is still controversial depending on the study [42]. CPN in pancreatic cancer had no survival benefit in two large randomized control trials [20, 47]. A recent randomized trial suggested that CPG might be superior to CPN for patients with pancreatic cancer [48]. The positive response rate at day 7 and the complete response rate were higher in the ganglia neurolysis group (75.5% vs. 45.5% and 50% vs. 18.2%, respectively). Further research needs to be conducted on the long-term benefits of CGN versus CPN for patients with pancreatic cancer.

- EUS-guided celiac plexus block and celiac plexus neurolysis are effective options to patients with refractory pain secondary to chronic pancreatitis and pancreatic cancer, respectively.
- A discussion with the patient about the indications, contraindications, risks, benefits, and long-term efficacy should be performed prior to performing the procedure ideally before the procedure date as opposed to open access scheduling.
- The endosonographer must master the anatomy of the pancreas, the splanchnic nerve, and the celiac plexus.
- The two most common EUS injection techniques are the central technique and the bilateral technique although the technique for obtaining the best response remains controversial.
- Bupivacaine (0.25%) is used for both celiac plexus block and celiac plexus neurolysis as an initial local anesthetic, whereas it is followed by either triamcinolone (40 mg) for CPB or ethyl alcohol (98%) for CPN, respectively.
- The most common complications are transient diarrhea, transient hypotension, and transient abdominal pain usually lasting for 48 h with supportive care.
- Pain relief on average lasts up to 12 weeks and repeat CPB/CPN can be performed; however, different studies show different results, and the effects on quality of life vary depending on the study.
- The available evidence is more conclusive for patients with pancreatic cancer; however, more long-term studies and randomized controlled trials need to be conducted.
- Initial data suggests that direct celiac plexus ganglia neurolysis is a safe and effective approach.

References

1. Ventafridda GV, Caraceni AT, Sbanotto AM, Barletta L, De Conno F. Pain treatment in cancer of the pancreas. Eur J Surg Oncol. 1990;16(1):1–6. Epub 1990/02/01
2. Lankisch PG. Natural course of chronic pancreatitis. Pancreatology. 2001;1(1):3–14. Epub 2002/07/18
3. Yan BM, Myers RP. Neurolytic celiac plexus block for pain control in unresectable pancreatic cancer. Am J Gastroenterol. 2007;102(2):430–8. Epub 2006/11/15
4. Wang PJ, Shang MY, Qian Z, Shao CW, Wang JH, Zhao XH. CT-guided percutaneous neurolytic celiac plexus block technique. Abdom Imaging. 2006;31(6):710–8. Epub 2006/12/08
5. Carroll I. Celiac plexus block for visceral pain. Curr Pain Headache Rep. 2006;10(1):20–5. Epub 2006/02/28
6. Hoffman BJ. EUS-guided celiac plexus block/neurolysis. Gastrointest Endosc. 2002;56(4 Suppl):S26–8. Epub 2002/09/26
7. Ventafridda V, Tamburini M, Caraceni A, De Conno F, Naldi F. A validation study of the WHO method for cancer pain relief. Cancer. 1987;59(4):850–6. Epub 1987/02/15
8. Kappis M. Erfahrungen mit local anasthesie bie bauchoperationen. Vehr Dtsch Gesellsch Chir. 1914;
9. Levy MJ, Wiersema MJ. EUS-guided celiac plexus neurolysis and celiac plexus block. Gastrointest Endosc. 2003;57(7):923–30. Epub 2003/05/31
10. Gress F, Schmitt C, Sherman S, Ikenberry S, Lehman G. A prospective randomized comparison of endoscopic ultrasound- and computed tomography-guided celiac plexus block for managing chronic pancreatitis pain. Am J Gastroenterol. 1999;94(4):900–5. Epub 1999/04/14
11. Ischia S, Ischia A, Polati E, Finco G. Three posterior percutaneous celiac plexus block techniques. A prospective, randomized study in 61 patients with pancreatic cancer pain. Anesthesiology. 1992;76(4):534–40. Epub 1992/04/01
12. Levy MJ, Topazian MD, Wiersema MJ, Clain JE, Rajan E, Wang KK, et al. Initial evaluation of the efficacy and safety of endoscopic ultrasound-guided direct ganglia neurolysis and block. Am J Gastroenterol. 2008;103(1):98–103. Epub 2007/11/01
13. Ward EM, Rorie DK, Nauss LA, Bahn RC. The celiac ganglia in man: normal anatomic variations. Anesth Analg. 1979;58(6):461–5. Epub 1979/11/01
14. Brown DL, Moore DC. The use of neurolytic celiac plexus block for pancreatic cancer: anatomy and technique. J Pain Symptom Manag. 1988;3(4):206–9. Epub 1988/01/01
15. Levy M, Rajan E, Keeney G, Fletcher JG, Topazian M. Neural ganglia visualized by endoscopic ultrasound. Am J Gastroenterol. 2006;101(8):1787–91. Epub 2006/06/20
16. Soweid AM, Azar C. Endoscopic ultrasound-guided celiac plexus neurolysis. World J Gastrointest Endosc. 2010;2(6):228–31. Epub 2010/12/17
17. McGreevy K, Hurley RW, Erdek MA, Aner MM, Li S, Cohen SP. The effectiveness of repeat celiac plexus neurolysis for pancreatic cancer: a pilot study. Pain Practice. 2013;13(2):89–95. Epub 2012/05/10
18. O'Toole TM, Schmulewitz N. Complication rates of EUS-guided celiac plexus blockade and neurolysis: results of a large case series. Endoscopy. 2009;41(7):593–7. Epub 2009/07/10
19. Wiersema MJ, Wiersema LM. Endosonography-guided celiac plexus neurolysis. Gastrointest Endosc. 1996;44(6):656–62. Epub 1996/12/01
20. LeBlanc JK, Al-Haddad M, McHenry L, Sherman S, Juan M, McGreevy K, et al. A prospective, randomized study of EUS-guided celiac plexus neurolysis for pancreatic cancer: one injection or two? Gastrointest Endosc. 2011;74(6):1300–7. Epub 2011/10/18
21. Pusceddu C, Mameli S, Pili A, Podda G. [Percutaneous neurolysis of the celiac plexus under CT guidance in the invasive treatment of visceral pain caused by cancer]. Neurolisi percutanea del plesso celiaco sotto guida TC nel trattamento invasivo del dolore viscerale da cancro. Tumori. 2003;89(4 Suppl):286–91. Epub 2003/08/09
22. Vranken JH, Zuurmond WW, Van Kemenade FJ, Dzoljic M. Neurohistopathologic findings after a neurolytic celiac plexus block with alcohol in patients with pancreatic cancer pain. Acta Anaesthesiol Scand. 2002;46(7):827–30. Epub 2002/07/26
23. Ascunce G, Ribeiro A, Reis I, Rocha-Lima C, Sleeman D, Merchan J, et al. EUS visualization and direct celiac ganglia neurolysis predicts better pain relief in patients with pancreatic malignancy (with video). Gastrointest Endosc. 2011;73(2):267–74. Epub 2011/02/08
24. Davies DD. Incidence of major complications of neurolytic coeliac plexus block. J R Soc Med. 1993;86(5):264–6. Epub 1993/05/01
25. Eisenberg E, Carr DB, Chalmers TC. Neurolytic celiac plexus block for treatment of cancer pain: a meta-analysis. Anesth Analg. 1995;80(2):290–5. Epub 1995/02/01

26. Pello S, Miller A, Ku T, Wang D. Hemorrhagic gastritis and duodenitis following celiac plexus neurolysis. Pain Physician. 2009;12(6):1001–3. Epub 2009/11/26
27. Gress F, Schmitt C, Sherman S, Ciaccia D, Ikenberry S, Lehman G. Endoscopic ultrasound-guided celiac plexus block for managing abdominal pain associated with chronic pancreatitis: a prospective single center experience. Am J Gastroenterol. 2001;96(2):409–16. Epub 2001/03/10
28. Sayed I, Elias M. Acute chemical pericarditis following celiac plexus block--a case report. Middle East J Anaesthesiol. 1997;14(3): 201–6. Epub 1998/09/30
29. Shin SK, Kweon TD, Ha SH, Yoon KB. Ejaculatory failure after unilateral neurolytic celiac plexus block. Korean J Pain. 2010;23(4):274–7. Epub 2011/01/11
30. Lalueza A, Lopez-Medrano F, del Palacio A, Alhambra A, Alvarez E, Ramos A, et al. Cladosporium macrocarpum brain abscess after endoscopic ultrasound-guided celiac plexus block. Endoscopy. 2011;43 Suppl 2 UCTN:E9–10. Epub 2011/01/29.
31. Mercadante S, Nicosia F. Celiac plexus block: a reappraisal. Reg Anesth Pain Med. 1998;23(1):37–48. Epub 1998/04/29
32. Loeve US, Mortensen MB. Lethal necrosis and perforation of the stomach and the aorta after multiple EUS-guided celiac plexus neurolysis procedures in a patient with chronic pancreatitis. Gastrointest Endosc. 2013;77(1):151–2. Epub 2012/05/26
33. Patt RB, Reddy S. Spinal neurolysis for cancer pain: indications and recent results. Ann Acad Med Singap. 1994;23(2):216–20. Epub 1994/03/01
34. Gress F. Endoscopic ultrasound-guided celiac plexus neurolysis. Gastroenterol Hepatol. 2007;3(4):279–81. Epub 2007/04/01
35. Noble M, Gress FG. Techniques and results of neurolysis for chronic pancreatitis and pancreatic cancer pain. Curr Gastroenterol Rep. 2006;8(2):99–103. Epub 2006/03/15
36. Lillemoe KD, Cameron JL, Kaufman HS, Yeo CJ, Pitt HA, Sauter PK. Chemical splanchnicectomy in patients with unresectable pancreatic cancer. A prospective randomized trial. Ann Surg. 1993;217(5):447–55. discussion 56–7. Epub 1993/05/01
37. Fujii L, Clain JE, Morris JM, Levy MJ. Anterior spinal cord infarction with permanent paralysis following endoscopic ultrasound celiac plexus neurolysis. Endoscopy. 2012;44 Suppl 2 UCTN:E265–6. Epub 2012/07/21.
38. Hardy PA, Wells JC. Coeliac plexus block and cephalic spread of injectate. Ann R Coll Surg Engl. 1989;71(1):48–9. Epub 1989/01/01
39. Appalaneni V, et al. EUS-guided celiac plexus neurolysis vs. block: assessing interference with pancreatic surgery and adhesions in a pig survival model. GIE. 2008;69(2):233–4.
40. Johnson CD, Berry DP, Harris S, Pickering RM, Davis C, George S, et al. An open randomized comparison of clinical effectiveness of protocol-driven opioid analgesia, celiac plexus block or thoracoscopic splanchnicectomy for pain management in patients with pancreatic and other abdominal malignancies. Pancreatology. 2009;9(6):755–63. Epub 2010/01/22
41. Muscatiello N, Panella C, Pietrini L, Tonti P, Ierardi E. Complication of endoscopic ultrasound-guided celiac plexus neurolysis. Endoscopy. 2006;38(8):858. Epub 2006/09/27
42. Leblanc JK, Rawl S, Juan M, Johnson C, Kroenke K, McHenry L, et al. Endoscopic ultrasound-guided celiac plexus neurolysis in pancreatic cancer: a prospective pilot study of safety using 10 mL versus 20 mL alcohol. Diagnos Therap Endosc. 2013;2013:327036. Epub 2013/02/01
43. Sahai AV, Lemelin V, Lam E, Paquin SC. Central vs. bilateral endoscopic ultrasound-guided celiac plexus block or neurolysis: a comparative study of short-term effectiveness. Am J Gastroenterol. 2009;104(2):326–9. Epub 2009/01/29
44. Puli SR, Reddy JB, Bechtold ML, Antillon MR, Brugge WR. EUS-guided celiac plexus neurolysis for pain due to chronic pancreatitis or pancreatic cancer pain: a meta-analysis and systematic review. Dig Dis Sci. 2009;54(11):2330–7. Epub 2009/01/13
45. LeBlanc JK, DeWitt J, Johnson C, Okumu W, McGreevy K, Symms M, et al. A prospective randomized trial of 1 versus 2 injections during EUS-guided celiac plexus block for chronic pancreatitis pain. Gastrointest Endosc. 2009;69(4):835–42. Epub 2009/01/13
46. Sey MS, Schmaltz L, Al-Haddad MA, DeWitt JM, Calley CS, Juan M, et al. Effectiveness and safety of serial endoscopic ultrasound-guided celiac plexus block for chronic pancreatitis. Endosc Intern Open. 2015;3(1):E56–9. Epub 2015/07/03
47. Wyse JM, Carone M, Paquin SC, Usatii M, Sahai AV. Randomized, double-blind, controlled trial of early endoscopic ultrasound-guided celiac plexus neurolysis to prevent pain progression in patients with newly diagnosed, painful, inoperable pancreatic cancer. J Clin Oncol. 2011;29(26):3541–6. Epub 2011/08/17
48. Doi S, Yasuda I, Kawakami H, Hayashi T, Hisai H, Irisawa A, et al. Endoscopic ultrasound-guided celiac ganglia neurolysis vs. celiac plexus neurolysis: a randomized multicenter trial. Endoscopy. 2013;45(5):362–9. Epub 2013/04/26

Flexible Robotic Endoscopy Systems and the Future Ahead

41

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Introduction

Computer and robotically assisted surgery was developed to overcome the limitations of minimally invasive surgical procedures as well as enhance the interventional capabilities of surgeons. The poster child for robotic surgery in the 2000s was the Da Vinci machine, which enhanced the visualization and manipulation abilities of laparoscopic surgeons. Originally developed for battlefield telesurgery by DARPA, it makes use of a master-slave configuration, in which the user sits at a master control terminal and remotely operates a slave robot. Other medical specialties have also embraced robotic technology to improve precision, safety and reliability. For example, ophthalmic surgery benefits greatly from handheld devices which filter out tremors from the surgeon's hand [1]. Neurosurgery requires thorough preoperative imaging and path planning which is then put into action by a flexible path following robot. Endovascular surgery is also heavily imaging based and benefits from the use of master-slave control interfaces to increase ergonomics and reduce fluoroscopy exposure to the surgeon [2].

In gastroenterology, robotics has been implemented in flexible endoscopes to increase their effectiveness and safety as well as to augment their therapeutic capabilities. Often, haustral folds create obstructions that the tip-mounted video camera cannot see behind. Robotic mechanisms have been added to the heads of endoscopes that let them bend 180° backwards to see behind the folds. Novel locomotion methods that reduce the amount of force applied to the intestinal walls and interventional endoscopes have also been developed. In the most common embodiment, instruments emerge from the tip of the endoscope into the camera's field of vision. These instruments are similar to those used in laparoscopic surgery, such as tissue graspers, electrocautery devices, and wire loops. They are usually cable actuated and controlled from the proximal end by the endoscopist. Endoscopes with two or more instrument channels allow bimanual grasping of tissue and/or resection ability. They are also robotically assisted, which offers an improvement to conventional surgical endoscopy by addressing some of the inherent challenges of providing enough force to distally mounted tools through a long and flexible conduit. The most promising flexible endoscopic robots being developed will be introduced further in this chapter, and a case series on endoscopic submucosal dissection (ESD) using one of the platforms will be presented.

Finally, natural orifice transluminal endoscopic surgery (NOTES) is a new paradigm that makes use of natural orifices to access the peritoneum for surgery, thus leaving no visible scars. Current technology limits it to transoral, transvaginal and transanal avenues of access, but with miniaturization even more may be possible. Much of the technology for NOTES is based on that of existing gastrointestinal surgery. Within this context, the future developments and possibilities of flexible robotic endoscopes will be discussed.

Robotic Endoscopy Systems

The current robotic endoscope platforms being developed are summarised in Table 41.1. Information is provided on their key features (degrees of freedom, dimensions) and

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readiness to market (clinical trials, regulatory approval) [3, 4]. Direct comparisons are not useful due to the differing areas of anatomy that they specialise in, for example, oropharyngeal vs colonic. Where they do operate in the same anatomical domain, at present there is insufficient clinical data to suggest the superiority of one device over another.

The diagnostic endoscopes presented employ unique methods to advance through the colon that reduce the amount of force exerted on the colon, reducing trauma to the endoluminal lining. These would be cumbersome to operate using a manual approach, so automation allows the endoscopist to focus on the task of identifying features of interest such as polyps and lesions.

The surgical endoscopes presented also benefit greatly from robotic assistance. Most surgical endoscopes make use of control tendons actuated at the proximal end to move distally mounted instruments. The convoluted path (tortuosity) of an endoscope through the lower GI tract and the bending of the endoscope tip into a retroflexed position (i.e. 180°) introduce friction between the tendons and their guide sheaths [5–11]. This friction leads to a sluggish response of the end effector to human commands made at the proximal end and a jerky start-stop motion of the surgical tools. These control problems can be mitigated by the introduction of a robotic controller which intelligently compensates for nonlinear and hysteretic friction effects [12–16]. Friction losses can also severely degrade the output force, so to maintain the payload of the end effectors for tissue manipulation, motorised actuation is desirable [10, 16–18].

In addition, better ergonomics are possible with robotics. The control system of manually operated endoscopes has been modelled after that of laparoscopic tools, which make use of control wheels and dials to directly control the tendons. This is unintuitive and results in a steep learning curve. As with the Da Vinci machine, robotics offers a more natural mapping of user motion to the movement of the surgical tools. Haptic feedback can also be incorporated, which improves the precision at which a surgeon can manipulate the tissue.

Diagnostic Endoscopes

Aer-O-Scope

The Aer-O-Scope is equipped with a front-facing camera and a 360° panoramic camera for viewing the side walls of the colon (see Figs. 41.1 and 41.2). This unique optical setup allows it to see behind haustral folds. Upon insertion, a balloon at the anal sphincter is used to make the colon airtight. Two balloons mounted at the tip of the scope are inflated with CO_2 gas to provide cushioning as it slides through the colon. Forward motion is achieved by pressurising the segment of colon between the proximal balloon and the middle balloon [19].

Endotics

The Endotics endoscope draws inspiration from the locomotive principle of an inchworm. It has two anchoring points, proximal and distal, which are alternately actuated using a vacuum suction mechanism. The middle section is able to contract and expand along its longitudinal axis (Fig. 41.3). By cycling between the four actuation mechanisms, it is capable of inching forwards or backwards [20].

Invendoscope

The Invendoscope aims to be a lightweight, single-use colonoscope that addresses the medical risk of cross-contamination from improperly sterilised endoscopes. It has a robotic hydraulically articulated tip for navigation and retrograde viewing. It uses a novel way of advancing through the colon, being surrounded by an air-filled inverted sleeve that cushions the lumen as the tip moves forward (see Fig. 41.4). This theoretically reduces the amount of force exerted on the colon [21]. In a comparison study between the Endotics and Invendoscope systems, it was shown to be faster at completing the colonoscopy, but induced greater levels of discomfort [22].

Neoguide

The Neoguide endoscopy system, recently acquired by Intuitive Surgical, consists of 16 individual segments that

Table 41.1 Current robotic endoscopy platforms

Name	Flexible length (cm)	Diameter (mm)	Number of instrument channels	Regulatory approval	Commercial status	Animal trials	Human trials
Aer-O-Scope	>150	–	–	FDA, CE	Under development	Yes	Yes
Endotics	~200	17	–	CE	Available	Yes	Yes
Invendoscope	200	–	1	FDA, CE	Under development	Yes	Yes
Neoguide	173	14–20	–	FDA	Under development	Yes	Yes
Flex	~50	Variable	2	FDA, CE	Only in Europe	Yes	Yes
i-snake	20	14	1	–	–	Yes	No
MASTER	154	22	2	–	Under development	Yes	Yes
Viacath	90	16	2	–	Available	Yes	–

Fig. 41.1 Omni-view cameras on tip of endoscope with inflated distal balloon (Reproduced with permission. Source [http://www.giview.com/contact-us.html])

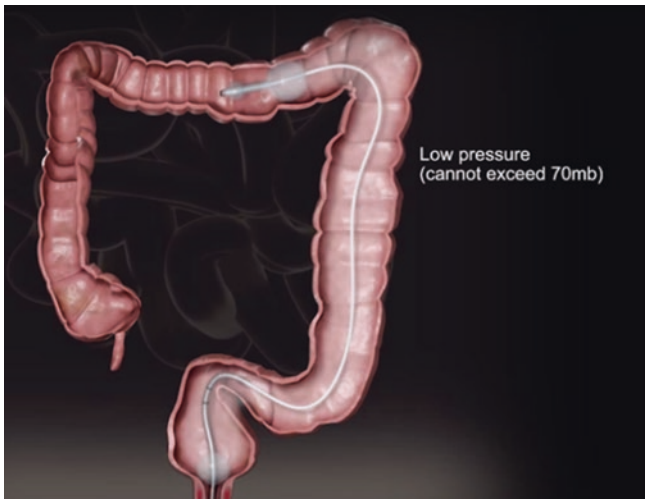

Fig. 41.2 Pneumatic intubation

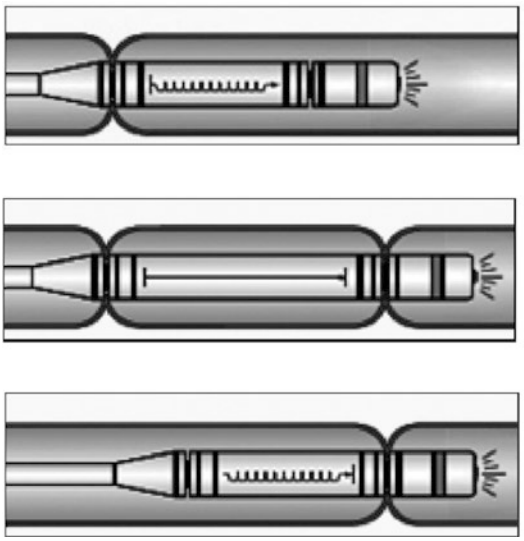

Fig. 41.3 Endotics principle of locomotion

can be programmed to change their shape (see Fig. 41.5). As the lead segment makes its way deeper into the colon, the rest will automatically change their shape to follow the path that has been defined. Each of the 16 segments has 2 degrees of articulation [23].

Surgical Endoscopes

Flex Robot

Medrobotics' Flex Robotic System, the product of research at Carnegie Mellon University, is a short flexible endoscope designed for transoral surgery (See Fig. 41.6). While transoral pathologies do not normally fall under the scope of gastrointestinal specialists, it has operating principles common to endoscopes. It has an overtube comprising many ball and cup vertebral segments. Articulation is achieved by motorised tensioning of a cable tendon system that runs through the overtube, which also houses a video camera at the distal tip. Due to an inner spine that can be stiffened, it is able to maintain the shape of the path travelled. Riding on the outside of the overtube are two instrument channels that allow various manual cable instruments to be inserted and controlled, such as graspers and monopolar cutters [24, 25].

i-Snake

The i-Snake, being researched at Imperial College London, is a short flexible robotic tool [26]. It has six segments linked by movable joints (see Figs. 41.7 and 41.8). Micromotors embedded within the segments enable it to move in 7 degrees of freedom by using miniature gears and pulleys. A video camera is mounted at the tip, and it also has an internal instrument channel for endoscopic tools. At present, the large size of the motor segments hinders the minimum radius of curvature that it can achieve, thus limiting it to peritoneal surgery.

MASTER

The Master and Slave TransEndoluminal Robot (MASTER), developed at Nanyang Technological University and commercialised under the company Endomaster, consists of a

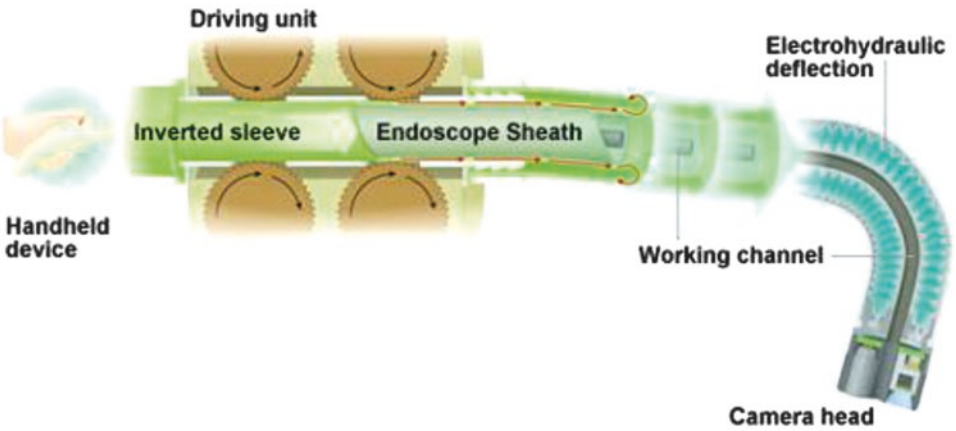

Fig. 41.4 Invendoscope operating principle (Reproduced with permission. Source: [http://www.invendo-medical.com/])

Fig. 41.5 Neoguide endoscope

Fig. 41.6 Graspers and video camera on Medrobotic's Flex

custom-developed endoscope that has an integrated videoscope and two instrument channels [27]. The instrument channels support a variety of instruments with cable articulation, such as electrocautery tools and 7 degree of freedom graspers (see Fig. 41.9). Clinical demonstrations have been performed, such as NOTES liver resection and endoscopic submucosal dissection (ESD) [28]. However, questions remain about sterilization procedures as it has not yet been granted FDA or CE mark approval. Detailed descriptions of ESD, full-thickness gastric wall resection, and hepatic wedge resection procedures will be given in the next section.

Viacath

The Viacath (Hansen Medical systems, USA), a flexible cable robot initially developed for endovascular and urological interventions, can also be used in the field of gastroenterology (see Fig. 41.10). It consists of a steerable overtube that houses a standard endoscope and two instrument channels. It shares its control interface and actuation mechanism with the Laprotek robotic-assisted laparoscopy system, also marketed by the same company. This facilitates tool changes. Initially it could only exert a weak tip force of 0.5 N, but the latest version reportedly can exert up to 3 N [23].

Endoscopic Submucosal Dissection with Master Robot

Endoscopic mucosal resection (EMR) is an endoscopic technique in which specimens of early-stage superficial lesions are resected. Most early-stage GI cancers are confined to the mucosal and submucosal layers and have not yet progressed to deep submucosal invasion or lymph node metastasis. Thus, early detection and removal lead to a high chance of patient survival; in contrast, the survival rate for advanced gastrointestinal cancers remains poor. It is also known that en bloc resection reduces the risk of residual cancer.

Endoscopic submucosal dissection (ESD) was developed as an improvement to EMR and provides the ability to resect larger lesions en bloc and with greater margins. It is increasingly recognised as a highly effective procedure for the treatment of early-stage gastric cancers. Compared with EMR, it reduces the rate of local recurrence from 15% to 1% and allows more accurate histological examination of the resected specimen [29]. However, en bloc dissection along the submucosal layer is difficult due to the technical limitations of current therapeutic endoscopes, which are equipped with poorly manoeuvrable cutting tools. The risk of procedural complications such as perforation and delayed bleeding means that ESD is performed by only the most skilled of endoscopy surgeons. A long procedure time adversely affects patient recovery after ESD procedures and may lead to ulceration and other negative effects [30]. A study conducted at Hiroshima University Hospital across 896 patients found that the incidence of intraoperative bleeding with ESD was 22.6% compared with 7.6% for EMR. Perforation was significantly higher at 53.8% with ESD compared with 2.9% for EMR [31]. Clearly, there is significant scope to reduce the incidence of trauma to the patient during ESD. The use of a robotic master-slave interface to carry out the procedure has been shown to reduce operating times and may enable novice surgeons to perform a satisfactory job.

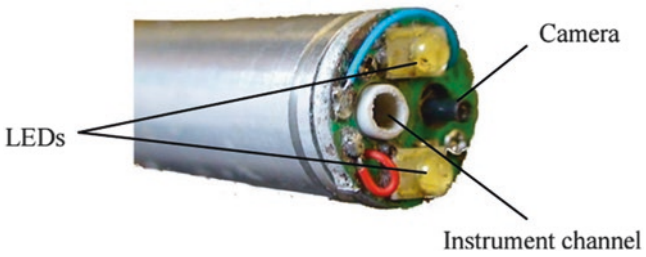

Fig. 41.7 Tip of the i-Snake

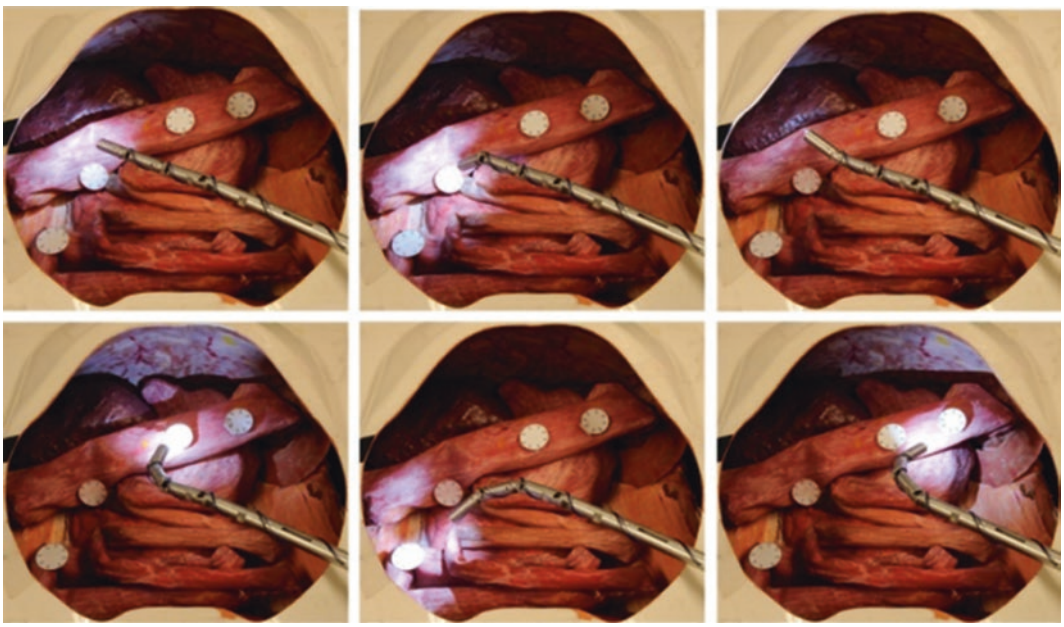

Fig. 41.8 Articulation of i-Snake

Fig. 41.9 Twin 7 DOF arms on Endomaster's MASTER robot (Reproduced with permission. Source: [www.endomastermedical.com])

Fig. 41.10 Viacath 6 DOF robotic arm

Indications

ESD can be considered for the removal of superficial premalignant and well to moderately differentiated malignant lesions in the GI tract. The Japanese Society of Gastrointestinal Endoscopists categorises superficial (type 0) lesions into polypoid and nonpolypoid categories, which are further subcategorised as shown in Fig. 41.11. The lateral extent of the lesion can be detected by methylene blue dye spraying and advanced imaging modalities such as narrowband imaging.

The depth of the invasion of the lesion can be determined by high-frequency endoscopic ultrasound (EUS), which produces a stratified image of nine separate layers (Fig. 41.12). The submucosa is divided into three layers, sm1, sm2 and sm3. The images produced can help in estimating the risk of lymph node metastases and thus the suitability of ESD in resecting the lesion.

Earlier techniques like EMR are limited to small (<20 mm) lesions or piecemeal resections of larger lesions. In contrast, ESD allows for the resection of large ulcerative lesions greater than 20 mm in diameter. High en bloc resection rates of 80–90% can be achieved with ESD compared with 50% for EMR [29]. This increases the accuracy of histopathological assessments, which in turn helps physicians to determine the best course of management for patients.

Contraindications

ESD is considered unsuitable when there is a suspicion of lymph node metastasis or deep tissue invasion by the lesion. In addition to EUS, submucosal invasion can also be detected by the injection of a saline solution into the submucosa underneath the lesion. This is known as the non-lifting test. If the lesion fails to elevate above the surrounding tissue, it is considered a positive test result. In this scenario, full-thickness gastrotomy resection or other more extensive methods are recommended.

The technical complexity of the operation leads to long procedure times (90 min compared with 30 min for EMR); hence it is contraindicated for patients with possible complications from premedication or who are susceptible to surgical stress. Factors increasing the difficulty of the operation include scarring on or around the lesion, which indicates a thin submucosal cushion and hence increased probability of perforation through the muscularis propria. The upper part of the stomach is also challenging due to its large vascular network, which can cause attempts at haemostasis to fail [34]. Because of these difficulties, ESD is generally not recommended for novice surgeons [35].

Instruments and Accessories

The first generation of the MASTER system consists of three major components: a master controller, a telesurgical workstation and a pair of slave arms equipped with a grasper and a monopolar electrocautery hook. The slave arms access the surgical site through the operating channels of a conventional forward-viewing therapeutic endoscope. The operation of MASTER robot is depicted in Fig. 41.13. The master controller has receptacles for the surgeon's right index finger and thumb and a handle for his/her left arm to grasp. These control the gripping action of the grasper and cutting motion of the monopolar diathermy 'L' hook, respectively. The current to the diathermy device is activated by a foot pedal. The

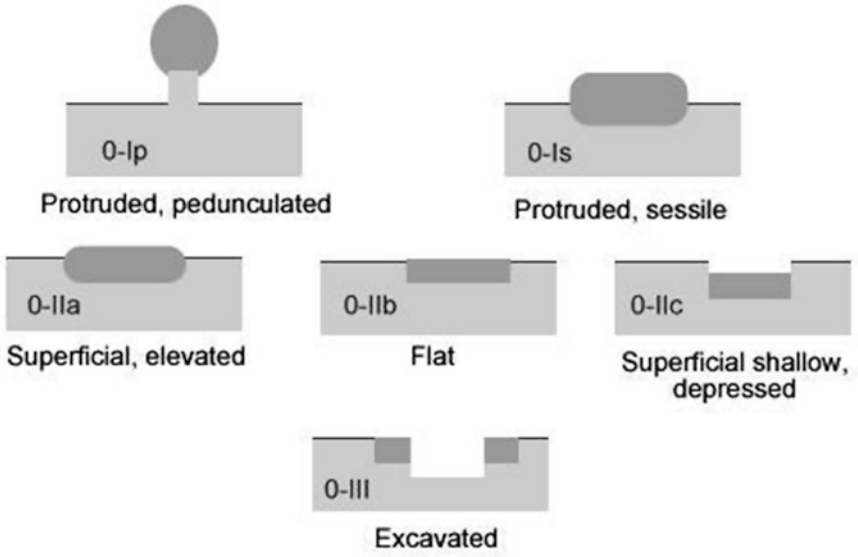

Fig. 41.11 Paris classification of superficial gastrointestinal neoplasms [32]

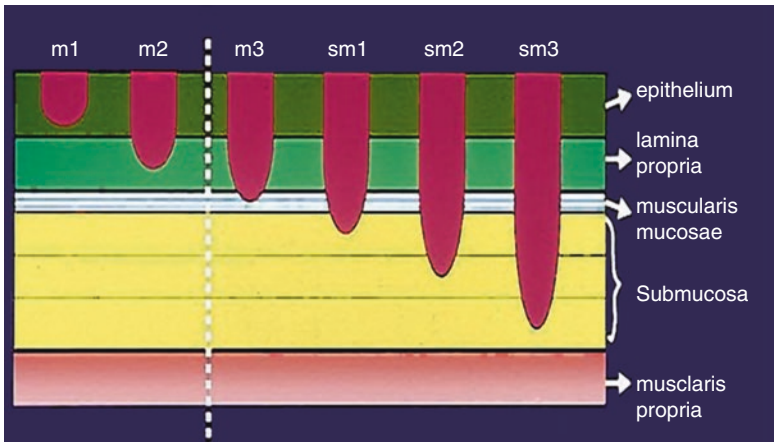

Fig. 41.12 Depth of lesion penetration as determined by high-frequency endoscopic ultrasound [33]

surgeon's hand motions are recorded by the robot arms using robotic 'proprioception'. These are converted by the master console into control signals, which are sent by data cable uplink to the slave manipulators. The slave motors then tension/slacken the tendons by appropriate amounts to mimic the user's hand motions on the slave robot. Each motor-tendon pair operates 1 degree of freedom of the slave arms. The surgeon is assisted by an endoscopist, who controls the macro-level positioning and orientation of the endoscope. Visual feedback to the surgical team is provided by the camera on the endoscope.

More recent iterations of the MASTER system feature interchangeable instruments such as injection needles, grasping forceps and various cautery devices. A version of electrocautery device that was developed for EMR is the insulated tip knife, which has a small ceramic ball attached to the tip of a cutting needle (Fig. 41.14). The ceramic ball restricts cutting to the lateral plane, preventing depthwise perforation of the muscularis propria.

Pre-procedure Preparation

The endoscope and the end effectors are sterilised by immersion in glutaraldehyde for 30 min. To clear the gastric cavity, patients have to fast for a minimum of 6 h before the procedure (fluids are allowed). They are sedated under general anaesthesia and ventilated via naso or orotracheal intubation. They are laid sideways in the left lateral position, which makes blood in the stomach gravitate towards the fundus and greater curvature.

Master-Assisted ESD Procedure

The ESD procedure consists of two main parts: marking of the lesion and submucosal dissection. The endoscopist first introduces a standard therapeutic videogastroscope into the patient and steers it to the surgical site (See Fig. 41.15). The lesion is circumferentially marked with electrocautery.

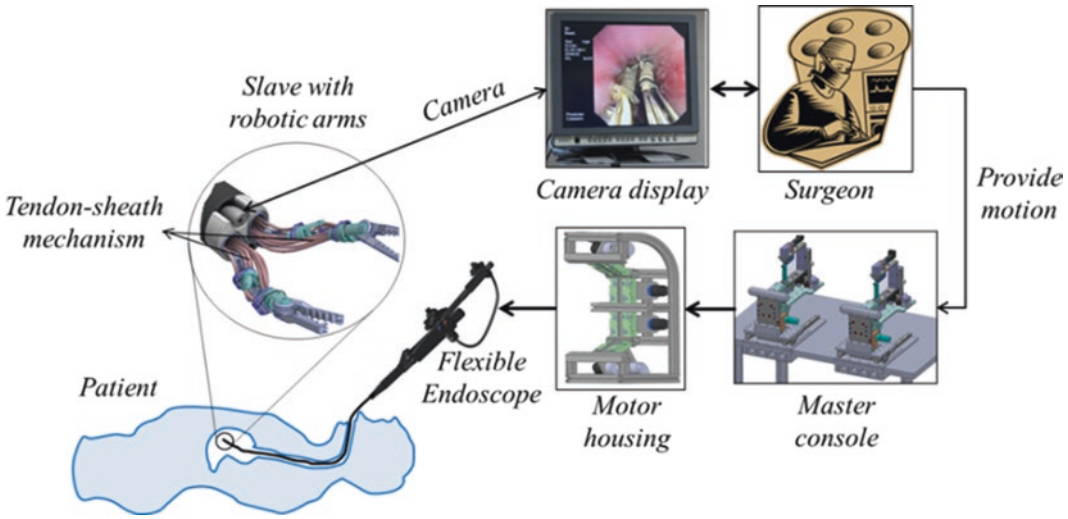

Fig. 41.13 Olympus insulated tip knives [36]

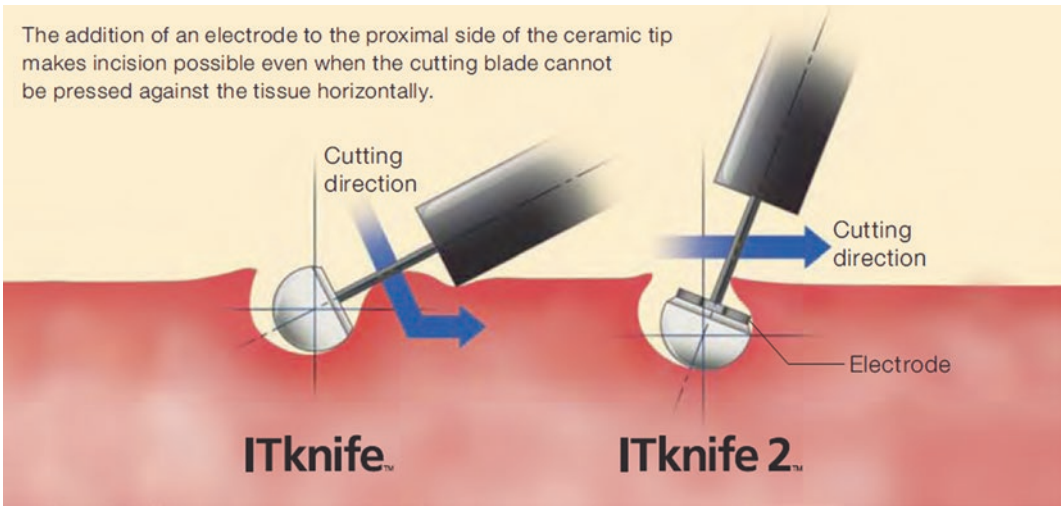

Fig. 41.14 Flow of operation for the MASTER robot

Then, fluid (mixture of 100 mL normal saline, 5 mL of indigo carmine/methylene blue and 1 mL of 1 in 10,000 epinephrine and sodium hyaluronate) is injected into the submucosa to elevate the lesion. The actual amount used depends on the size of the lesion and swelling response to the fluid. A lack of elevation response may indicate that the lesion has deeply invaded the submucosa or metastasised into the lymph nodes, in which case ESD would not be able to excise the entire lesion but could still offer useful histopathology information. Next, a small incision is made at the distal end of the lesion using a needle knife or dual knife. The remaining circumference of the lesion is then scribed with an insulated tip knife.

The conventional endoscope is removed, and the MASTER-equipped endoscope is inserted to conduct the robotic submucosal dissection. For the first-generation MASTER, the grasper arms are unable to fully retreat into the endoscope so an overtube must be used during its introduction to prevent damage to the tracheal lining. The grasping arm is used to grasp and retract the tumour-side open edge of the mucosa in order to expose the submucosa. The cautery arm is then able to perform dissection of the submucosa.

Post-ESD Management

After the procedure, the patient's vitals such as blood pressure, pulse and arterial oxygen content are monitored hourly. They are prescribed with a high dose of proton pump inhibitor to limit the production of gastric acid, thus reducing the occurrence of strictures. Follow-up endoscopy is performed 3 months later to confirm that the ESD-induced ulcer has healed and that the tumour has not recurred.

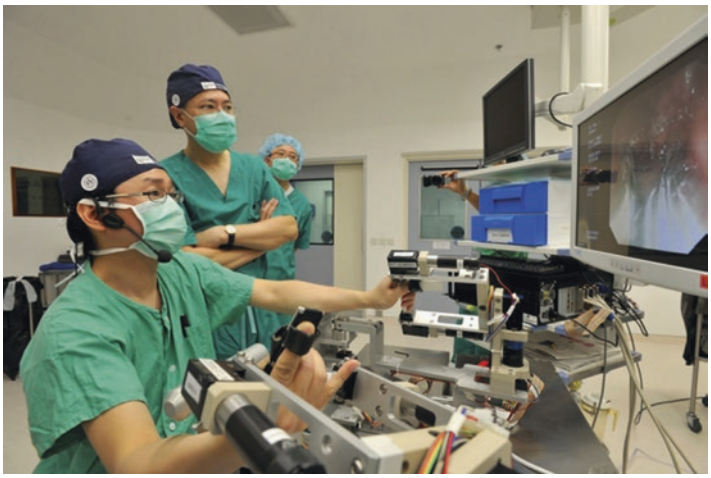

Fig. 41.15 Clinical setup for the performance of robotic ESD, with one endoscopist holding the endoscope while the surgeon performs submucosal dissection using the robotic arms

Table 41.2 Procedure timing in minutes for MASTER ESD

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Centre	India	India	India	Hong Kong	Hong Kong
Lesion marking	3	4	4	2	1
Submucosal injection	3	2	2	3	3
Circumferential mucosal incision	4	18	15	5	7
Insertion of overtube	4	4	4	5	5
Exchange of the endoscope	3	3	3	3	3
Robotic submucosal dissection	19	5	3	50	16
Total procedure time	26	36	31	68	35

Results of Clinical Trials

A multicentre prospective endoscopic submucosal dissection (ESD) study has been performed [27]. Five patients with a diagnosis of early-stage gastric neoplasia, limited to the mucosa, were recruited from two centres. The results are given in Table 41.2.

All patients underwent successful MASTER-assisted ESD (See Fig. 41.16). The mean submucosal dissection time was 18.6 min (median, 16 min; range, 3–50 min). No perioperative complications were encountered. All patients were discharged from the hospital within 3 days after procedures. Two patients were found to have intramucosal adenocarcinoma, one had high-grade dysplasia, one had low-grade dysplasia, and one had a hyperplastic polyp. The resection margins were clear of tumours in all five patients. No complications were observed at the 30-day follow-up examination (Fig. 41.17). Follow-up endoscopic examinations revealed that none of the patients had residual or recurrent tumours.

Full-Thickness Gastric Resection with Master Robot

Gastrointestinal stromal tumours (GIST) originate from the interstitial cells of Cajal in the connective tissue, or stroma, of the stomach, rather than the mucosal lining. Because they occur on the muscularis propria, mucosal and submucosal dissections are ineffective forms of treatment. Laparoscopic gastric wedge resection has become the gold standard for removal of GIST, being a short procedure with reduced trauma that allows for next-day discharge of the patient. In this surgical procedure, access to the resection site is obtained through the abdomen. The desired use of robotic endoscopy to carry out the resection encounters several challenges. Firstly, insufflation of the GI tract is lost when the resection is carried out. Secondly, the submucosal techniques from ESD provide insufficient tissue retraction and exposure. Lastly, the luminal defect created by the dissection cannot be closed by endoclipping, and the first generation of the MASTER robot provides only one grasper which is insufficient for suturing. To overcome these barriers, a clinical approach has been developed that uses the MASTER as a platform for retraction and dissection and the Apollo Overstitch as a device for tissue approximation [37].

Indications

GIST is a rare form of cancer and comprises only 1% of GI tumours. However, almost one third of GIST masses are malignant or at high risk of malignance. Adjuvant therapies are ineffective, leading to high mortality rates. Masses can be

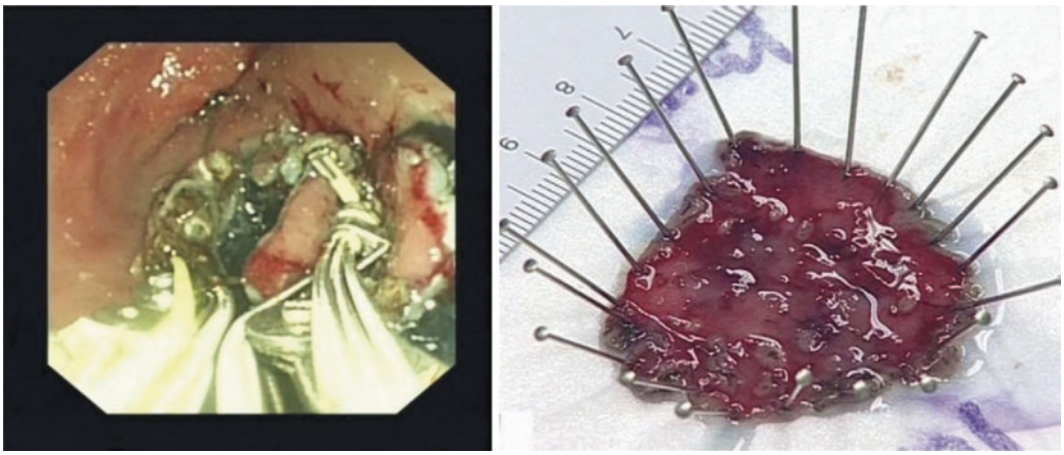

Fig. 41.16 ESD result: (*Left*) The procedure of ESD by MASTER with adequate retraction to demonstrate the submucosal plane for dissection; (*Right*) Specimen after MASTER ESD

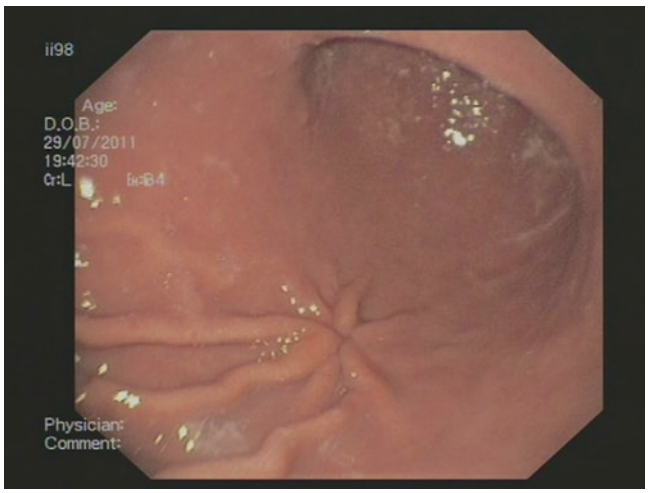

Fig. 41.17 Thirty-day postoperative endoscopic picture

classed as having metastatic potential based on their size and on the histological analysis of tissue samples obtained by diagnostic endoscopy. In one study, more than 5 mitoses per 50 high-powered fields and having a maximum diameter greater than 10 cm indicated an 86% chance of eventual metastasis [38]. In contrast, being below the threshold for both indicators led to only a 2–3% chance of metastasis, and so in these cases the tumour may be regularly monitored instead. Five centimetres in diameter has been suggested as the predictive threshold for malignancy and hence surgical treatment.

Procedure

The procedure consists of four main parts. First, using a single-channel endoscope, the anterior wall of the stomach is slung to the abdominal wall and affixed using a Loop Fixture II device. Second, the gastric lesion is circumferentially marked using a needle knife. A mixture of saline and indigo carmine/methylene blue is injected to elevate the lesion. A mucosal incision is made at a point on the circumference with an IT knife and a needle knife. Third, the endoscope is withdrawn and the MASTER is introduced via an overtube. The mucosal incision is completed around the lesion to expose the muscularis propria, which is then grasped and incised to the serosa. The full-thickness resection is completed using retraction provided by the grasper and dissection with the electrocautery hook. At this point, a loss of insufflation occurs. However, the fixtures from the Loop Fixture II device provide enough traction to keep the luminal space from collapsing. Finally, the luminal defect is closed using the Overstitch endoscopic suturing device (Fig. 41.18).

Results of Preclinical Trials

Preclinical trials were conducted on two nonsurvival porcine specimens with weights of 30 and 35 kg [37]. The average dimensions of the specimens removed were 50 mm by 20 mm. Successful closure of the defects was achieved with satisfactory gastric distension, evidenced by the absence of gas leakage afterwards (See Fig. 41.19). No injury to adjacent organs was observed. All results are given in Table 41.3.

Natural Orifice Transluminal Endoscopic Surgery with Master Robot

Natural orifice transluminal endoscopic surgery (NOTES) refers to a class of procedures in which an endoscope is passed through a natural orifice and then through an incision

Fig. 41.18 Apollo Overstitch system mounted on a dual-channel endoscope

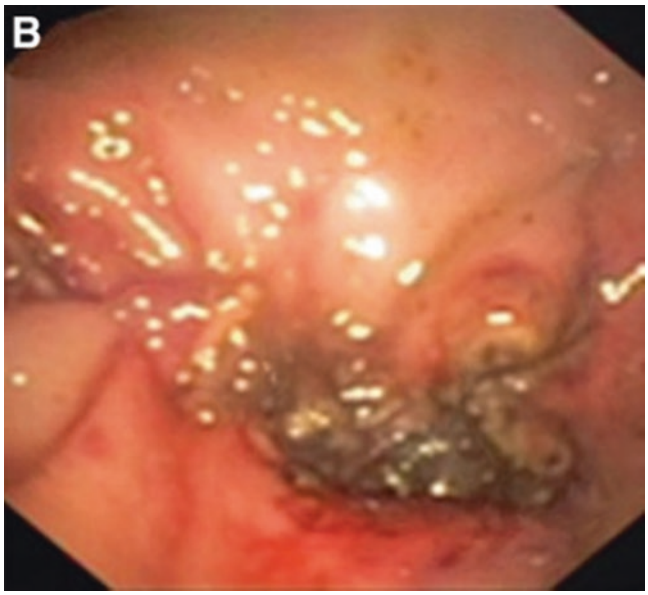

Fig. 41.19 Closure of gastric luminal defect after Overstitch suturing

in the stomach, colon, vagina or bladder. This allows surgery to be performed in the abdomen without external scars. It has been touted as the next evolution in minimally invasive surgery after laparoscopic surgery. However, a new class of surgical instrument has to be developed before NOTES becomes feasible for widespread use, as the current instrumentation adapted from laparoscopic surgery possesses inadequate dexterity and is non-ergonomic.

Hepatic wedge resection is one such procedure in which access can be readily obtained through the gastric wall. Essentially, it is the dissection of the liver to remove tumours through a hole created in the stomach wall. The liver is classified into eight functional segments according to the blood supply from the hepatic artery and portal vein. Large metastases increase the likelihood that anatomic amounts, i.e. entire segments will have to be removed. Thus, bulk tissue manipulation and effective bleeding control are required during the surgery. Means of closing the gastrotomy and providing insufflation for the peritoneum and stomach are also key requirements. Preclinical investigations have been conducted to determine the suitability of the MASTER platform in conducting hepatic wedge resection [28].

Procedure

Subjects are deprived of food for a period of 18 h prior and sedated immediately before the surgery. Intubation is performed with an endotracheal tube and general anaesthesia administered. Throughout the surgery, oxygen is supplied through a ventilator. Heart rate and oxygen saturation are monitored every 20 min.

A sterile overtube is advanced into the oesophagus with a standard gastroscope. The stomach is irrigated with 10% povidone-iodine antibacterial solution and normal saline to clear the cavity of effluent. The gastroscope is then withdrawn and a dual-channel endoscope bearing the MASTER slave arms is inserted. The monopolar cautery hook makes a 10 mm linear incision on the anterior wall of the stomach (See Fig. 41.20), about 15–20 cm from the gastroesophageal junction. The endoscope then passes through the incision into the peritoneum. The endoscope is flexed to achieve optimal visual registration of the liver (See Fig. 41.21). Once the segment to be dissected has been identified, the robotic arms are advanced towards it. The grasper elevates and secures the segment, allowing the cautery hook to dissect it in the appropriate plane. Haemostasis of the cut edges is achieved with the cautery hook. The excised liver segment and the endoscope are then retracted through the gastrotomy and out of the mouth. The gastrotomy can then be closed through suturing or endoclipping.

Results of Preclinical Trials

Two porcine subjects successfully underwent natural orifice translumenal hepatic wedge resection using the MASTER.

Tissue segments of 14 by 8 by 5 mm and 21 by 10 by 7.6 mm were excised and retrieved en bloc. After the operation, the animals were euthanised without closure of the gastrotomy. The procedure time for the MASTER robot is given in Table 41.4.

Table 41.3 Procedure time for MASTER full thickness resection

	Case 1	Case 2
Total procedural time	56 min	70 min
Operative time for full-thickness resection using MASTER	44 min	52 min
Operative time for closure of gastrotomy using Overstitch	12 min	18 min
Full gastric distension after the procedure	Yes	Yes
No. of overstitches applied to close the gastric luminal defect	2	1
Complications during the procedure	Nil	Diathermy injury to anterior abdominal wall

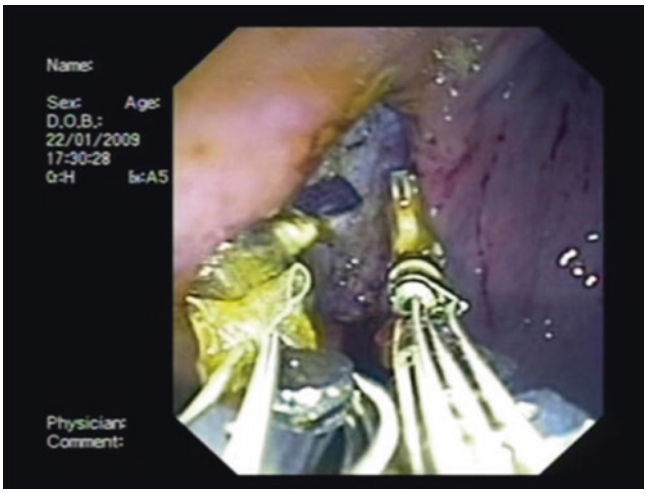

Fig. 41.20 Performance of gastrotomy on the anterior wall of the stomach

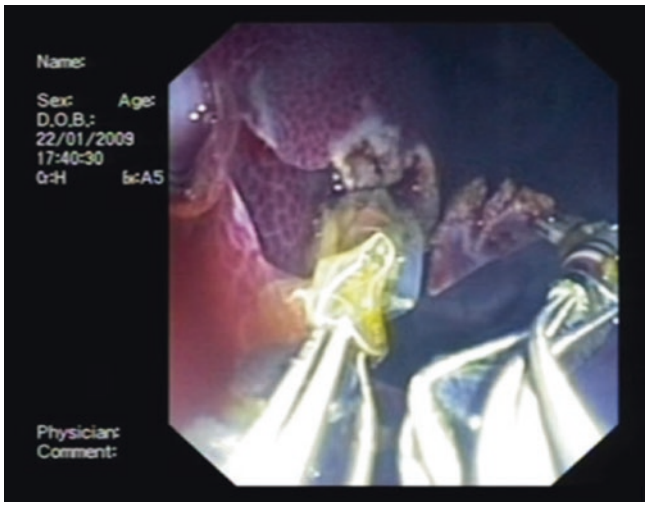

Fig. 41.21 Dissection of the liver segment

Table 41.4 Procedure time for MASTER NOTES surgery

	Case 1	Case 2
Total procedural time	10.2 min	8.5 min
Operative time for gastrotomy and approach to liver segment	2.0 min	2.5 min
Operative time for electrosurgical excision	8.2 min	6.0 min
Sufficient grasping tension applied to tissue	Yes	Yes
Fewer than three attempts at cutting through the liver with monopolar hook at 80 W	Yes	Yes
Complications during the procedure	Nil	Nil

Assessment of the Master Robotic Endoscopy System

ESD is a difficult procedure because of the lack of a dexterous and ergonomic platform for performing the dissection. Unlike laparoscopy, in which bimanual operation and triangulation of the instruments are possible through different access ports, therapeutic endoscopes make use of a single arm mounted coaxially with the endoscope to manipulate tissue. The high dexterity twin instrumentation of the MASTER robot helps to overcome these limitations. Triangulation is achieved through the bifurcation of the arms at their proximal base joints and re-convergence at the distal joints. Motorised actuation overcomes the tendon friction accumulated along the tortuous endoscope path. An ergonomic human machine interface enables intuitive mapping of user-to-slave motion and greatly reduces the learning curve.

A study was conducted to determine the effect that the MASTER robot had on the learning curve for ESD [39]. Three expert ESD clinicians, three non-expert ESD clinicians and three novice nonclinicians were recruited to perform ESD on an ex vivo porcine model using the MASTER. The expert clinicians had each performed more than 100 ESD procedures. The non-expert clinicians had performed less than ten each, while the novices were engineers who had no prior experience performing the procedure. The novices were able to understand and carry out the ESD procedure within 20 min, showing that the learning curve could be significantly shortened and procedure times reduced. Compared with years of training needed for endoscopists to perform ESD, an intensive 1–2 week training duration is sufficient to perform it using the MASTER.

The second generation of the MASTER robot features fully interchangeable instruments that access the surgical site through a conventional endoscope. This obviates the need to swap out the MASTER endoscope for injection of the elevation fluid and allows the full complement of surgical endoscopic tools to be used, such as biopsy forceps, injection needles, snares and coagulation devices. It is expected to

improve the ease of operation further and enable a wide variety of procedures such as full-thickness resection and NOTES to be performed reliably.

Future of Robot-Assisted Endoscopic Surgery

Robotic therapeutic endoscopes capable of a variety of procedures from GI surface dissection to transendoluminal peritoneal surgery will become commercially available in the near future. This pace of technological development is driven by clinical needs; in line with changing global demographics, the incidence of GI cancer (an age-related disease) is expected to increase by 6% per annum. Aside from GI cancer, other diseases and complications treatable by endoscopy include gastroesophageal reflux disease (GERD) and ulcers in the upper GI, diverticulitis, haemorrhoids, irritable bowel syndrome (IBS) and Crohn's disease in the lower GI. Government-led screening programs will reveal growths at an early stage before they become symptomatic, and patients can opt for their pre-emptive removal by ESD before they advance beyond the submucosal layer. Technical improvements to the tools and interfaces of robot-assisted endoscopic surgical platforms will enhance the capabilities of surgeons, thus allowing them to undertake more ambitious surgeries and push the envelope, especially in the field of NOTES.

Enhancements to Tools and Interfaces

Better robotic tools and interfaces are the key to improving the feasibility of NOTES procedures and other gastroenteric treatments. However, some technical challenges need to be addressed before surgeons can be convinced of its efficacy. These include (i) ensuring adequate dexterity, strength, and size of the slave arms, (ii) precision of the slave arms, (iii) function-specific end effectors, and (iv) the addition of haptic feedback to the system.

Dexterity, Strength and Size

From a design perspective, the strength, dexterity and miniaturisation of a robot arm are competing parameters. A balance has to be struck when developing a robotic arm for a desired task.

Dexterity of the slave arms is required to enable triangulation of instruments and tissue manipulation tasks such as suturing, grasping, retraction/exposure and traction/countertraction. The human arm has 7 degrees of freedom of motion (shoulder pitch, yaw, roll, elbow pitch, roll and wrist pitch, yaw). In an endoscopic surgery, the elbow and wrist joints are employed the most by the surgeon as large-scale relocation is achieved by movement of the entire endoscope. The grasping motion of the fingers also adds another degree of freedom. Hence, at least four DOFs are required for the slave arms, five DOFs if grasping of tissue is required, in order to adequately replicate the configuration of the surgeon's hand and wrist.

Miniaturisation of tools is synonymous with minimally invasive surgery. Current therapeutic dual-channel endoscopes are about 12.8 mm in diameter, limiting the possible size of instruments. This in turn limits the raw strength available for manipulation of tissue and forward cutting traction (push or pull) on electrocautery devices. Furthermore, due to friction losses throughout the flexible sheath, the actual force required by the cables at the proximal end could be as high as 100 N (emphasising the need for robotics to assist in applying these loads). Possible alternatives like distal tip-mounted actuators are not powerful enough for effective tissue manipulation, but could prove useful for locking or trigger mechanisms.

Precision

The precision of minimally invasive tools, defined as the robotic arms following the user-desired path as closely as possible, is paramount to ensuring patient safety and operation success. In addition, the accurate control of flexible endoscope also minimises the error. Precision can help prevent accidental perforations in ESD and enable the efficient application of haemostasis cautery. Precision can be improved by stiffening the endoscope near the surgical site, i.e. it must be flexible enough to navigate through the GI tract to the site yet stiff enough to prevent flopping of the arms when forces are being exerted on tissue. The path following overtubes used in Medrobotic's Flex is one such innovation. Position-sensing feedback and stick-slip friction modelling are also needed to compensate for the jerky motion of cable-controlled arms. This can be achieved using the miniaturisation of sensors, which is currently a field of burgeoning scientific interest. Examples include fibre Bragg grating sensors that consist of a fibre-optic cable running along the length of the endoscope or stretchable MEMS sensors; these can be used to detect its flexed shape. Better spatial cues are also necessary for surgeons, as the narrow angle of image feed from an endoscope can cause surgeons to be disorientated. Studies have shown that in laparoscopic surgeries, this is a significant factor that causes damage to vital structures in an operation [40–44].

End Effectors, Imaging Modalities, Auxiliary Instruments

Despite the encouraging trials performed with the MASTER, more effective instrumentation is needed to make it robust enough for clinical use. More powerful electrosurgery instruments would provide additional headroom to manage any

unforeseen major bleeding. More controlled ways of supporting the stomach walls after the loss of insufflation due to gastrotomy could also be developed.

The use of interchangeable instruments, a concept present in normal endoscopes, would allow function-specific end effectors to be inserted for the appropriate task. For example, high payload arms could be used for the manipulation of bulk tissue, while closure of the gastrotomy could be performed by high dexterity arms or specialised suturing tools (similar to the Overstitch endoscopic attachment). Another innovation will be the development of in vivo imaging modalities that allow one-stop diagnosis and treatment of precancerous tissue. Techniques like Raman spectroscopy and multimodal imaging will allow near instantaneous histopathological assessments at the biomolecular level [45].

Haptic Feedback

Haptic feedback refers to the somatosensory and proprioceptive stimulation of the user by the machine as a means of conveying information [46–49]. The controllers used in advanced master-slave surgical robots have built-in electronic sensors to detect the relative positions of the human wrist and fingers. They then employ force actuators to adjust the ease at which a user can move his interfacing appendages around in space; this makes it possible to feedback to the user a range of conditions being experienced by the slave robot. For example, a resistance-free sensation is felt by the user when the robot is moving through air, but this is dynamically altered into a mushy, damped feeling when contact is made with soft tissue.

The use of haptics improves the ergonomics of using the machine and, crucially, increases patient safety. The absence of haptic feedback on the Da Vinci machine has often been cited as a contributory factor towards surgeon error. With feedback to the surgeon, accidental damage to delicate tissues can be avoided. Software constraints can also be implemented to prevent the over exertion of force. However, challenges remain in integrating force sensors into the small distal tips of the robotic slave arms. The miniaturisation of force and pressure sensors should improve this aspect of surgical robots in the near to mid future.

Innovations in Surgical Procedures

In the long term, minimally invasive surgery will continue to gain popularity due to the reduction in surgical trauma, which offers better recovery and cosmetic results. Unpredictable factors like antibiotic resistance may also hasten the transition to minimally invasive approaches, as they offer a lower risk of infection than open surgery [50, 51]. Natural orifice transluminal endoscopic surgery is a promising and novel field of surgery that stands to benefit from this evolution. The GI tract runs along the length of the body, offering access to most areas of the peritoneum. Many surgeries could potentially be converted from laparoscopic or open methods to NOTES. For gastroenterologists, collaborations with other specialties will become necessary in order to develop innovative natural orifice surgical approaches which take advantage of the capabilities of robotic platforms.

Currently, robot-assisted endoscopic instruments do not possess the stability, strength and precision to perform advanced manoeuvers on a risk-free and reliable basis. These technical issues are the focus of many research groups and surgical technology companies, but in the meantime, one can expect to see hybrid procedures that leverage on the individual strengths of endoscopic and laparoscopic approaches. For example, opening and closure of a gastrotomy can be done using laparoscopic instruments with a peritoneal approach, while a cholecystectomy can be endoscopically performed through the gastrotomy and tissue removed through the mouth [52]. Capsule endoscopy is also a good approach for pre-diagnostic before surgery [53–57].

Eventually, advances in technology will place intuitive, multirole therapeutic endoscopes in the hands of surgeons. These would allow complex surgical procedures like ESD and NOTES to be performed by surgeons with less experience or skill, thus benefitting a wider population of patients. The technology will also enable more difficult and innovative procedures to be attempted by accomplished surgeons who wish to differentiate themselves and push the boundaries of what is medically possible.

Conclusions

- Robotics enables a variety of unconventional actuation strategies to be used for endoscopes, resulting in reduced trauma to the GI tract.
- For transmission of force to distally mounted endoscopic instruments, robotically actuated tendon sheath mechanisms are the current state of the art.
- Robotics in surgical endoscopy enables an ergonomic mapping of the surgeon's movements to remotely controlled slave arms, facilitating tissue manipulation.
- The learning curve for difficult procedures such as endoscopic submucosal dissection and full-thickness resection can be significantly reduced.
- Improved surgical outcomes are also observed from clinical and preclinical trials.
- The technology behind master-slave surgical robotics will continue to mature, with the addition of position and force sensors enabling better control and tactile feedback.
- More robotic-assisted GI luminal and NOTES surgeries are expected to be conducted in the future, and gastroenterologists will have a key collaborative role to play.

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References

1. Microsurgery device reduces surgeon tremor. Available: http://www.nibib.nih.gov/news-events/newsroom/microsurgery-device-reduces-surgeon-tremor.
2. Antoniou GA, Riga CV, Mayer EK, Cheshire NJW, Bicknell CD. Clinical applications of robotic technology in vascular and endovascular surgery. J Vasc Surg. 2011;53:493–9.
3. Patel N, Darzi A, Teare J. The endoscopy evolution: 'the superscope era'. Frontline Gastroenterol. 2015;6:101–7.
4. Yeung BPM, Gourlay T. A technical review of flexible endoscopic multitasking platforms. Int J Surg. 2012;10:345–54.
5. Bardou B, Nageotte F, Zanne P, de Mathelin M. Design of a telemanipulated system for transluminal surgery. In: Engineering in medicine and biology society, 2009. EMBC 2009. Annual international conference of the IEEE; 2009, p. 5577–82.
6. Bardou B, Nageotte F, Zanne P, Mathelin M. Design of a Robotized Flexible Endoscope for natural orifice transluminal endoscopic surgery. In: Garbey M, Bass BL, Collet C, Mathelin M, Tran-Son-Tay R, editors. Computational surgery and dual training. Boston: Springer US; 2010. p. 155–70.
7. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. An investigation of friction-based tendon sheath model appropriate for control purposes. Mech Syst Signal Process. 2013;42:97–114.
8. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Nonlinear modeling and parameter identification of dynamic friction model in tendon sheath for flexible endoscopic systems. In: ICINCO 2013 – proceedings of the 10th international conference on informatics in control, automation and robotics, vol. 2, Reykjavik, Iceland; 2013, p. 5–10.
9. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Dynamic friction-based force feedback for tendon- sheath mechanism in NOTES system. Int J Comput Electr Eng. 2014;6:252–8.
10. Hassani V, Tjahjowidodo T, Do TN. A survey on hysteresis modeling, identification and control. Mech Syst Signal Process. 2014;49:209–33.
11. Nguyen TL, Do TN, Lau MWS, Phee SJ. Modelling, design, and control of a robotic running foot for footwear testing with flexible actuator. In: Presented at the 1st international conference in sports science & technology (ICSST), Singapore; 2014.
12. Do TN, Tjahjowidodo T, Lau MWS, Yamamoto T, Phee SJ. Hysteresis modeling and position control of tendon-sheath mechanism in flexible endoscopic systems. Mechatronics. 2014;24:12–22.
13. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Adaptive control of position compensation for cable-conduit mechanisms used in flexible surgical robots. In: ICINCO 2014 – proceedings of the 11th international conference on informatics in control, automation and robotics, Vienna, Austria; 2014. p. 110–7.
14. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Nonlinear friction modelling and compensation control of hysteresis phenomena for a pair of tendon-sheath actuated surgical robots. Mech Syst Signal Process. 2015;60:770–84.
15. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Adaptive control for enhancing tracking performances of flexible tendon–sheath mechanism in natural orifice transluminal endoscopic surgery (NOTES). Mechatronics. 2015;28:67–78.
16. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. A new approach of friction model for tendon-sheath actuated surgical systems: non-linear modelling and parameter identification. Mech Mach Theory. 2015;85:14–24.
17. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Adaptive tracking approach of flexible cable conduit-actuated NOTES systems for early gastric cancer treatments. In: Filipe J, Gusikhin O, Madani K, Sasiadek J, editors. Informatics in control, automation and robotics, vol. 370: Springer International Publishing Switzerland; 2016. p. 79–97. https://link.springer.com/chapter/10.1007/978-3-319-26453-0_5.
18. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Enhanced performances for cable-driven flexible robotic systems with asymmetric backlash profile. In: Technologies for practical robot applications (TePRA), 2015 IEEE international conference on; 2015, p. 1–6.
19. Horise Y, Nishikawa A, Sekimoto M, Kitanaka Y, Miyoshi N, Takiguchi S, et al. Development and evaluation of a master-slave robot system for single-incision laparoscopic surgery. Int J Comput Assist Radiol Surg. 2012;7:289–96.
20. Cosentino F, Tumino E, Passoni GR, Morandi E, Capria A. Functional evaluation of the Endotics system, a new disposable self-propelled robotic colonoscope: in vitro tests and clinical trial. Int J Artif Organs. 2009;32:517–27.
21. Balasundaram I, Al-Hadad I, Parmar S. Recent advances in reconstructive oral and maxillofacial surgery. Br J Oral Maxillofac Surg. 2012;50(8):695–705.
22. Tumino E, Cosentino F, Passoni GR, Rigante A, Barbera R, Tauro A, Cosentino PE. Robotic colonoscopy. Osaka: InTech; 2011. https://www.intechopen.com/books/colonoscopy/robotic-colonoscopy.
23. Patel N, Seneci C, Yang GZ, Darzi A, Teare J. Flexible platforms for natural orifice transluminal and endoluminal surgery. Endosc Int Open. 2014;2:E117–23.
24. Johnson PJ, Serrano CMR, Castro M, Kuenzler R, Choset H, Tully S, et al. Demonstration of Transoral surgery in cadaveric specimens with the Medrobotics flex system. Laryngoscope. 2013;123:1168–72.
25. Medrobotics. Medrobotics company website. Available: www.medrobotics.com.
26. Shang J, Noonan DP, Payne C, Clark J, Sodergren MH, Darzi A, et al. An articulated universal joint based flexible access robot for minimally invasive surgery. In: 2011 IEEE international conference on robotics and automation (ICRA); 2011, p. 1147–52.
27. Phee SJ, Reddy N, Chiu PWY, Rebala P, Rao GV, Wang Z, et al. Robot-assisted endoscopic submucosal dissection is effective in treating patients with early-stage gastric neoplasia. Clin Gastroenterol Hepatol. 2012;10:1117–21.
28. Phee SJ, Ho KY, Lomanto D, Low SC, Huynh VA, Kencana AP, et al. Natural orifice transgastric endoscopic wedge hepatic resection in an experimental model using an intuitively controlled master and slave transluminal endoscopic robot (MASTER). Surg Endosc Other Intervent Tech. 2010;24:2293–8.
29. Tajika M, Niwa Y, Bhatia V, Kondo S, Tanaka T, Mizuno N, et al. Comparison of endoscopic submucosal dissection and endoscopic mucosal resection for large colorectal tumors. Eur J Gastroenterol Hepatol. 2011;23:1042–9.
30. Toyokawa T, Inaba T, Omote S, Okamoto A, Miyasaka R, Watanabe K, et al. Risk factors for perforation and delayed bleeding associated with endoscopic submucosal dissection for early gastric neoplasms: analysis of 1123 lesions. J Gastroenterol Hepatol. 2012;27:907–12.
31. Oka S, Tanaka S, Kaneko I, Mouri R, Hirata M, Kawamura T, et al. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer. Gastrointest Endosc. 2006;64:877–83.
32. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc. 2003;58:S3–43.
33. Greenwald BD, Roberts KE. Endoscopic mucosal resection [Online]. Available: http://emedicine.medscape.com/article/1891659-overview#a1.

34. Kume K. Endoscopic mucosal resection and endoscopic submucosal dissection for early gastric cancer: current and original devices. World J Gastrointest Endosc. 2009;1:21–31.
35. Yoshida N, Yagi N, Inada Y, Kugai M, Yanagisawa A, Naito Y. Prevention and management of complications of and training for colorectal endoscopic submucosal dissection. Gastroenterol Res Pract. 2013;2013:287173.
36. Olympus. Endoscopic submucosal dissection product catalog. Tokyo: Olympus Corporation; 2017.
37. Chiu PW, Phee SJ, Wang Z, Sun Z, Poon CC, Yamamoto T, et al. Feasibility of full-thickness gastric resection using master and slave transluminal endoscopic robot and closure by overstitch: a preclinical study. Surg Endosc. 2014;28:319–24.
38. Judson I, Demetri G. Advances in the treatment of gastrointestinal stromal tumours. Ann Oncol. 2007;18(Suppl 10):x20–4.
39. Chiu PW, Phee SJ, Bhandari P, Sumiyama K, Ohya T, Wong J, et al. Enhancing proficiency in performing endoscopic submucosal dissection (ESD) by using a prototype robotic endoscope. Endosc Int Open. 2015;3:E439–42.
40. Yamashita Y, Kimura T, Matsumoto S. A safe laparoscopic cholecystectomy depends upon the establishment of a critical view of safety. Surg Today. 2010;40:507–13.
41. Way LW, Stewart L, Gantert W, Liu K, Lee CM, Whang K, et al. Causes and prevention of laparoscopic bile duct injuries: analysis of 252 cases from a human factors and cognitive psychology perspective. Ann Surg. 2003;237:460–9.
42. Do TN, Seah TET, Phee SJ. Design and control of a novel mechatronic tracheostomy tube-inserted suction catheter for automated tracheal suctioning. In: The 7th IEEE international conference on cybernetics and intelligent systems (CIS) and the 7th IEEE international conference on robotics, automation and mechatronics (RAM) (CIS-RAM), Angkor Wat, Cambodia; 2015, p. 228–233.
43. Do TN, Seah TET, Phee SJ. Design and control of a mechatronic tracheostomy tube for automated tracheal suctioning. IEEE Trans Biomed Eng. 2016;63:1229–38.
44. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Position control of asymmetric nonlinearities for a cable-conduit mechanism. IEEE Trans Autom Sci Eng. 2016;PP:99.
45. Wang JF, Lin K, Zheng W, Ho KY, Teh M, Yeoh KG, et al. Simultaneous fingerprint and high-wavenumber fiber-optic Raman spectroscopy improves in vivo diagnosis of esophageal squamous cell carcinoma at endoscopy. Sci Rep. 2015;5:12957.
46. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Dynamic friction model for tendon-sheath actuated surgical robots: modelling and stability analysis. The proceedings of 3rd IFToMM international symposium on robotics and mechatronics, Singapore; 2013, p. 302–11.
47. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Real-time enhancement of tracking performances for cable-conduit mechanisms-driven flexible robots. Robot Comput Integr Manuf. 2016;37:197–207.
48. Do TN, Tjahjowidodo T, Lau MWS, Phee SJ. Performance control of tendon-driven endoscopic surgical robots with friction and hysteresis. arXiv preprint arXiv:1702.02063, 2017.
49. Do TN, Phee SJ. Haptic feedback in natural orifice transluminal endoscopic surgery (NOTES). arXiv preprint arXiv:1606.07574, 2016.
50. Nau P, Ellison EC, Muscarella P Jr, Mikami D, Narula VK, Needleman B, et al. A review of 130 humans enrolled in transgastric NOTES protocols at a single institution. Surg Endosc. 2011;25:1004–11.
51. Schmidt A, Meier B, Caca K. Endoscopic full-thickness resection: current status. World J Gastroenterol. 2015;21:9273–85.
52. Voermans RP, Henegouwen MIV, Bemelman WA, Fockens P. Hybrid NOTES transgastric cholecystectomy with reliable gastric closure: an animal survival study. Surg Endosc Other Intervent Tech. 2011;25:728–36.
53. Do TN, Seah TET, Ho KY, Phee SJ. Correction: development and testing of a magnetically actuated capsule endoscopy for obesity treatment. PLoS One. 2016;11:e0151711.
54. Do TN, Seah TET, Yu HK, Phee SJ. Development and testing of a magnetically actuated capsule endoscopy for obesity treatment. PLoS One. 2016;11:e0148035.
55. Do TN, Ho KY, Phee SJ. A magnetic soft endoscopic capsule-inflated intragastric balloon for weight management. Sci Rep. 2016;6:39486.
56. Do TN, Phan PT, Ho KY, Phee SJ. A magnetic soft endoscopic capsule for non-surgical overweight and obese treatments. 2016 IEEE/RSJ international conference on intelligent robots and systems (IROS); 9–14 October 2016, p. 2388–93.
57. Le HM, Do TN, Phee SJ. A survey on actuators-driven surgical robots. Sens Actuators A Phys. 2016;247:323–54.

Device Development and Accessories

42

Vihar Surti

Introduction

Development of novel medical technologies is a core reason for the historical growth in endoscopic procedures. Between 1968 and 1990, the introduction of technologies for clinical procedures such as endoscopic retrograde pancreatography (ERCP), colonoscopic polypectomy, and endoscopic ultrasonagraphy led to the golden era of innovation in endoscopy [1]. Clinicians are instrumental in the development of new technologies and procedures. Adequate integration of clinicians into the device development process is an important factor to improve its outcomes [2, 3]. Therefore, it is beneficial for physicians, fellows, nurses, and technicians in the field of gastroenterology to gain an understanding of the device development process.

Medical Device Development Process

The development process for medical devices includes several milestones. The nomenclature and characterization of milestones can often vary for medical device developers; however, Fig. 42.1 provides a simplified overview [4–6]. Milestones are commonly grouped within development phases [4–7]. Figure 42.2 denotes the phases utilized for the purposes of this discussion.

The purpose of the development process is to solve a need and convert the conceptual solution into a marketable device. Progression through each phase of development therefore increasingly defines the conceptual solution and decreases its number of undefined design variables (Fig. 42.3a) [8]. The conceptual solution is defined the least during the discovery phase and fully defined into a product at the end of the commercialization phase. Phases with a higher number of undefined design variables correlate to greater flexibility and decreased predictability. This means a higher development cost for a design change but an improved accuracy of predicting the launch date progressively with each phase (Fig. 42.3b,c) [8]. Communication of launch dates throughout the development process is especially important since it is a determining factor for product success [9]. Since the highest number of undefined variables in the development process occurs during the discovery phase, design teams have a unique challenge in prevailing through it. The latter phases benefit from teams utilizing a systematic and structured approach, whereas the discovery phase is often unstructured [8]. Consequently small companies such as startups have greater success in the earlier stages, whereas, large companies are often superior at navigating optimization through commercialization [2].

Design Controls

Design controls are a systematic and structured approach for evolving the design. The Code of Federal Regulations (CFR), Title 21, Part 820, requires medical device manufacturers to utilize design controls in their development process [10]. Design controls begin after the creation of the conceptual solution at the end of the discovery phase. It extends from the optimization phase to commercialization. The utility of design controls increases the probability of the device meeting its intended use after launch [11]. The sections within design controls are:

Design and Development Planning
Design Input
Design Output
Design Review
Design Verification
Design Validation
Design Transfer
Design Changes
Design History File

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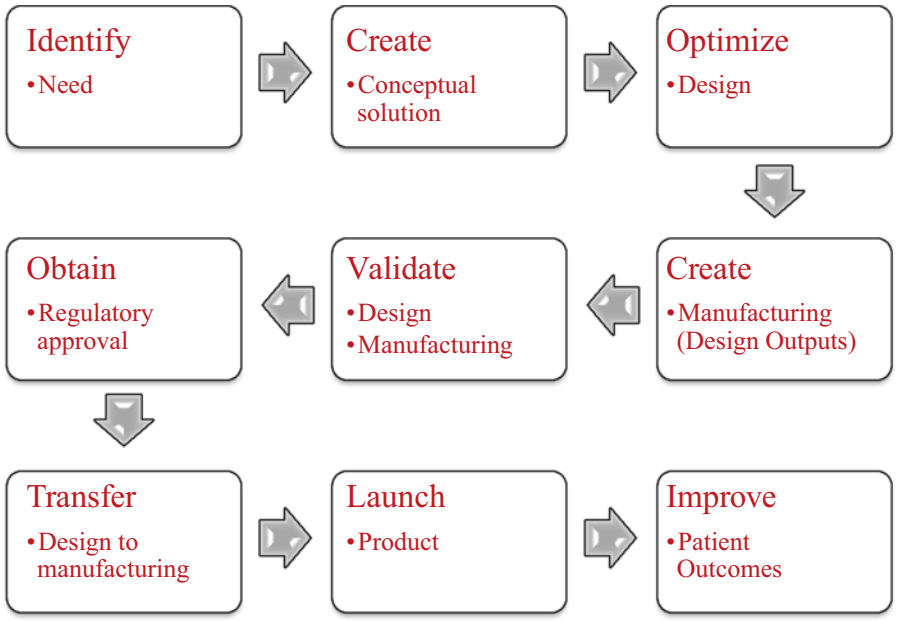

Fig. 42.1 Milestones of medical device development

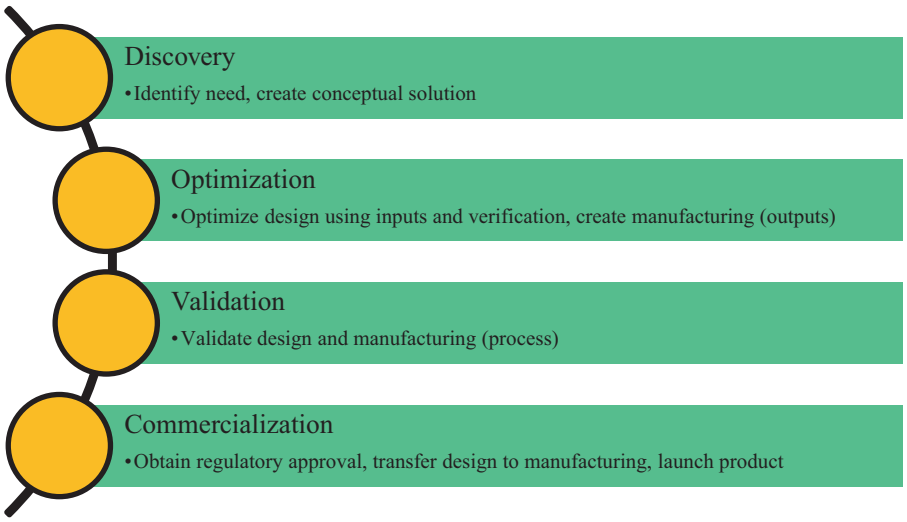

Fig. 42.2 Phases of device development

The CFR and FDA's Design Control Guidance (DCG) for Medical Device Manufacturers provides definitions and expectations for each of these sections [10, 11]. Due to the diversity of medical devices, the execution of each section varies across the industry; however, proper utility of the process can lead to early detection of design errors in development [11]. The design history file is the accumulated documentation output of all design control sections. The file must be accessible for the life of the device. Any device changes that invalidate information within the file require an update of the relevant activities. It serves as a device reference guide for the manufacturer or a regulatory body throughout the device life cycle.

Hypothetical Case Study

Consider that a clinician identifies a need for a stiffer snare for polypectomy. After partnering with a design team, a prototype is created. The first prototype with a minor increase in wire diameter combined with a novel metal alloy meets the stiffness expectations of the clinician. The design team comprehensively identifies any additional design inputs, and the prototype, with its manufacturing process, is optimized in one cycle. The device is successfully validated with the initial animal study. The device design data is submitted to regulatory agencies globally. All agencies approve the device without any delays. The product is launched globally and

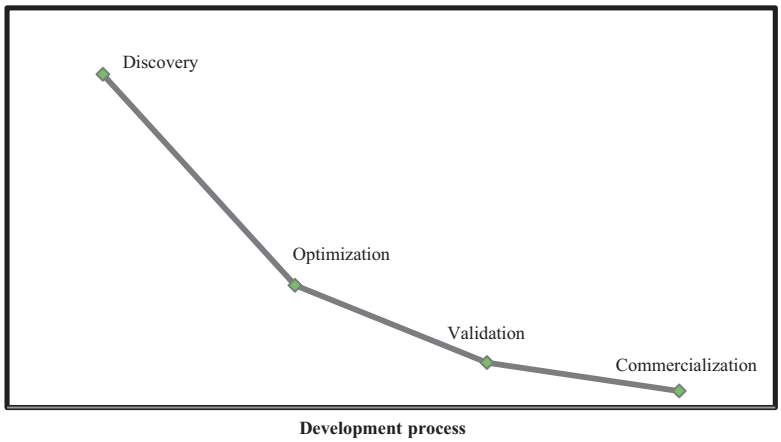

Fig. 42.3 (**a**) Undefined design variables. (**b**) Error in predicting launch date. (**c**) Adaptive to design changes with minimal cost impact

quickly generates excitement. This excitement, when combined with minimal training needed for proper device use, creates significant market demand. The manufacturer is able to meet the demand due to well-designed manufacturing processes and systems. The device is produced reliably without any unanticipated concerns for safety or efficacy. Patient outcomes are vastly improved, and the technology is considered a significant innovation for the clinical area.

Discussion on Device Development Process

This hypothetical case study is an idealistic representation of the development pathway of a new device. Realistically, the pathway is commonly highly iterative and convoluted. Each milestone has potential for delays and failure. A reliable manufacturing process may be unattainable due to the inherent complexity of the conceptual solution. The novel alloy chosen in the case study may have been insufficiently developed for high-volume utility. Continuous amendments to the design inputs may result in a perpetual cycle of redesigns and eventual abandonment of the device. Insufficient funds to support the development effort are a common issue for start-ups [7]. Communication, commitment, and teamwork deficiencies can result in an inability to overcome development barriers [9, 12]. A change in the competitive market while the device is within the development process can obsolete its benefits. These are only a few reasons for setbacks in the process. Consequently, many devices never exit the development process with significant cost to device manufacturers.

Discovery

Discovery is about selecting the ideal design from a field of possibilities [6]. Hence, creativity is an important trait in the discovery phase to create a robust landscape of possibilities. If available ideas are poor, the final choice will consequently be poor. The future value of the chosen design and its viability can be a difficult assessment Often, the benefits of the selection have to be weighed against the cost and commitment required for the development process. There are two significant choices in this phase [6, 8]. The first is to select a need to address. The second is to select a concept that potentially solves the need. Whether the selections are right can only be measured after device launch and directly correlates to its success [8]. As a result, poor performance during the discovery phase can have a costly outcome. High demand within the market segment of the clinical area is an indicator of a strong performance in the discovery phase.

Identify the Need

For medical devices, needs can be categorized as clinical or market. Clinical needs are opportunities to significantly improve the safety and/or efficacy outcomes for a clinical problem. Market needs, as defined for this discussion, are opportunities derived through market competition by offering incremental improvements for safety and/or efficacy. An observed deficiency in the operating ease of a band ligation device for the treatment of esophageal varices is a hypothetical example of a market need. The primary purpose to address such a need is to provide clinicians a choice in the market for a user-friendly version. Although such an improvement may lead to a slight reduction in procedure time due to device ease, the overall gain in safety and efficacy outcomes for the patient is minimal. In contrast, prior to band ligation, surgery was the only available option to treat variceal bleeding. In this historical scenario, the desire for an endoscopic alternative to surgery is an example of a clinical need, which led to significant gains in patient outcomes for safety and efficacy [13].

Conceptual Solution

Solutions for clinical needs result in disruptive technologies. Conversion from surgical to endoscopic management of variceal bleeding led to changes in procedure volume for surgeons and endoscopists. Hospital systems see changes in procedure room designs or staff job functions due to such technology. Competitive device manufacturers may be forced to adapt as well. Market-leading devices may become obsolete. As a result the entire supply chain between device manufacturers and material suppliers can be disrupted.

Solutions for market needs result in incremental technologies. This does not indicate that such technology cannot result in a transformation of a market. The introduction of a disruptive technology may provide significant gains in patient outcomes, but its penetration in the market may be hindered due to a variety of other shortcomings. Therefore, incremental improvements to the initial disruption can provide the necessary trigger for improved outcomes for the total patient population in a clinical area [14]. An assessment by competitors on shortcomings of the initial disruptive technology can yield multiple market needs [14]. Addressing these needs with incremental improvements leads to a maturation of the technology for the clinical area. Another disruptive event in the same clinical area can initiate a second chain reaction of incremental solutions (Fig. 42.4).

Three areas of expertise are required for successful completion of the discovery phase for medical devices (Fig. 42.5). Deficiencies in clinical, technology, or market knowledge for the design team can result in a long discovery phase or a flawed device concept. Generally, knowledge required for creating an incremental conceptual solution is easier to gain. While for disruptive technologies, sufficient knowledge may not exist in at least one area and may require new research. For example, for the discovery of capsule endoscopy to occur, new expertise in technology related to semiconductors, integrated circuits, and illumination was necessary [15]. New expertise in human physiology specific to the understanding of the small bowel was also needed [15]. Once the technology and clinical expertise had matured, the conceptual solution of capsule endoscopy was created.

Therefore, expertise in the three areas is necessary for the completion of the discovery phase; however, a revelation in any one of the areas may result in the initiation of the phase. New knowledge of the market may uncover a market need, while new clinical knowledge reveals a clinical need. The creation or new understanding of a technology can stimulate discovery by allowing a previously unresolved clinical or market need to be addressed [6].

Historical Case Study

Sivak (2004) discusses the discovery phase for the first snare device for colonoscopic polypectomy [16]. In 1969, Dr. Shinya identified surgical resections of polyps as an opportunity for a new clinical need. Based on his market assessment, 30% of surgical resections were for polyps. His goal was to convert those to an endoscopic approach. However, to generate a conceptual solution, he required engineering expertise. So, after partnering with Mr. Ichikawa, an Olympus Optical engineer, they attempted to create a solution. Several barriers existed for them. The only type of endoscope that existed at the time was a gastroscope, and clinical knowledge for techniques in colonoscopy was insufficient. After acquiring a new colonoscope, Dr. Shinya was initially able to visualize the cecum in 10% of procedures. With advances in

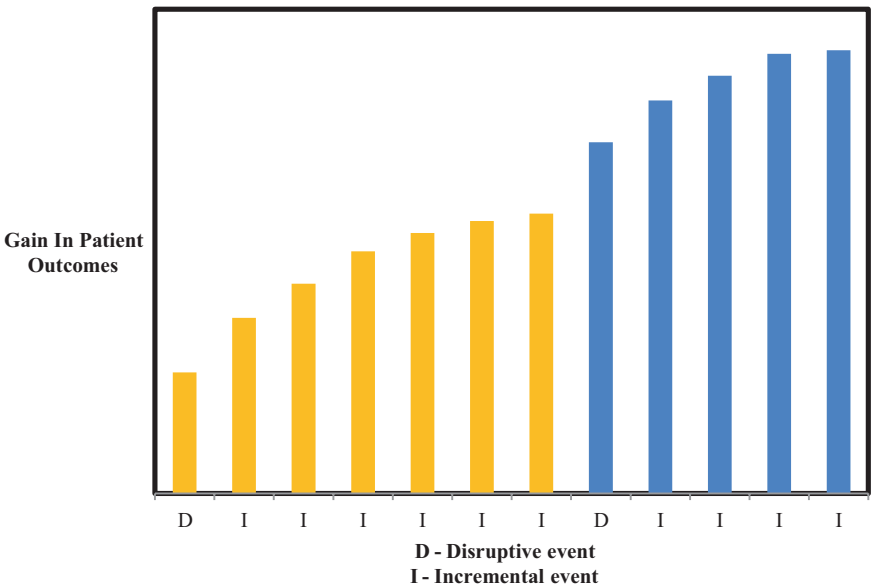

Fig. 42.4 Benefit to patient outcomes by technological advances

Fig. 42.5 Areas of expertise needed to create a medical device conceptual solution

colonoscope design and technique, his success rate improved to 60%. He practiced his technique while performing colonoscopy during colonic surgery. With gains in clinical expertise in colonoscopy and technological advances of the colonoscope, work began on generating a solution for endoscopic polypectomy. Dr. Shinya and Mr. Ichikawa evaluated consequences of electrosurgical currents and device designs in animal studies. In 1969, they generated the conceptual solution of a snare. The idea was not patented. The FDA did not have any regulations for medical devices, so in 1970, Dr. Shinya reported the first 11 clinical cases of colonoscopic polypectomy.

Discussion of Barriers to Disruptive Technology in Endoscopy

The case study of colonoscopic polypectomy is an example of disruptive technology to solve a clinical need. Deficiencies in clinical knowledge of colonoscopy and endoscope technology were addressed before the conceptual solution for polypectomy was discovered. Today, there are increased barriers to disruptive technology than during the invention of the snare [2, 3, 17]. Barriers specific to endoscopy include challenges to collaboration, increased development cost, and progression of laparoscopic surgery.

Dr. Shinya and Mr. Ichikawa freely collaborated at the time. In the current environment, compliance laws and compensation framework increase the difficulty of collaboration between industry and clinicians [2, 18]. Dr. Shinya was the owner of his ideas, but more often today medical institutions own the clinician's ideas. The medical device industry has to adhere to compliance laws to prevent any impropriety in relationships with clinicians. Therefore, medical institutions and industry generate legal contracts that take months, if not years, to negotiate the terms of collaboration. Collaboration does not always evolve into success. Consequently, a graveyard of wasted contracts symbolically represents another barrier to innovation. A different model for some academic institutions is to encourage collaboration between their clinical and engineering centers [7]. Ownership and compensation for ideas is predetermined by the rules of the institution. However, the challenge for this approach is to bridge the gap in engineering expertise within an academic institution to that within the medical device industry [17]. Endoscopic accessory companies, for example, have acquired expertise in catheter technology through years of experience. Engineering centers in academic institutions may have to generate adequate fundamentals in catheter technology prior to addressing a newly identified clinical need. Collaboration between expert clinicians in the field of gastroenterology and industry engineers with experience in endoscopic devices is optimal for a successful discovery phase.

There are also increased costs in the current environment. In calculating the value of a clinical or market need, medical device companies factor in the cost of global regulations, contracts, reimbursements, and development timelines [1, 6, 18]. Generally, these factors are costlier for bringing technology to the market that addresses clinical needs than for market needs. In addition to higher complexity for the previous cost factors, clinical needs often require clinical trials to validate the improvement in patient outcomes. To assess all these factors, device companies utilize filtering processes in the discovery phase to be selective in the needs that they will pursue [6]. Companies with an internal culture of innovation are successful in selecting and delivering disruptive technology to the market [12]. Other companies utilize such filtering processes to gravitate toward market needs, since the cost and return of investment is easier to predict. Generally, large companies minimize financial risk and bet on incremental technologies, while small companies such as startups tend to deliver more disruptive technologies [4, 9, 17].

The conversion from surgical to endoscopic procedures is a fundamental pathway for disruptive technology in endoscopy. Generally, such conversions lead to significant increases in patient outcomes due to the high risk of surgery when compared to endoscopy. However, the conversion of open surgical techniques to laparoscopy has reduced the surgical risks. Maturity of some of these laparoscopic surgical procedures has also further decreased the overall risk to the patient. Therefore, the potential gain in patient outcomes may not be sufficiently significant for a clinical area to warrant the conversion to an endoscopic approach. Natural orifice transluminal endoscopic surgery (NOTES) is an endoscopic approach for performing procedures in the peri-

toneal cavity by breaching the gastrointestinal lumen. Coomber (2012) reviewed available evidence from clinicians using the NOTES approach for cholecystectomy rather than laparoscopy [19]. Due to the high quality threshold of laparoscopic cholecystectomy, a high level of clinical evidence is required for NOTES as an approach. The incremental gain in patient outcome when compared to laparoscopy has been a barrier in the adoption of the NOTES cholecystectomy. To maximize the utility of the NOTES approach, it is beneficial to select a procedure that maximizes the predictive gain in patient outcomes. Significant decreases in laparoscopic surgical risks are a deterrent for the entry of disruptive endoscopic technology.

Optimization

With the realization of the conceptual solution, the next step in the development process is to optimize the design. Design inputs, design verification, and design outputs are sections of design controls utilized in this phase and are explained in detail within the CFR and DCG [10, 11]. A summary of these concepts will be further discussed for this phase. The overall objective of this phase is to convert a rudimentary prototype into a manufacturable version. A successfully conducted optimization phase results in a device that performs consistently and reliably in the market.

Design Inputs

Inputs are classified into three types of requirements: functional, performance, and interface. Functional requirements result in attribute verifications. Such verifications are binary and assess for the presence or absence of an observation. For a snare, the presence of a snare head within colonoscopic view after extension from its catheter would be an example of a functional requirement. Performance requirements quantify the quality of a function. Adding a force requirement to assess the ease of extending the snare head converts the previous functional requirement into a performance requirement. Interface requirements can be either functional or performance based and are essential for compatibility with the user, the patient, or other compatible devices. For endoscopic accessories, the inputs related to endoscope compatibility would be categorized as interface requirements. Interface requirements for the user are also known as usability requirements and are addressed by human factors engineering. Minimizing device failures by eliminating user errors is a key element of human factors engineering [20].

Design Outputs

Design outputs are generated from the design process to address the inputs. The physical form of the device is a design output. Other outputs include, but are not limited to, engineering drawings, manufacturing specifications, or instructions for use (IFU). A snare that must pass through a 2.8 mm pediatric colonoscope is an example of an interface design input. For such an input, a specific catheter design characterized by its outer diameter for fit and material type for flexibility, are design outputs selected during the design process. A variety of design output combinations can successfully address a design input. Therefore, excellence in determining design outputs is based on a design team's proficiency in the design process.

Design Verification

The activity to evaluate whether the outputs meet the inputs is known as design verification. Design verification is utilized to determine whether the device is built right. For the previous case, verification would include an assessment of ease for snare catheter passage within the 2.8 mm pediatric colonoscope. Some other types of design verification include visual checks for labeling content accuracy or testing of a mechanical joint to a requirement. Two specific design verifications to further explore are biocompatibility testing and risk analysis. A fixed design input for all medical devices is that the device has to be reasonably safe for use while performing its intended purpose. Biocompatibility testing evaluates the safety profile of materials (outputs) selected for the device, while a risk analysis verifies safety of the overall design and manufacturing outputs to address the safety input.

The ISO 10993 series on biological evaluation of medical devices is a set of standards used by regulatory agencies for biocompatibility evaluation of a marketed medical device [21]. It provides guidance on the testing recommended based on duration and type of tissue contact (Fig. 42.6). The standard also details testing methods and evaluation requirements. Claiming compliance to the standard for a device provides an easy assurance to regulatory agencies that the materials have an acceptable safety profile for human contact.

ISO 14971 provides definition and guidance for medical device risk [22]. There are several components of a risk analysis, but the overall objective is to reduce harm to the patient or user due to a device hazard. Figure 42.7 provides an algorithm in determining risk. Hazards are inherent to all medical devices and in combination with the context of the clinical procedure, known as sequence of events, can lead to hazardous situations. Harm is a result of the hazardous situation,

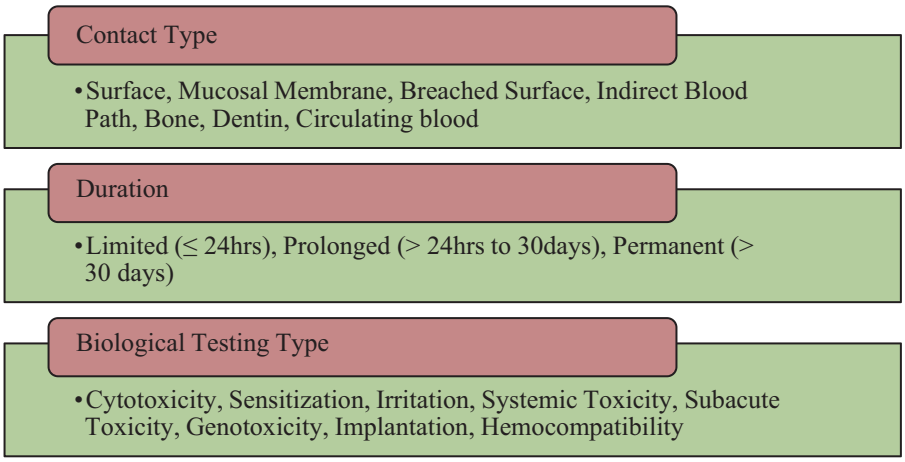

Fig. 42.6 Biocompatibility variables [21]

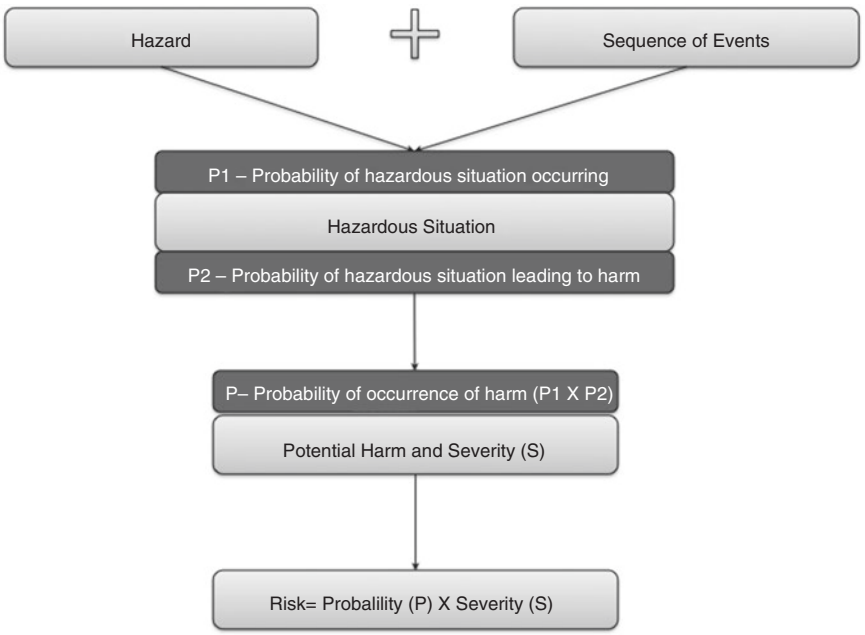

Fig. 42.7 Risk analysis [22]

and risk is the combination of the probability of occurrence and severity of harm. In the case of the snare, consider the sequence of events where the clinician unknowingly exposes the tip of the snare head, denoted in Fig. 42.8, from the catheter, and while maneuvering the endoscope in position for a polyp, aggressively contacts the tip to the colon wall. By itself the events have no consequence; however, when combined with a hazard of a tip that is sharp, a hazardous situation of bleeding can occur due to trauma to the colonic wall. The potential harm to the patient may be negligible for an oozing bleed that ceases on its own. However, if the bleeding is significant, the potential harm could be a drop in blood pressure. The severity of the bleed combined with its probability of occurrence determines the risk of a sharp snare tip.

The hazard of a sharp tip can be present due to a variety of factors. The sharp tip may have been inherently designed as such or may be a result of a manufacturing process that yields inconsistent tip sharpness. It could also be a result of a failure in the tip that exposes a sharp element. All these lead to the same harm; however, the probability of occurrence of the harm and therefore the resulting risk can vary based on the reasoning for tip sharpness. Design teams cannot determine an accurate understanding of the risk profile without clinical knowledge. Collaboration with clinicians is critical for progressing through this design verification activity [9].

Hypothetical Case Study

Figure 42.8 shows a conceptual model of a snare joint that securely attaches the drive cable to the snare wires. The two snare wires are attached to the drive cable by an adhesive designated by the boxed area in the diagram. The designer proceeds to systematically analyze the joint based on a vari-

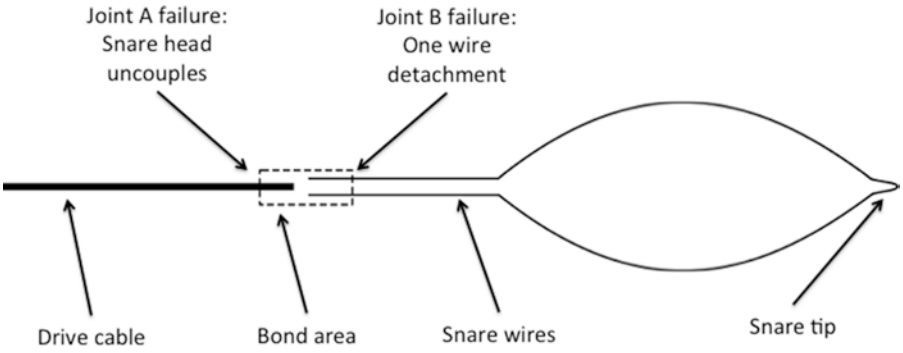

Fig. 42.8 Snare design

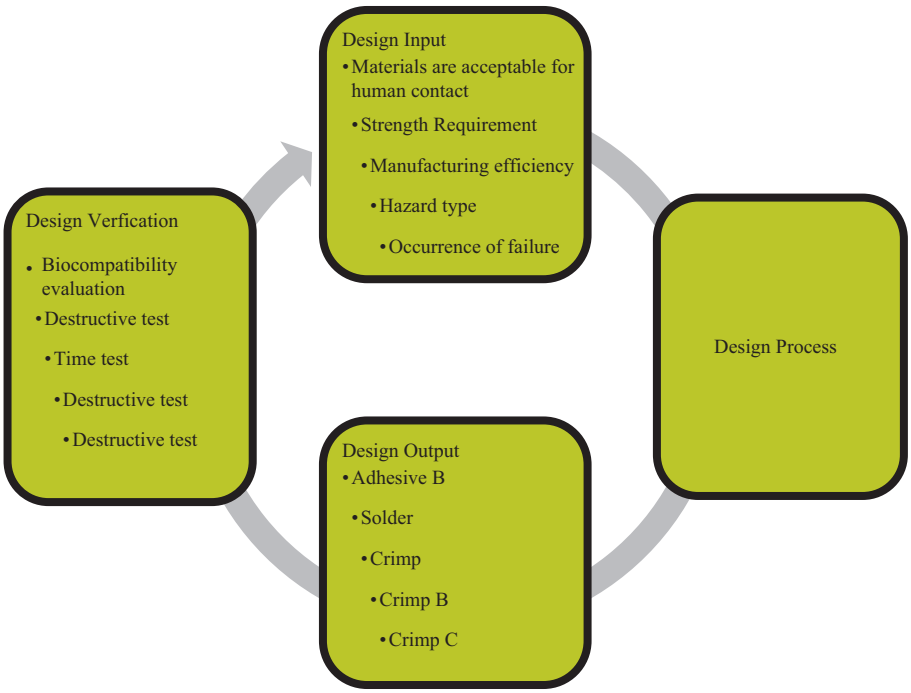

Fig. 42.9 Optimization cycle

ety of design inputs (Fig. 42.9). The first input indicates that the materials chosen must be acceptable for human contact. The initial adhesive A is deemed to have an unacceptable safety profile; therefore the designer selects an adhesive B as the output from the design process. Adhesive B is subjected to biocompatibility evaluation and is considered to be acceptable. Next, the joint is reviewed for strength. Based on similar devices in the market, the strength requirement for the joint must be 5lbs. Although the adhesive joint meets the requirement initially, within 6 months of manufacturing, the joint weakens to below the requirement. The manufacturing of the joint is modified from an adhesive to a solder process to conform to the input. The design is then reviewed with manufacturing personnel. The review concludes that the solder process is onerous to effectively meet the forecasted market demand. Alternately, a metal tube crimped around the three wires is consequently determined to be a more efficient manufacturing method. After determining that all the previous requirements are met, a risk analysis of the joint is conducted with a clinician. A concern is uncovered about the type of failure at the joint. If the failure occurs such that the metal tube separates from the drive cable, designated as Joint A failure in the diagram, the entire snare head would uncouple into the patient. However, if one of the snare wires were to consistently fail first as shown in the diagram as Joint B failure, then the inoperable device would still remain intact. Consequently to reduce the device risk, the designer shortens one end of the snare wire within the metal tube. Design verification is conducted to verify that the snare wire consistently detaches from the metal tube instead of the drive wire. To further reduce risk, the occurrence of the failure is analyzed. Based on similar devices, a failure no greater than 1 in 10,000 is expected. Utilizing statistical methods, a sampling of devices is used to determine the failure rate. The crimp design is incrementally optimized until the failure rate is below the expected rate.

Deficiencies in the Optimization Phase

The previous case study illustrates the iterative nature of the optimization phase. Although it portrays an inefficient iteration of a joint design by considering each input sequentially, some amount of iteration is unavoidable. An exhaustive inputs list for the entire device prior to initiating the design process allows design teams to concurrently address the inputs [6, 17]. Instead of five design iterations in the previous scenario, the same result may be achieved in two, reducing development time and cost. However, a complete design input list at the beginning of the design process is idealistic, and hidden inputs are often uncovered later in the development process [6].

Changes in sales forecast of a new device can impact manufacturing inputs. The design team utilizes these inputs to select the manufacturing methodology during the design process. For example, assigning an operator for device assembly may be adequate if the predicted annual sales are low. If the predicted annual sales are high, some level of automation may be needed for the assembly instead. Therefore, an accurate sales forecast of the device early in the optimization phase can result in a thorough list of manufacturing inputs. For incremental technology, clinician feedback combined with available market research data for comparable devices can easily be used to determine the forecast. For disruptive technology, the forecast may be more difficult to realize and requires an in-depth analysis by clinicians and the design team. Development time and cost can be minimized by an accurate sales forecast early in the development process.

Changes in the competitive landscape during the development process can cause the design team to retreat within the optimization phase or back to the discovery phase. A new product launch by a competitor that includes additional safety features or benefits could diminish the value of the potential device. Consequently, it is conceivable that new inputs are introduced to the potential device in order to increase gains in patient outcomes. Such instances are unpredictable; however, having shorter development cycles minimizes the risk of such disruptions and allows design teams to rapidly adapt.

Specific to endoscopic accessories, the interaction between the accessory and the endoscope is important for effective function. A significant challenge to designing accessories is compensating for the different variations of endoscopes in the market. In addition to multiple models of endoscopes available from a scope manufacturer and multiple endoscope manufacturers, the repaired and aged versions of each present a difficult design challenge. Based on technical review conducted by the American Society of Gastrointestinal Endoscopy, there were 27 different colonoscopes offered in 2011 [23]. A simple device like a snare may not be impacted significantly by these variants, but more intricate devices could be. Such interface inputs may not be easily uncovered or verified in the development cycle. In some instances, if verification cannot be conducted, it is necessary to narrow the compatibility conditions on the product label to limit potential malfunctions.

Validation

The CFR and DCG provide requirements for validations, which are conducted after completion of all iterative changes to design and manufacturing processes [10, 11]. Design validations assess whether the right design has been built for the intended use. In contrast, design verification assesses whether the design is built right. Design validation evaluates the device against its user needs and intended use. The intended use is the stated clinical purpose of a device. Process validation evaluates the built device to the design intent.

Design Validation

Often, simulated conditions are utilized in design validations to appropriately challenge the device design. An assessment of simulation accuracy is an important activity to perform prior to validation. When adequate simulated conditions cannot be achieved to evaluate safety and efficacy, actual conditions are utilized in the form of clinical trials. Clinicians are instrumental in this assessment. Development cost and time is significantly reduced for medical device companies if simulated conditions can be successfully utilized instead of clinical trials [17]. However, the decision for the need of a clinical trial must be made based on the ability to adequately evaluate the design. Device manufacturers often conduct clinical trials outside of the United States to reduce cost and time [17]. Incremental technology used in high-risk procedures and disruptive technology commonly require clinical trials. Additionally, the decision to conduct a clinical trial can be predetermined due to regulatory requirements.

Process Validation

If a device were to only be built once, design validation would be sufficient. Designing and constructing a building would be such an example. However, this is generally not the case for medical devices. Hence, process validation is needed to determine whether every device manufactured meets its design intent. A set of devices is never identically built even from the same manufacturing time. Slight variations exist within the materials utilized, the operator assembling the device, or performance changes in manufacturing equipment.

Therefore, devices are manufactured to be within a range of performance established from design activities. Each manufactured device and its performance requirements are inspected to be within the acceptable range. However, certain performance requirements, such as the strength of a joint, cannot be practically inspected without damaging the device. Process validation is therefore utilized to test a sampling of the devices before and during manufacturing to analyze the performance. Design validation is used to predict acceptable clinical performance of the design during its market life cycle, while process validation is used to predict acceptable manufacturing performance for a set production time period. Conducting process validations on devices manufactured under simulated launch conditions is critical to expose unknown manufacturing deficiencies.

Hypothetical Case Study

Consider the optimized stiffer snare device again. For validation of the design, a test method is required to adequately simulate conditions. The design team and clinician debate various simulations found within the literature research. A porcine animal study is agreed upon for validation. Porcine colonic mucosa is verified to be similar to humans. For simulating a polyp, the clinician injects fluid between the layers of the colon wall. The resulting dome shape is considered an adequate polyp simulation. The clinician proceeds to use the prototype and successfully completes the polypectomy. Another polyp simulation is created. A new prototype is handed to the clinician; however, the clinician prefers to use the first prototype to simulate the use of one snare in a patient with multiple polyps. The design team did not account for such a requirement, and the snare wires damaged from the initial polypectomy fail to exit the catheter for the second polypectomy. The clinician and design team discuss the criticality for performing multiple polypectomies in a patient with the same device. After deeming it to be important, the failure of the validation is noted. The design team reverts the project back into the optimization phase to make design improvements for the new requirement.

Validation Lessons

Adequate simulations for device interactions with the patient, users, compatible devices, operating environment, and storage environment have to be considered. The case study provides an example of a simulation designed to account for the user and the patient. By utilizing a clinician, as opposed to nonclinical personnel, the clinical situation of multiple polyps was added to the validation. Additionally, the accuracy of the simulated polyp sufficiently challenged the device and rendered it unusable for a second instance. The case study simulation can be improved for other interactions. Utilizing a variety of commonly available endoscopes while performing simulated polypectomy would be an example of evaluating the device-to-device compatibility. Subjecting the snare devices to a shipping simulation prior to performing the design validation addresses the storage environment. Lastly, assessing the legibility of markings on the device handle in a simulated dark procedure room addresses the operating environment. A simulation must be designed with a thorough understanding of all device interactions for an adequate design validation

Simulating the worst-case conditions of a clinical case is an important consideration for design validation. Consider a device that is subjected to bending during a clinical case where an increase in procedure time results in an increase in bending cycles. If the number of bending cycles were counted in each case for a hundred cases, Fig. 42.10 would represent the hypothetical data. Based on the data, the device can be subjected to bending cycles in the range of 2 to 18. However, based on the highest frequency of cases with a common procedure time, ten would represent the nominal bending cycles. If all device failures were to occur after 14 bending cycles, as represented by the shaded region in the graph, a design validation simulation under nominal conditions would be inadequate. If a simulation included 20 bending cycles, the device would fail and further design optimization would be required for a robust design. Since a failure may never be fully mitigated and the shaded region may represent an extremely small percentage of clinical cases, judgment has to be utilized on whether the simulation for 20 bending cycles is excessive. Engineering devices for excessive requirements result in lengthy development cycles and high development costs. An adequate analysis on the magnitude of worst-case is an important consideration in determining the quality standard for a device.

Collaboration with clinicians to review the validation simulation can minimize deficiencies [9]. However, some deficiencies may not be obvious even by clinician review. Therefore it is important for design teams to observe similar clinical procedures. This may be a simple task for incremental technology. However, for disruptive technology a representative procedure may not be available. As a result, it may be difficult to achieve an accurate simulation for disruptive technology, and a clinical trial may be the only avenue for an adequate evaluation.

Commercialization

Commercialization is the last phase of the design and development process. Regulatory approval and design transfer prior to launch are the milestones for this phase. With

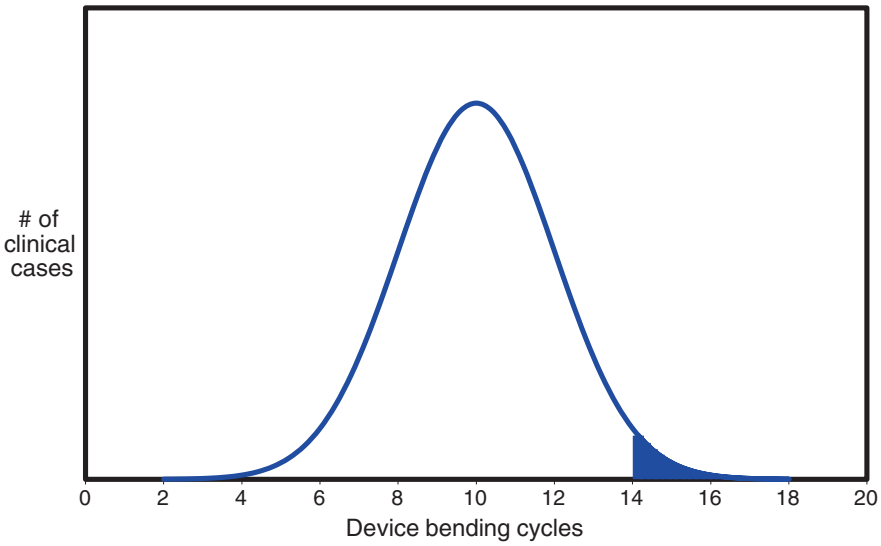

Fig. 42.10 Filled area represents the number of cases where devices failed

completion of design activities in the previous phases, the primary focus in this phase is to accurately communicate the design details. Design teams communicate the information to regulatory agencies, manufacturing, marketing, and sales teams.

Design Transfer

Design transfer is the final step of design controls prior to a new device launch and is explained in the CFR and DCG. It is the final documented review added to the design history file prior to its completion. A history file provides information on all completed activities. However, the manufacturer requires a subset of manufacturing information transferred for production of the device. Incomplete or inaccurate information transferred can lead to unreliable device performance in the market. This is analogous to an incorrectly communicated recipe of a new dish. The deficiency in device manufacturing may not be apparent at the onset of the launch. Sometimes such deficiencies are exposed years later. Minor adjustments made to the manufacturing process can creep the device performance outside of expectations in the absence of communicated design boundaries. Consequently, design transfer is an important review for product quality.

Regulatory Approval

Medical devices can be released to the market after obtaining regulatory approval. Each country has a specific set of requirements for the regulatory approval process. The focus of the discussion here will be on the regulatory processes for the United States and European Union.

In the United States, the requirements for the device are determined by its risk classification (Fig. 42.11) [7]. Low-, moderate-, and high-risk devices are classified as I, II, or III, respectively. Most class I devices do not require notification to the FDA. Class II devices generally require a 510 k submission. The submission is an accumulation of information from design controls that supports the safety and efficacy of the device. In some instances clinical study data may be required to support the submission. A 510 k submission also requires an assessment that the device is substantially equivalent to a device previously cleared by the FDA. Previously cleared devices are known as predicates. The selected predicates for the assessment have to be denoted in the submission. Common endoscopic accessories generally follow the regulatory pathway for Class II devices. Class III devices always require clinical study data. Prior to obtaining clinical data for Class II or III, an investigational device exemption (IDE) is required. The FDA utilizes the IDE to review the adequacy of the device for clinical trial. Agreement on trial design and expectations of device performance are some of the important elements of the IDE process. Another pathway for a Class III device, where the treatment population does not exceed 4000 cases annually, is humanitarian device exemption. In such devices, safety has to be addressed, but efficacy may be theoretical at approval. The reduced threshold allows for flexibility in providing treatment options for rare disorders.

For the European Union, requirements for releasing a medical device to the market are outlined in the Medical Device Directive (MDD). Per the MDD, devices are classified into four categories: I, IIa, IIb, and III. The essential requirements for each classification are included in the various annexes of the MDD. Unlike the centralized FDA in the United States, competent authorities (CA) from every country in the European Union establish and monitor compliance

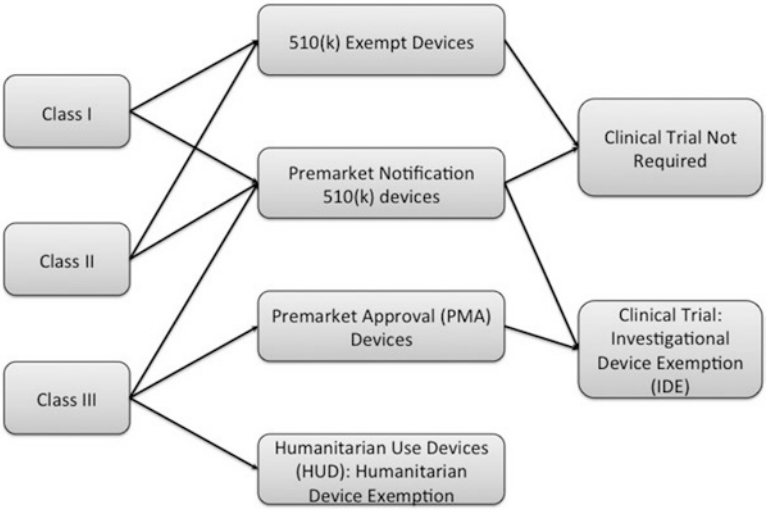

Fig. 42.11 Regulatory pathway in the United States for medical devices

of the MDD requirements. A difference from the United States is CAs utilize notified bodies to enforce regulatory compliance. These organizations are commercial entities and independent of the government. They review and audit the device documentation from the manufacturer against the essential requirements. If the requirements are met, the manufacturer is provided the approval to place a CE mark on the labeling of the device. This symbol represents compliance to the MDD requirements and allows the manufacturer to market the device anywhere within the European Union.

Time of approval for a medical device between the United States and European Union is a significant matter for debate. Approval time for Class I/II is considered similar in the two regions [24]. For Class III devices, a considerable difference in time exists. High-risk devices gain approval in Europe approximately on average 4 years prior to the United States [18]. Adequate data does not exist to determine the effectiveness of the two regulatory systems. Premature approval of an unready technology can lead to harm in patient populations. However, delay in access to the latest technology is also a source of potential harm for patients. Such measures are difficult to quantify and study.

Hypothetical Case Study

The manufacturer determines that the stiffer snare is a Class II device in the United States. Since the FDA has cleared several snare devices in its history, sufficient predicates are available. Class II device submissions may require a clinical study, and an analysis is conducted on the differences between the new snare and the predicates. The manufacturer deems a clinical study is not needed since the differences are minimal. A 510(k) document is created based on the design history file and submitted to the FDA for a 90-day review. FDA clears the device after their review period. In parallel, the manufacturer determines that for the European Union, the snare is a Class IIb device. The information from the design history file is placed into a technical file that is utilized by a notified body to audit in the future. The CE mark is acquired within a week.

Discussion on Delay for Regulatory Approval

Disagreement in the assessment of device safety is a major source of regulatory delay. Although, regulatory agencies utilize risk classifications to categorize new technology, multiple pathways exist for each classification resulting in ambiguity of direction. Risk assessment can also be inconsistent within regulatory agencies depending on the reviewers. Risk assessments are generally qualitative, rather than quantitative. Therefore, the experience and knowledge of the reviewer can be a factor on determinations of risk. Medical advisors for regulatory agencies can also have different assessments on device safety compared to device companies. Several discussions between medical device manufacturers and regulatory agencies on safety outcomes may be required resulting in regulatory delays [24].

For the United States, debate over efficacy requirements of a new technology can also result in significant delay. The European Union requires device manufacturers to show that the new technology is able to perform its intended purpose. In contrast, FDA requires data that the device is reasonably effective. Agreement between the FDA and the medical device industry on defining reasonable effectiveness may only be achieved after much debate and delay. The difference in requirements for efficacy between the European Union and United States is a major reason for differences in approval times for Class III devices [24].

Conclusion

Clinician involvement is critical throughout the medical device development process [9, 18]. Collaboration between clinicians and medical devices manufacturers can result in a robust conceptual solution within the discovery phase. In the optimization phase, clinicians are instrumental in determining a comprehensive list of design inputs. Accurate simulations or trials require significant consultations with clinicians in the validation phase. During the commercialization phase, medical device manufacturers and regulatory agencies employ medical advisors to accurately review safety and efficacy of a device.

For any technological advance in medicine, an overall assessment of risk versus benefit for the patients is a key element of ethical concern. All medical devices are flawed due to human engineering and carry risks to the patient [18]. Whether a device design is good enough or risks have been adequately mitigated requires sound knowledge and judgment. Discussions and debates are essential for medical device companies to elucidate these topics. Clinicians are essential in ensuring the discussions and debates are thorough during the entire device development process.

References

1. Sivak MV. Gastrointestinal endoscopy: past and future. Gut. 2006;55(8):1061–4.
2. Rosenberg N, Gelijns AC, Dawkins H, editors. Sources of medical technology: universities and industry. Washington, DC: National Academies Press; 1995.
3. Chatterji AK, Fabrizio KR, Mitchell W, Schulman KA. Physician-industry cooperation in the medical device industry. Health Aff. 2008;27(6):1532–43.
4. Medina LA, Kremer GEO, Wysk RA. Supporting medical device development: a standard product design process model. J Eng Des. 2013;24(2):83–119.
5. Pietzsch JB, Shluzas LA, Paté-Cornell ME, Yock PG, Linehan JH. Stage-gate process for the development of medical devices. J Med Devices. 2009;3(2):–021004.
6. Santos IC, Gazelle GS, Rocha LA, Tavares JMR. An ontology model for the medical device development process in Europe. In: The 1st international conference on design and processes for medical devices-PROMED 2012; 2012.
7. Ham ST. Mapping the medical device development process. 2010.
8. Kim J, Wilemon D. Focusing the fuzzy front–end in new product development. R&D Manag. 2002;32(4):269–79.
9. Brown A, Dixon D, Eatock J, Meenan BJ, Young T. A survey of success factors in new product development in the medical devices industry. In: Engineering management conference, 2008. IEMC Europe 2008. IEEE International. IEEE; June 2008, p. 1–5.
10. Code of Federal Regulations. 21 CFR Part 820.30. Design controls; 2014.
11. Food US, Administration D. Design control guidance for medical device manufacturers. In: Center for Devices and Radiological Health. Rockville: United States Food and Drug Administration; 1997.
12. Tellis GJ. Disruptive technology or visionary leadership?*. J Prod Innov Manag. 2006;23(1):34–8.
13. Rajoriya N, Tripathi D. Historical overview and review of current day treatment in the management of acute variceal haemorrhage. World J Gastroenterol WJG. 2014;20(21):6481.
14. Christensen C. The innovator's dilemma: when new technologies cause great firms to fail. Boston: Harvard Business Review Press; 2013.
15. Pan G, Wang L. Swallowable wireless capsule endoscopy: progress and technical challenges. Gastroenterol Res Pract. 2012;2012:1–9.
16. Sivak MV. Polypectomy: looking back. Gastrointest Endosc. 2004;60(6):977–82.
17. Kaplan AV, Baim DS, Smith JJ, Feigal DA, Simons M, Jefferys D, Fogarty TJ, Kuntz RE, Leon MB. Medical device development from prototype to regulatory approval. Circulation. 2004;109(25):3068–72.
18. Citron P. Ethics considerations for medical device R&D. Prog Cardiovasc Dis. 2012;55(3):307–15.
19. Coomber RS, Sodergren MH, Clark J, Teare J, Yang GZ, Darzi A. Natural orifice translumenal endoscopic surgery applications in clinical practice. World J Gastrointest Endosc. 2012;4(3):65–74.
20. Vincent CJ, Li Y, Blandford A. Integration of human factors and ergonomics during medical device design and development: It's all about communication. Appl Ergon. 2014;45(3):413–9.
21. ISO 10993-1:2009, Biological evaluation of medical devices – part 1: Evaluation and testing within a risk management process.
22. ISO 14971:2007, Medical devices – application of risk management to medical devices.
23. Varadarajulu S, Banerjee S, Barth BA, Desilets DJ, Kaul V, Kethu SR, Pedrosa MC, Pfau PR, Tokar JL, Wang A, Song LMWK. GI endoscopes. Gastrointest Endosc. 2011;74(1):1–6.
24. Kramer DB, Xu S, Kesselheim AS. Regulation of medical devices in the United States and European Union. N Engl J Med. 2012;366(9):848–55.

NOTES: Past, Present, and Future

43

John H. Rodriguez and Jeffrey Ponsky

Introduction

Surgery has always gravitated around a balance between safety and efficacy. Surgeons have been on a constant crusade to make their operations better, safer, and more recently less invasive. The quest toward minimal access surgery has been a constant evolution. Minimally invasive surgery has evolved from multiple angles that have somewhat completed each other. Perhaps laparoscopy has been the area that has witnessed the fastest growth and universal acceptance. It has pushed common open operations to the point of obsolete. Laparoscopy has become the new standard of care. In a similar way, endoscopy has evolved to become an invaluable tool in the diagnosis and management of pathology in the gastrointestinal tract. Many procedures that are now routinely done through minimal access approaches were not even thought as possible less than a century ago. The aim of this chapter is to describe the historical evolution of flexible endoscopy to natural orifice translumenal endoscopic surgery (NOTES), examine some of the current applications, and seed some thoughts for the future.

History

The path to modern-day surgical endoscopy has been a slow evolution fueled by medical innovation. Technology has been a limiting factor at many stages, as our minds have moved faster that our tools. Early pioneers worked with rigid scopes and very rudimentary optics, but this new technology marked the birth of minimally invasive surgery. In the 1950s, flexible surgical endoscopy was introduced and started a revolution. Early developers were unaware of the immense potential this new technology had to offer. With new technology came new frontiers and allowed the transition from diagnostic to therapeutic procedures. This gave early endoscopists for the first time the means to not only diagnose pathology but also to perform therapeutic procedures while maintaining minimal access.

The first therapeutic procedures performed with a flexible endoscope involved removal of pathology limited to the mucosa of the gastrointestinal tract. Polypectomy probably offered the first sight that the combination of endoscopic visualization of the GI tract and special tools would allow more advanced procedures. In the 1970s, endoscopic retrograde cholangiopancreatography was first described. This innovative new procedure made possible the concept of intervention beyond the lumen of the gastrointestinal tract. Endoscopists were now aware that intervention in structures immediately adjacent to it was possible. This was the first breakthrough procedure that demonstrated that intervention beyond the boundaries of the lumen of the gastrointestinal tract but through a natural orifice was possible. To this point, no violation of the gastrointestinal tract was necessary. A few years later, the description of percutaneous endoscopic gastrostomy (PEG) marked a milestone in the evolution of advanced intervention through an endoscopic approach. This new procedure had the same results as a well-established operation (gastrostomy), but was now possible through a technique that required no direct access to the peritoneal cavity. It also proved the concept that purposeful violation of the gastrointestinal tract through endoscopic intervention was possible.

The next phase in the development of NOTES evolved from the idea that intervention was possible beyond the limits of the gastrointestinal tract. Continuity or contiguity of the lumen of the bowel was no longer a limiting factor, and remote organs became a target. The first published experience of natural orifice translumenal endoscopic surgery (NOTES) came in 2004 and was described by Dr. Kalloo from the Johns Hopkins Hospital. His team performed a diagnostic peritoneoscopy and liver biopsy through an

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incision in the gastric wall using a standard endoscope. The gastrotomy was then closed using standard endoscopic clips. This breakthrough procedure was the birth of NOTES and broke barriers that had been previously established. It also introduced new dilemmas. The idea of violating a normal organ such as the stomach to treat a diseased one was not universally welcomed. Technology available at the time was also a huge limiting factor.

Despite the controversy, the NOTES movement gained momentum in the mid to late 2000s. At this time, several proceduralists started to experiment with the new technology. Initial experience was limited to animal models both in vivo and ex vivo. The feasibility and safety was then tested, and multiple animal survival studies were published. It seemed that the possibilities were endless. Different procedures were reported and consisted mainly of lymphadenectomies, gastrojejunostomy, and cholecystectomy. The common access site was the stomach, likely due to easy access and for being such a robust and well-vascularized organ.

The new idea became very attractive to other specialists, who evaluated other access sites other than the mouth. Gynecologists and urologist used the vagina for common access for natural orifice surgery. Multiple case reports and small series have surfaced and include hysterectomy, nephrectomy, oophorectomy, and natural orifice translumenal endoscopic surgery-assisted ovarian cystectomy (NAOC). Once again, this emerging technique raised many questions that challenged its clinical application. The main concern involved the concept of violating an intact organ to gain access to structures that would be otherwise accessible through laparoscopy or minilaparotomy. To this point, laparoscopy had already established itself as a universally accepted technique with innumerable applications. Laparoscopy also became the standard of care to which NOTES was being compared, specially, at a time when laparoscopic boundaries were being pushed further by smaller and more advanced instruments, better optics, as well as single incision and single port applications. The safety and the challenges being raised seemed to place a halt on the rapid expansion of NOTES techniques and applications.

Gastroenterologists and surgeons understood the need for responsible expansion of the new technique. In 2005, the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR) was constituted by a group of experts from the American Society of Gastrointestinal Endoscopy (ASGE) and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). The group of experts recognized the obstacles and developed a list of guidelines that needed to be followed in order to further develop NOTES techniques and applications. In Europe, the EURO-NOTES clinical registry was started as a combined effort from members of the European Association for Endoscopic Surgery (EAES) and the European Society of Gastrointestinal Endoscopy (ESGE). The goal was to promote the development of NOTES applications within a controlled and responsible innovative environment.

NOSCAR established a blueprint upon which NOTES cases could be studied and introduced. IRB application and approval was paramount to each intervention. Early studies of the efficacy of NOTES were performed at several centers. Initial studies examined the safety and efficacy of peritoneal examination with NOTES. Such a study was performed for staging of malignancy prior to pancreaticoduodenectomy at Ohio State University. Another such feasibility study was carried out at Case Western Reserve University. These studies documented and verified the feasibility and safety of NOTES. An early report of a NOTES procedure was published by Marks et al. and described reestablishing a PEG tract, "PEG rescue" after premature removal of the PEG tube.

Bessler and his colleagues published the first report of transvaginal cholecystectomy, while others continued to pursue transgastric cholecystectomy. All of these procedures were of the hybrid variety, employing laparoscopic observation of the procedure.

It soon became apparent that transgastric NOTES was difficult and cumbersome. The problem of leakage from the gastric closure continued to plague the technique. Manipulation and retraction of tissue was difficult. New instruments were developed for retraction, dissection, and suturing. In the meantime, transvaginal surgery became more widespread and employed rigid scopes through the vagina, simulating a vaginal laparoscopy.

Colonic procedures were performed through a transrectal approach and were effective but not widely practiced.

Despite the loss of momentum in the late 2000s, a large number of NOTES procedures have been performed worldwide, mostly in the area of gastrointestinal surgery. Cholecystectomy through a transvaginal or transgastric approach has been the most popular operation performed to this day. Over a decade has passed since the introduction of this new technology. Unfortunately, the anticipated hype and potential have not been quite met. The hurdles that we faced at the introduction of this new technology remain the same more than 10 years later. But the focus of safer and less invasive procedures has not been lost. The lack of universal acceptance and application, as well as technical challenges, has stalled the technology. In comparison, laparoscopy has continued to evolve, and boundaries have been pushed beyond imagination.

But the lessons learned from NOTES have led to a revolution in endoscopic surgery. Although limited to the gastroin-

testinal tract, many of these modern procedures have evolved from technology and technical lessons learned from NOTES. Once again, patient safety and optimal outcomes have remained as the main objectives. Operations such as peroral endoscopic myotomy (POEM), endoscopic submucosal dissection (ESD), and peroral pyloromyotomy (POP) are direct descendants of NOTES. In the same fashion, colorectal surgeons have developed more advanced techniques such as transanal endoscopic microsurgery (TEMIS) which evolved from natural orifice surgery.

The expansion of NOTES has been significantly limited by medical technology available at this time. However, we have witnessed a tremendous growth of procedures that have derived from the origins of NOTES. Modern application of such techniques has evolved into a new concept of "intramural surgery." Operations such as POEM, ESD, TAMIS, and transvaginal gynecologic surgery have all derived from the concept of natural orifice interventions. NOTES will continue to evolve and expand, and unexpected indications and applications will continue to emerge. The future of these developments will depend on advances in the technology used for suturing, tissue division, hemostasis, and the overall application and accessibility of this technology. Many different technologies are currently being developed to try to fill gaps between feasibility and common application of NOTES.

Suggested Readings

1. Chukwumah C, Zorron R, Marks JM, Ponsky JL. Current status of natural orifice translumenal endoscopic surgery (NOTES). Curr Probl Surg. 2010 Aug;47(8):630–68. https://doi.org/10.1067/j.cpsurg.2010.04.002.
2. Giday SA, Kantsevoy SV, Kalloo AN. Principle and history of natural orifice translumenal endoscopic surgery (NOTES). Minim Invasive Ther Allied Technol. 2006;15(6):373–7.
3. Gumbs AA, Fowler D, Milone L, Evanko JC, Ude AO, Stevens P, Bessler M. Transvaginal natural orifice translumenal endoscopic surgery cholecystectomy: early evolution of the technique. Ann Surg. 2009;249(6):908–12.
4. Marks JM, Ponsky JL, Pearl JP, McGee MF. PEG "Rescue": a practical NOTES technique. Surg Endosc. 2007;21(5):816–9. (Surgical Endoscopy Springer Link) Manuscript , 4/3/2007.
5. Meining A, Feussner H, Swain P, Yang GZ, Lehmann K, Zorron R, Meisner S, Ponsky J, Martiny H, Reddy N, Armengol-Miro JR, Fockens P, Fingerhut A, Costamagna G. Natural-orifice transluminal endoscopic surgery (NOTES) in Europe: summary of the working group reports of the Euro-NOTES meeting 2010. Endoscopy. 2011;43(2):140–3. https://doi.org/10.1055/s-0030-1256128.
6. Nikfarjam M, McGee MF, Trunzo JA, Onders RP, Pearl JP, Poulose BK, Chak A, Ponsky JL, Marks JM. Transgastric natural-orifice transluminal endoscopic surgery peritoneoscopy in humans: a pilot study in efficacy and gastrotomy site selection by using a hybrid technique. Gastrointest Endosc. 2010 Aug;72(2):279–83. https://doi.org/10.1016/j.gie.2010.03.1070.
7. Ponsky JL, Kalloo AN, Pearl JP. How will NOTES influence gastroenterology? AGA Perspectives. 2007;3(2):4–5.
8. Rattner D, Kalloo A. ASGE/SAGES working group on natural orifice translumenal endoscopic surgery. Surg Endosc. 2006;20(2):329–33.

Part II

Procedure Units, Quality and Efficiency

How to Set Up an Endoscopy Center

44

Lavanya Viswanathan and Satish S.C. Rao

Introduction

As the landscape of global healthcare shifts from "volume-based care" to "value-based care," it is more essential than ever to think of each medical decision from a patient-centered care model. This principle is particularly important when planning a gastroenterology/hepatology procedural unit. The design should be thoughtful and comprehensive, ensuring that all gastroenterological procedures can be performed under one roof while preserving the highest standards of healthcare delivery.

Delivery of high-quality healthcare is as much about the infrastructure and aesthetics as it is about the personnel. When designing an endoscopy center, it is essential to plan a unit that complements the practice of endoscopists and hepatologists [1] within a thriving gastrointestinal unit.

In this chapter, we discuss a model approach for designing a gastroenterology procedure unit, primarily drawing upon our experience in designing a brand new endoscopy center from scratch. Clearly, the proposed design assumes there is space available and that it is a new project and not one of redesign or refurbishment as this will require a different approach. We have outlined the major areas of concern when planning an endoscopy center, but it is important to customize plans to fulfill individual operational needs.

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Designing a Gastrointestinal Procedural Unit

Location, planning, flexibility, and a team-based approach are essential for designing a successful center. In addition to the gastroenterologists and surgeons, who are the major stakeholders, the design team should include representation of several key players who are summarized in Table 44.1. It is also useful to create an advisory board comprising of senior leadership, key stakeholders, and outside consultants with experience in developing and operating an endoscopy center.

During the initial planning stages, it is critical not only to consider the current volume of patients and procedures (Table 44.2) but also to anticipate future needs and plan the space accordingly. For example, an endoscopy unit designed to serve a community will have different demands than an academic facility associated with a hospital. It is also important to look at every aspect of patient flow including the transitions from the check-in area, patient and family waiting lounge, preparation rooms and procedure rooms to the recovery suites, and checkout area. Planning should allow for a smooth transition between these various stations and, as far as possible, maintain a unidirectional flow while maintaining patient privacy throughout. It is also important to consider if this will only serve as an outpatient ambulatory center or a mixed unit that caters to both outpatients and inpatients. Finally, it is important to visit at least two to three endoscopy centers, as a team (gastroenterologists, architect, engineer, and endoscopy nurses) not only to learn about the optimal design but also to learn about missteps and design flaws that were not foreseen and how to avoid them.

The initial steps include developing a detailed business plan that outlines the immediate and projected needs of the procedural unit, discussing with the architects and engineers about an estimated budget outlay for the project, and applying for building regulations and permits. The next stage is to identify a proper location. Thereafter, the most critical step is

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Table 44.1 Design team members

Gastroenterologist
GI surgeon
Endoscopy nurses
Gastroenterology technicians
Motility nurses
Hospital epidemiology director
Safety officers
Patient representative
Anesthesiology director
Experienced architects and engineers
Equipment purchase consultants
Radiologist
Interior designers

Table 44.2 Common procedures performed in an endoscopy unit

Endoscopy/gastroscopy Endoscopic band ligation
Endoscopic stenting
Enteroscopy
Laser argon plasma coagulation and tumor ablation (Barryx)
Percutaneous endoscopic gastrostomy/jejunostomy
Videocapsule endoscopy Colonoscopy with water immersion and CO_2 inflation Polypectomy including complex polypectomy Achalasia/esophageal stricture dilation under fluoroscopy Deep/device-assisted enteroscopy or small bowel endoscopy Fecal microbiota transplantation (FMT) Endoscopic celiac plexus block/neurolysis Endoscopic mucosal resection (EMR) Endoscopic mucosal dissection (EMD) Endoscopic therapy for Barrett's esophagus Endoscopic ultrasound (EUS, both diagnostic and therapeutic) Endoscopic retrograde cholangiopancreatography (ERCP) Biliary/pancreatic stone extraction, stenting, and cyst gastrostomy Cholangioscopy Liver biopsy (percutaneous/transjugular) Fibroscan of liver

detailed and meticulous planning with the architectural team and innumerable revisions to the plan taking into consideration patient flow and aesthetics. This process can take many months, is painstaking, and can be exhausting, but ultimately is the most important step, as fixing design flaws is extraordinarily expensive and time consuming and can lead to significant delays in completing the project. The time spent with architectural designing is well worth the wait. Once the design is ready, the next step is to identify a suitable engineering firm to construct the project. This is also the time to seek the necessary permits such as certificate of need, which is a requirement in many states in the USA, and seek fire marshal and epidemiology approval. This initial process can take up to a year. Most importantly, the team should come up with a detailed timeline of the construction that is realistic and acceptable. Once the plans are ready and permissions secured, the actual construction process can begin, and this can take up to 18 months depending on the size of the project. So, from a timeline perspective, it can take between 2 and 3 years from inception to completion of a new endoscopy unit (Table 44.3).

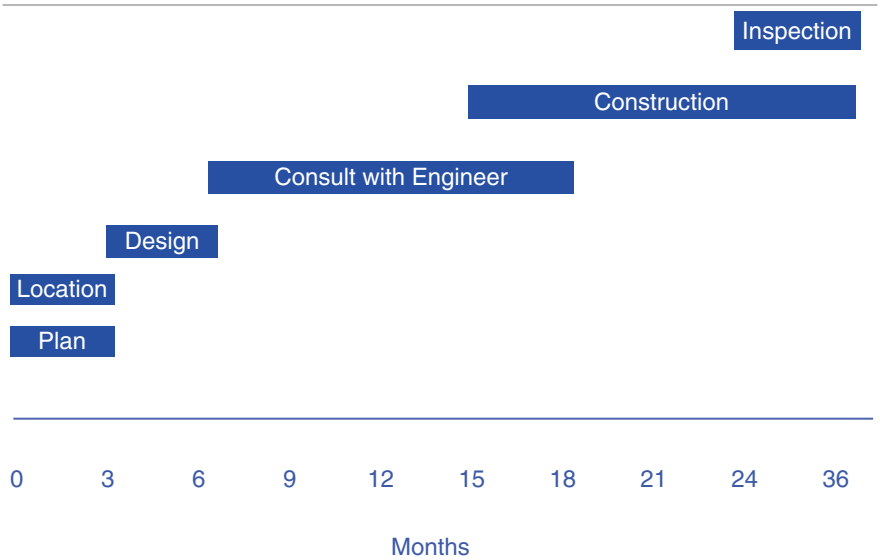
Key Elements of a Comprehensive Gastrointestinal Procedural Suite

A successful unit will encompass facilities that will provide an infrastructure for all aspects of GI care. Our outpatient GI endoscopy and motility center is housed within a 43,000 ft^2 purpose-built Digestive Health Center. This includes 22 bays, which include 12 patient preparation suites, 10 recovery suites, 6 spacious endoscopy rooms, 3 advanced endoscopy and fluoroscopy suites, a 5-room GI motility suite, nurses' station, endoscopy precinct, physician reporting room, anesthesiology room, and a staff lounge. It is unique in that it is a freestanding unit which includes an Outpatient GI Clinic and Administrative and Faculty Offices connected to each other on the same floor within the department. The entire unit is connected to the main hospital which facilitates easy transfer of inpatients for procedures and also to the intensive care unit in case of emergency.

Endoscopy Staff

One cannot overstate the importance of exceptionally trained staff to help make the endoscopy experience less stressful and more pleasant for the patient. When anticipating staffing needs, it is important to take into consideration the patient volume and number of procedures scheduled daily. Endoscopy is a team activity, and our staff prepare the patient for each procedure both physically and mentally [2]. Ideally, an endoscopy unit staffing plan should include an endoscopy manager and charge nurse in order to help with the day-to-day operation of the unit. According to Medicare guidelines, a registered nurse (RN) must be available on site during all hours of operation of a hospital or an endoscopy center [1]. Two staff members should be allotted per procedure room, and one must be a registered nurse (RN). For example, if there are five procedure rooms, ten staff members must be available at all times, of which five must be registered nurses. There should be a total of at least two RNs in the pre- and postoperative areas. Additionally, at least two endoscopy technicians should be assigned to endoscope/instrument reprocessing. It would be wise to hire nurse educators to help speak with patients both before and after procedures and to counsel them appropriately while going over physician recommendations in greater detail. Friendly, knowledgeable, and efficient staff who similarly believe in a patient-centered approach are essential to provide excellent patient care in an endoscopy center.

Table 44.3 Endoscopy unit planning timeline



1. Develop a business plan and select a location (3–6 months)
2. Design the unit with an architect or design consultant (3–6 months)
3. Work with an engineering consultant to obtain necessary permits and regulatory approvals before building (may take up to 1 year)
4. Construction (may take up to 18 months)
5. Final inspection
6. Move in

Patient Lounge (Waiting Room)

The patient experience starts when he/she walks into the waiting room to check in for the procedure. The waiting room should be conducive for the patient to mentally prepare for the procedure and should feel roomy, uncluttered, and inviting. This can be achieved by employing calming wall colors, neutral furniture, and vibrant wall art (Fig. 44.1). Literature regarding what to expect with each procedure should be readily available. Placing friendly well-dressed reception staff to greet the patient will serve to allay fears even before the patient is called back for the procedure. Short media clips shown on monitors that showcase successful patient stories and introduce individual faculty and team members can be very helpful.

Patient Preparation Suite

Once the patient is called for the procedure, he/she is led to the preparation suite (Fig. 44.2). Here, the patient undergoes the initial intake assessment and pre-sedation assessment by a gastroenterologist and anesthesiologist. If possible, invite the patient to bring his/her family member or friend to join and keep a few chairs in the room to facilitate this. It would be practical to have a few bariatric chairs available if needed. This area will look more aesthetically pleasing with wide-open hallways and spacious, well-lit rooms.

Most endoscopy preparation areas separate patients with cloth curtains. However, this does not allow for much privacy. Patients are already anxious while awaiting the procedure and can be negatively affected by hearing bad news from the next room or feel uncomfortable having a frank discussion with providers for fear of unintentionally disclosing personal details to a neighbor. This can be solved by separating individual patient suites with solid walls, which will also serve to maintain HIPAA compliance (Fig. 44.2).

The patient feels more welcome when greeted with a ready-made set of gown, socks, and a towel laid on the bed. A small locker should be available for patients to store belongings and valuables [3]. Similar to the patient lounge, consider painting preparation rooms with calming colors. One may consider a mural on the ceiling as the patient is usually lying on the bed. A television mounted high up on the wall can also help to distract and keep the patient occupied.

All equipment, such as the computer and other monitors, should be foldable and extendable so they can be flushed with the wall when not in use to make the room feel more spacious. Standard supplies such as gloves, sterile needles,

Fig. 44.1 Patient lounge area with open floor plan and vibrant wall art

Fig. 44.2 Preparation suite with solid walls, a mobile vital signs monitor, and chairs

vacuum, air, oxygen, and suction ports are mounted along the wall. Dual lighting features are also useful if the patient prefers to dim the room or is irritated by bright light. A unique feature of our endoscopy unit is our mobile vital signs monitoring which is mounted on the patient's bed and travels with the patient to provide continuous monitoring before, during, and after the procedure without interruption and feeds wirelessly and directly into the patient's electronic chart.

It is very important to have plenty of easily accessible bathrooms, especially for patients who have undergone bowel preparation before the day's procedure. The usual ratio is one bathroom per ten endoscopic procedures per day [1]. Our endoscopy center has 3 bathrooms for 12 preparatory rooms. It would also make better sense to place colonoscopy patients closer to the bathrooms. The central nursing hub should be strategically placed so that the nursing staff can keep a close eye on all patients and be easily accessible. Monitoring dashboards at the reception area and nurses' station allow nursing staff to give status updates to family members. Dashboards in the precinct serve to alert techs, nurses, and endoscopists as to when a patient is ready in the room for a procedure or when a procedure has been completed to facilitate efficient turnover for the next procedure.

Endoscopy Suites

The endoscopy area is generally the workhorse of any endoscopy unit. The number of procedure rooms is often determined by the case volume of the facility. Procedures require several personnel in addition to the endoscopist, specialized equipment, and essential paraphernalia every day. A standard endoscopy suite is between 145 and 300 ft^2 in size depending on whether anesthesia is needed for the procedure, but if more room is allowed, it can make setup and movement more convenient for both the patient and medical staff [1]. All personnel should be able to move comfortably around the patient at any time during the procedure. All doors should be wide enough for the patient's bed to go through comfortably. Use wall space with labeled shelves to easily access necessary supplies. Plan accordingly to place a counter just behind the assistant so he/she does not need to go far to collect and prepare biopsy samples or procure endoscopic accessories during the procedure. There should be an OSHA-approved sink with sink guard to avoid contaminating samples [5, 6]. A large mounted screen on the wall will make it easy to watch during the procedure (Fig. 44.2). Place the monitor at a comfortable height so as to avoid being blocked by other staff in the room but can be tilted to avoid strain on the endoscopist. It is worth considering installing the more recent panoramic 330 or 360° view scopes and equipment as compared to the traditional, forward-viewing 170° viewing endoscopes that could miss lesions. The oxygen delivery system and other essential gadgets should not interfere with a free movement in the endoscopy room. It is essential to maintain silence and unnecessary conversation to minimum during procedures.

Confocal microscopy and cholangioscopy are another promising advancement which may allow us to make tissue diagnoses during endoscopic investigation. Procedure suites should have a crash cart strategically located and available to facilitate rapid resuscitation.

Traditionally, air is infused through the endoscopes for luminal distension during a standard endoscopy. However, air escapes into the bowel and cannot be sucked out adequately, often leaving the patient with a distended abdomen that can be uncomfortable, especially when performing prolonged and difficult procedures. However, the use of CO_2 which is fully absorbed, as opposed to air, will obviate this undesirable problem. Consider installing piped CO_2 gas in each room along with air, vacuum, and oxygen (Fig. 44.3). This is likely to become an industry standard in the future. Adequate number of outlets for power and for oxygen, air, and suction preferably at two locations within each room is desirable. Ideally, the anesthesiologist should be involved in designing these outlets.

Importantly, during the construction stage, attempts should be made to mock an entire procedure to systematically examine the logistics and flow during endoscopic procedures. Special attention should be paid to how room setup is affected when the patient is turned around within the procedure room. A trial run should be done to test patient flow from the preparation suite to the recovery suite with all key personnel, so as to remedy any problems with room design and flow. Also in academic training facilities, scope guides can be useful to learn how to minimize loops when advancing a colonoscope. Finally, placing two computer stations side by side for use by a trainee and staff physician or nurse to review electronic medical record information, radiographs, or document, the endoscopy findings in a timely manner can be useful (Fig. 44.4).

Advanced Endoscopy Suites

Advanced endoscopy suites are essential for modern procedure units and facilitate performance of more invasive diagnostic and therapeutic measures for pancreatobiliary and other common conditions. Because fluoroscopy is involved, it is crucial to keep safety and function in mind when planning this area. The room should be bigger than a standard endoscopy room, usually 250–350 ft^2, and must be carefully designed using simulations to accommodate the fluoroscopy units, the Berchtold-like beams, so that equipment can be moved around depending on the needs of each case. Newer GI-dedicated fluoroscopy units such as Omega Systems may be preferred because of their unique features over conven-

Fig. 44.3 Endoscopy suite with large adjustable wall monitor, wall-mounted air, vacuum, oxygen, and pipe CO_2 (insert)

Fig. 44.4 Endoscopy suite with physician workstation, endoscopy cart, and specimen collection area

tional fluoroscopy units, although the latter can be adapted. The rooms must be lead-lined for protection from radiation exposure. Create an area outside the rooms for lead shields so that staff can hang their coats securely and wear their shields before entering the rooms (Fig. 44.5). Alternatively, radiology lead shield screens can be set up in the room for those who do not wish to wear lead protection.

While standard endoscopes such as the gastroscope, enteroscope, colonoscope, and sigmoidoscope are all forward-viewing instruments, advanced endoscopic proce-

Fig. 44.5 Area for hanging lead vests, used for fluoroscopic procedures

Fig. 44.6 Advanced endoscopy suite with C-arm. Diathermy (*A*), fluoroscopic image monitor (*B*), endoscopic image monitor (*C*), nursing documentation computer (*D*), boom (*E*), anesthesia cart (*F*), fluoroscopy bed (*G*)

dures require more specialized equipment. For example, the duodenoscope is a side-viewing endoscope designed for use in ERCP, primarily. They are equipped with an elevator lever positioned at the opening of the accessory channel and maneuvered by a cable operated from the control section. A cholangioscope is a thin caliber endoscope that is passed through the instrument channel of a duodenoscope and inserted intraductally for direct imaging of the biliary and pancreatic ducts. Echoendoscopes are a hybrid instrument that combines flexible endoscopy with high-resolution ultrasound imaging.

Rooms can have ceiling-mounted, moveable booms or fixed systems per preference and should be large enough to comfortably fit a fluoroscopy bed, C-arm, anesthesia equipment, as well as all personnel and the patient. Separate display monitors for fluoroscopy, endoscopy, and ultrasound images that can be appropriately placed per endoscopist's preference during the procedure are recommended (Fig. 44.6). All display

Fig. 44.7 Advanced endoscopy suite with fluoroscopy bed (*A*) and multiple cameras (*B*) for video transmission for teaching purposes

screens can be controlled with a master remote if any particular image needs to be highlighted to others in the room. Specialized fluoroscopy beds for optimal imaging during the procedure are available as are jackknife beds for better patient positioning. Tertiary care centers may incorporate strategically positioned cameras to transmit procedures for training and CME purposes (Fig. 44.7). Plenty of lockable storage space should be allocated for easy access to accessories needed during the procedure.

Recovery Suite

A recovery suite is necessary to monitor patients after the endoscopic procedure. In keeping with unidirectional flow, the preparation, endoscopy, and recovery suites can be arranged in a horseshoe pattern to efficiently utilize space. While the recovery bed capacity is a notorious bottleneck in most endoscopy units, it is important to plan a ratio of at least one recovery bed per procedure room, with the ideal ratio being 1:2.5 [5, 6]. For example, for 5 endoscopy suites, there should be 13 recovery rooms. The preparation and recovery suites should be in close proximity to a medication preparation room containing intravenous fluids and controlled drugs and the central nurses' station. This makes it easier for staff to keep an eye on either suite as the day progresses. The recovery side has fewer bathrooms than the preparatory side but can otherwise be similar in design. Additionally, one room should be built with negative pressure ventilation, as an isolation unit for patients with serious communicable diseases.

Motility Laboratory Suite

The advantage of having a comprehensive GI motility laboratory is to study the pathophysiology of various neurogastroenterology and motility (NGM) disorders [7, 8]. These disorders affect 40% of the population. Consequently evaluation of NGM disorders is an essential component of the diagnostic spectrum of GI evaluation [7, 8]. Ideally, this should be located adjacent to a GI procedural suite for optimal convenience, both for the patient and the physician, and to facilitate performance of both motility and endoscopy procedures that may be needed in some patients. A comprehensive motility laboratory requires specific planning to have an organized approach to specific testing. Separate rooms for performing upper and lower GI motility procedures are preferable. A room dedicated to performing hydrogen and methane breath tests with a place to analyze breath samples and another room for patients to sit comfortably and collect breath samples over 3–8 h will help with both the accurate administration of testing and patient comfort.

Table 44.4 Procedures commonly performed in motility unit

Esophageal and impedance manometry
Ambulatory pH monitoring
Esophageal balloon distension test
Breath hydrogen and methane testing (glucose, fructose, lactose, fructan)
24-h gastric-duodenal manometry
24-h colonic manometry
High-resolution or 3-D anorectal manometry
Translumbar and transsacral motor evoked potential test
Biofeedback therapy for chronic constipation and fecal incontinence
Repetitive translumbar/transsacral magnetic stimulation therapy
3-D and pelvic ultrasound
Gastric and rectal barostat (sensation/tone/compliance)
Wireless motility capsule
Esophageal and rectal distensibility/compliance (EndoFLIP)

A motility testing room must be a minimum of 150–200 ft^2 and should contain a comfortable and well-padded exam bed that can be converted into a chair if needed and can be easily raised or lowered. The lab must be equipped with the appropriate equipment to perform studies [6]. Because motility procedures are performed without sedation, and these patients are often anxious and nervous, wall colors and decorations should be aesthetically appealing to put the patient at ease. A private bathroom within the motility laboratory is preferable, especially for anorectal studies.

The minimum testing capability needed to be considered a motility laboratory includes esophageal manometry, esophageal pH monitoring, and anorectal manometry [7, 8]. Of course, more specialized centers may include more sophisticated equipment according to the needs of the patient population. In a comprehensive digestive disease center like ours, for example, the laboratory offers other diagnostic tests such as breath testing and wireless motility capsule test for assessment of regional and whole gut transit [7, 8] (Table 44.4). Finally, a dedicated nurse and/or technician is needed to perform the appropriate testing. This person should have the right temperament and must be compassionate and patient.

Endoscope Maintenance and Storage

Endoscopic equipment can either be purchased or leased depending on the institution and available resources. Ideally, reusing fewer instruments efficiently is less costly than purchasing a large inventory of instruments that are largely underused. It is recommended to allocate one colonoscope, gastroscope, and sigmoidoscope for every 350 procedures each year; one duodenoscope and endoscopic ultrasound (EUS) scope for every 150 procedures per year; one light source and processor per endoscopic procedure room; and one scope reprocessor for every 1000 procedures per year. At least one pediatric scope should be available. It may not be economical, for example, to purchase instruments that would be infrequently used or would require a specific skill set not represented by the endoscopist. In high-volume endoscopy centers, it is usually more cost-effective to buy rather than lease equipment.

Fig. 44.8 Endoscopic aerator for storage of endoscopes

There should be easy access to the central endoscopy precinct where clean scopes are vertically hung and displayed. Employ an aerator to keep scopes dry and increase the longevity of the equipment [2] (Fig. 44.8). This area can also store equipment such as various stents and more specialized instruments needed for more advanced cases.

Blanket warmers can be placed in this central area if patients need warm blankets during the procedure. A refrigerator dedicated to the storage of fecal samples for use of fecal microbiota transplantation may be useful in the storage area.

Finally, adequate storage space should be available within the endoscopy suite, preferably 1–2 small rooms, where less commonly used equipment and ancillary equipment can be stored to declutter the endoscopy unit.

Endoscope and Instrument Cleaning and Sterilization

With increasing reports of endoscopically transmitted infections, it is important to design separate endoscopy cleaning and sterilization rooms and to ensure a unidirectional flow of soiled equipment from the endoscopy room to the scope cleaning room and from there to the sterilization room and back to the storage precinct. Unidirectional flow must be maintained in order to prevent cross-contamination and maintain hygiene of both the scopes and the rooms. A window separating soiled from clean areas should be available to prevent contamination. The endoscopy cleaning room should be stocked with the appropriate equipment and supplies for cleaning and disinfection of endoscopes and accessories [6]. Cleaning areas should have adequate ventilation to protect the staff per OSHA guidelines and be effectively sealed from the rest of the facility to keep infection contained [4]. Maintaining an organized flow is important to avoid introducing infectious pathogens to the patients.

Family Consultation Room

Although every precaution is taken to minimize risks and provide a positive experience for each patient, adverse events do occur and are a reality in an endoscopy suite. For this reason, each facility should have a quiet, private room away from the hustle and bustle of the endoscopy center. The room should be large enough for the provider, staff member, patient, and family to sit and discuss significant results or adverse events without the restriction of time or interruptions.

Provider and Staff Areas

Staff should have a designated lounge in which to convene, eat meals, and relax. This also serves to keep staff interactions private and provide a space to unwind and build collegiality between members of the team. Ideally, this should be located in a peripheral area which does not have cross traffic between patient areas to maintain privacy.

Summary

A meticulously designed and comprehensive gastrointestinal procedural suite will provide a positive experience for both the patient and family who are often apprehensive in getting a procedure. Also it reassures and comforts them that they are in the safe hands of a thoughtful and compassionate team. A positive working and learning environment will lead to increased efficiency in the workplace and a more pleasant experience for patients and staff. A properly designed endoscopy unit can provide the "value-based care" ideal that we should all strive to provide as healthcare providers.

References

1. Ginsberg GG, Gostout CJ, Kochman ML, Norton ID. Clinical gastrointestinal rndoscopy. 2nd ed. Philadelphia: Elsevier Saunders; 2005.
2. Cotton PB, William CB. Practical gastrointestinal endoscopy the fundamentals. 5th ed. Malden: Blackwell; 2003.
3. American Society for Gastrointestinal Endoscopy. Establishment of gastrointestinal areas. Gastrointest Endosc. 1999;50:910–2.
4. American Gastroenterological Association. AGA standards for office-based gastrointestinal endoscopy services. Gastroenterology. 2001;121:440–3.
5. Wayne JD, Aisenberg J, Rubin PH. Practical colonoscopy. West Sussex: Wiley Blackwell; 2013.
6. Larson DE, Ott BJ. The structure and function of the outpatient endoscopy unit. Gastrointest Endosc. 1986;32:10–5.
7. Parkman HP, Orr WC. The gastrointestinal motility laboratory. Gastrointest Endosc Clin N Am. 2009;19:171–84.
8. Rao SSC, Parkman HP. Advanced training in neurogastroenterology and gastrointestinal motility. Gastroenterology. 2015;148(5):881–5.

Sedation and Monitoring in Endoscopy

45

Gajen Perry, Edward Gibson, and Rajvinder Singh

Introduction

The following chapter offers a comprehensive description of the role and methods for sedation and monitoring of a patient during endoscopy. It examines the current practices and guidelines produced by various gastroenterology societies and reviews several newer options and their possible suitability in different clinical situations.

Endoscopy is an invasive procedure that can produce pain and discomfort. It often requires adequate sedation, or even general anaesthesia for successful completion. This becomes even more important during advanced endoscopic procedures such as EUS or ERCP which can be especially uncomfortable for the patient and often take longer. Not only do patient and proceduralist satisfaction scores improve following the administration of sedation, but procedural efficiency and success also increases.

Procedural sedation and/or analgesia as it pertains to endoscopy, refers to a drug-induced tolerance of the pain and discomfort associated with the procedure [1, 2]. Desired outcomes include amnesia of distressing events and adequate analgesia [1]. The aim is not a total lack of response to painful stimuli, but rather to facilitate the completion of a planned medical procedure while maximizing patient comfort [1]. In order to accomplish this, it is often necessary to use a range of sedation options during a single procedure. Although it may seem in some circumstances that no sedation, or light sedation would be suitable for a given procedure, patient factors or proceduralist preferences may warrant a more profound level of sedation and/or analgesia [1, 2].

Sedation/Analgesia

Sedation exists as a spectrum and can range from conscious to deep [1]. Conscious sedation is a drug-induced state of decreased consciousness during which patients are able to maintain airway patency, spontaneous ventilation and cardiovascular function [1]. Conscious sedation can be achieved through a variety of drugs including propofol, benzodiazepines and/or opioids. These drugs are sometimes used alongside local anaesthetic agents [1]. The primary goal of conscious sedation is to maintain a safe environment in which loss of consciousness is unlikely [1]. Deeper sedation by contrast, is a drug-induced state of decreased consciousness that can rapidly progress to unconsciousness, during which time patients are only able to respond to painful stimuli [1]. Consequently, it is often associated with loss of airway protection, inadequate ventilation and/or impaired cardiovascular function [1, 2]. The risk profile is similar to that of general anaesthesia and thus requires an equivalent level of support [1, 2].

Analgesia refers to the elimination, or at least impairment, of pain perception [1]. The drugs used to achieve this can act locally, by interrupting nerve conduction, or generally, by inhibiting the central nervous system's ability to process pain [1]. There are a wide variety of medications that can be used for this purpose including lignocaine, methoxyflurane or nitrous oxide [1]. General anaesthesia is a drug-induced, total loss of consciousness and perception of pain [1]. It is characterized by a complete lack of meaningful response to any stimulus, loss of all protective airway reflexes, and significant depression of respiratory and cardiovascular function [1]. General anaesthesia requires the presence of an anaesthetist, or other appropriate trained and credentialed medical specialists [1, 2].

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It is important that all medical practitioners administering procedural sedation and/or analgesia understand that it exists as a continuum and that the progression from complete consciousness through to general anaesthesia is not defined by discrete stages [1, 2]. The effect, and associated margin of safety of the drugs in sedation and/or analgesia vary between patients and the transition from sedation to loss of consciousness can be swift and unexpected [1]. Therefore, the administration of sedative or analgesic drugs requires the ability to anticipate and manage a number of potential risks including: depression of protective airway reflexes and loss of a patent airway; depression of cardiorespiratory function; drug interaction or adverse reactions, including anaphylaxis; or increased sensitivity to administered drugs [1]. It is also vital that the practitioner be able to dynamically alter the level of sedation and/or analgesia as needed by the proceduralist and/or patient [1].

Practical considerations

- Sedation is a spectrum, ranging from conscious to deep.
- Deep sedation is often associated with a loss of airway protection and impaired ventilation/cardiovascular function.
- Analgesia is the reduction, or elimination, of pain perception.
  - It can act peripherally on local nerves or ventrally on the brain and spinal cord.
- General anaesthesia is drug-induced total loss of consciousness and perception of pain.
- Any practitioners who administer sedation or analgesia must be trained to anticipate and manage all potential risks.

Propofol

Propofol is a short-acting sedative drug first introduced in the 1980s for the induction and maintenance of anaesthesia [3]. It has some amnesic properties but is completely devoid of analgesic effects [3]. Much of the controversy surrounding propofol and its use by non-anaesthetists has to do with an American Food and Drug Administration product label indicating that propofol "should be administered only by persons trained in the administration of general anaesthesia." [3] This warning along with its ability to produce apnoea or general anaesthesia, without a specific reversal agent led to propofol's restriction to anaesthetists/intensivists [3, 4]. However, since that time worldwide interest in propofol has expanded rapidly, and its uses now include monitored anaesthesia care (MAC) and procedural sedation [3]. Propofol uptake among proceduralists has been so fervent in part because it provides more rapid induction of sedation, quicker recovery and faster discharges than traditional methods of sedation and/or analgesia [3–6]. In fact, as both monotherapy, and in combination with low-dose opioids, propofol use leads to lower rates of cardiorespiratory complications [2, 7]. When compared to the more traditional regimen of midazolam-fentanyl, propofol-fentanyl combination therapy achieves deeper sedation more often while maintaining shorter induction, recovery and discharge times. Even in children, propofol has been shown to provide better procedural analgesia, via an amnesic effect, and behavioural control as compared to midazolam [6]. The role of propofol in procedural sedation during endoscopy is well established and is now being used routinely by anaesthetists, proceduralists and specially trained nursing staff, largely replacing the 'traditional sedation' regimen of benzodiazepines with or without opioids [3–7].

Non-anaesthesiologist-Administered Propofol Sedation

Endoscopist-directed propofol sedation (EDP) or non-anaesthesiologist-administered propofol (NAAP) has been shown to be a safe and effective alternative to traditional methods for a number of years [7]. A landmark international study in 2009, looking at over 640,000 cases found that EDP had a mortality rate which was lower than endoscopist-delivered benzodiazepines with or without opioids, and comparable to that of general anaesthesia administered by anaesthetists [7]. Worldwide experience has identified a role for NAAP in low-risk patients [3, 6]. In fact, many of the main endoscopy and anaesthetics societies around the world now recognize the role of, and establish the guidelines for NAAP in gastrointestinal endoscopy [1, 6]. The safe use of propofol by non-anaesthetists is true for both monotherapy and combination therapy regimens [7]. More specifically there is a wealth of evidence showing that NAAP is equivalent to, or safer than, standard sedation with respect to hypoxia, hypotension and bradycardia during upper endoscopy and colonoscopy [3, 6]. Much of the evidence for NAAP has been demonstrated primarily in low-risk patients, however more recent work has found it to be a safe and effective alternative in carefully selected average- and high-risk patients as well [6]. In these patients, a weight-based propofol dosing system resulted in a lower rate of complications, faster recover times and higher patient/proceduralist satisfaction ratings [6]. New evidence suggests that propofol's safety and efficacy remains true even for more complicated, lengthier procedures like EUS and ERCP, however this requires further research [2, 6].

The European Society for Gastrointestinal Endoscopy (ESGE), European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) and the European Society of Anaesthesiology published a guideline on non-anaesthetist administration of propofol in 2010 [2]. At that time the evidence, and thus their recommendation, was strongly in favour of NAAP as a safe and effective standard for procedural sedation [2]. Those guidelines have since been updated by the ESGE and ESGENA in 2015, at which time their recommendation of NAAP has grown stronger [2]. The European guideline concludes that NAAP is safe and found that propofol-based sedation showed similar rates of adverse effects, better and quicker sedation, greater patient cooperation, increased post-procedural patient satisfaction and decreased recovery/discharge times [2]. Specifically, when looking at hypoxia and hypotension, multiple meta-analyses have shown no significant differences between propofol-based and traditional sedation [2, 3]. Rather, it was found that fewer cardiorespiratory complications occurred with propofol [2, 3, 6].

A more specific version of NAAP is nurse-administered propofol sedation (NAPS) which is rapidly expanding throughout Europe [2, 6]. NAPS was first introduced in 2003 in the United States [6]. It originated as a protocol, designed in conjunction with an anaesthetist, whereby propofol was administered as monotherapy, in bolus form, by trained registered nurses under the supervision of a physician proceduralist [6]. When accompanied by the requisite training, and instituted according to established protocols, NAPS in properly selected patients has been shown to be safe [6]. Evidence now confirms that NAPS can be used in more advanced EUS and ERCP as well, however higher than average propofol doses may be required [8]. The safety of NAPS can be bolstered further using techniques such as target-controlled infusion (TCI) [4]. The combination has been shown to be more effective, and associated with lower rates of adverse events than manually controlled infusions [4]. TCI will be covered further in the section regarding the administration of propofol sedation.

Beyond the recognized safety and efficiency of NAAP, its use carries significant implications for procedure cost [2]. A study of the cost-effectiveness of endoscopist-directed propofol versus the traditional anaesthetist-led model in the setting of colorectal cancer screening, found that anaesthetist involvement in colonoscopy can increase the procedural cost by 20% [2]. This amounts to a potential savings of $3.2 billion in the United States alone [2].

Method of Administration

In the event of non-anaesthetist-administered sedation and/or analgesia, propofol monotherapy is the preferred regimen [2]. There is no evidence that additional drugs (benzodiazepine/opioid/ketamine) lead to a decrease in adverse events, however they can decrease the overall dose of propofol required [2]. Low-dose midazolam can also help facilitate intravenous line placement particularly in children, the highly anxious or patients suffering from dementia [4, 9]. This combination therapy is referred to as balanced propofol sedation (BPS), consisting of propofol with low-dose opioids or benzodiazepines [4]. The aim of BPS is to counteract the narrow therapeutic range and associated risk of apnoea when propofol is used in painful procedures [4]. As propofol has no analgesic properties, for certain procedures, BPS enhances the effectiveness of sedation while allowing lower doses of individual drugs [4].

It may be best to administer the propofol via intermittent bolus infusion or perfusor systems, such as TCI [4]. This is an automated system which employs pharmacokinetic modelling to determine optimal drug infusion rates [4]. TCI takes into account patient age, weight and desired plasma propofol concentration [4]. The advent of TCI has eliminated the peak concentrations caused by bolus infusions, and has been shown to be effective in avoiding over- and under-sedation [5]. It has been shown to be the sedation regime most effective at reducing the dose of sedative agents [4]. As such, its use in NAAP and NAPS is linked to shorter recovery time despite maintaining similar levels of sedation [4]. To increase the safety profile, it is recommended to establish an upper limit to the propofol target in TCI, reducing the risk of sudden respiratory depression in patients who prove difficult to sedate [4]. Similarly, the use of computer-assisted personalized sedation (CAPS) devices with propofol administration has been demonstrated to produce equivalent levels of sedation, with no change in rates of adverse events, when comparing proceduralist-led teams with the traditional anaesthetist-led model [10]. There is a growing body of evidence that for certain patients and procedures (e.g. ERCP), patient-controlled sedation (PCS) allows for decreased doses of propofol, lower sedation levels, similar patient satisfaction scores and shorter discharge times [2]. As with patient-controlled analgesia (PCA), patient factors such as confusion, age and comprehension will play a significant role in the suitability of PCS [2].

In select patients, such as those with mild to moderate COPD, intermittent bolus infusion of propofol/midazolam has proven more effective and safer, with less respiratory compromise than continuous infusions [2]. During the use of intermittent bolus infusion, titration must be based on assessments of the patient's sedation [2, 11]. In the event of stable vital signs, movement (extremities, eyebrows, noise making), respiration (depth and frequency) and time (respirations remaining stable for prolonged periods) are examples of the criteria used to determine the need for further propofol boluses [2, 11]. Titration of propofol based on movement/sounds (event dosing) is recommended for the experienced nurse, while time-based dosing, or a combination of both, is recommended for the inexperienced nurse [2, 11].

Pre-procedure Selection/Assessment

As with all procedures, it is essential that informed consent be obtained from the patient, or a person entitled to consent on behalf of the patient, as per applicable local legislation [1]. Where possible, the patient should be provided with written information outlining the nature of the procedure, associated risks, preparation instructions and what to expect on completion including immediate- and long-term recovery (after discharge) [1]. This can often be done in the setting of a preadmission clinic during which time the patient can be further assessed [1].

All patients must be assessed before procedural sedation and/or analgesia is undertaken, including a detailed history, examination and review of relevant investigations [1, 2]. The nature of the procedure and the patient's risk factors must be taken into consideration before determining the nature of sedation and/or analgesia required [1]. The history should include the current problem for which the patient is undergoing the procedure, all pre-existing medical/surgical comorbidities, any previous sedation and/or anaesthesia, current medications, allergies, last meal and exercise tolerance or functional status [1, 2]. The patient should be examined with respect to their airway, including false/damaged/loose teeth, their Mallampati score, respiratory and cardiovascular function and any other systems identified as potential problems during the history [1, 2].

The aim of the assessment is to identify those patients who are at increased risk of airway, respiratory or cardiovascular compromise during the course of procedural sedation and/or analgesia [1, 2]. These patients include, but are not limited to: the extremes of age, those less than 2 years old, and the elderly; patients with significant cardiovascular, cerebrovascular, respiratory, hepatic or renal disease; morbid obesity; a history of stridor, snoring or obstructive sleep apnoea; a history of difficult intubation or suspicion of the same due to facial/oral abnormalities, limited neck or cervical spine mobility; active gastrointestinal bleeding particularly if causing shock; severe anaemia; high risk of aspiration of gastric contents; and patients who may be tolerant to sedative agents [1, 2]. The patients belonging to the aforementioned list, or those with ASA or Mallampati scores ≥ 3, warrant the presence of an anaesthetist during the procedure, or at the very least a referral to a high-risk anaesthetic preadmission clinic [1, 2].

Training

Training is crucial to the institution of NAAP as there is strong evidence to show lower sedation-related complication rates among advanced experience level nurses (≥ 100 NAAP procedures) [2]. Endoscopists and registered nurses have been shown to be good candidates for training in NAAP however, given the difference in experience and knowledge between nursing staff and medical officers, it may be appropriate to offer separate training programmes for both parties [2, 3, 11]. In general, NAAP training courses should include theoretical and practical components, with both being assessed via examination [2].

Bases on experience in ALS/ACLS training, multifaceted interdisciplinary programmes are more effective than single interventions or unstructured, self-directed learning [3]. Training should consist of didactic teaching, airway workshops, simulation training and preceptorship [3]. Didactic teaching should include an in-depth overview of propofol covering its pharmacology and dosing [3]. The discussion should cover propofol's role in the continuum of sedation and the pre-procedural, intra-procedural, and post-procedural patient assessments required for its use [3]. Background study is recommended as an adjunct to all structured teaching [3]. All participants should be required to obtain a passing score on an examination that assesses their understanding and knowledge of all concepts taught [3].

The airway workshop should teach all practitioners to recognize and manage airway and ventilation complications [3]. This should include airway assessment, manual airway manoeuvres, the use of oral and nasopharyngeal airways, and bag-mask ventilation [3]. It is important as part of the airway skills that all NAAP practitioners have undertaken BLS/ALS prior to commencement [3]. During the workshop, advanced monitoring in the form of cardiac telemetry and capnography can be reviewed [3]. Using high-fidelity patient simulators, clinical scenarios can be reproduced in the simulation lab to provide opportunities to manage critical events [3]. Instructors can observe teams enacting a clinical situation and on its completion facilitate a discussion around the process, debriefing any significant errors [3]. Preceptorship under the stewardship of an anaesthetist, or appropriately qualified proceduralist, is recommended for any institute commencing propofol sedation regimens [3]. Following the initial programme, there should be a schedule of periodic refresher courses for all NAAP practitioners, similar to the strategy employed by ALS2 [3].

Prior to the institution of NAAP, it is recommended that local guidelines are developed in conjunction with the Department of Anaesthetics [11]. International experience shows that the combination of protocols and the associated training programmes leads to improved efficacy of sedation and lower complication rates [2, 3, 11]. In an ideal setting, a unified set of national, or even international, guidelines and training courses should be developed, and endorsed, by endoscopic/gastroenterological and anaesthetic societies [2, 3, 11].

Practical considerations

- Propofol is a short-acting sedative drug, completely devoid of analgesic properties.
- While initially only used by anaesthetists/intensivists, it has gained popularity as the drug of choice for nurse/proceduralist administered anaesthesia.
- It allows more rapid induction of sedation, quicker recovery and faster discharges.
- Non-anaesthesiologist-/anaesthetist-administered propofol (NAAP) has been proven to be a safe and effective alternative to traditional methods of sedation.
- Many of the main endoscopy and anaesthetics societies around the world recognize the role of and have established guidelines for NAAP in gastrointestinal endoscopy.
- There are many methods of propofol administration including balanced propofol sedation (BPS), target-controlled infusion (TCI), computer-assisted personalized sedation (CAPS) and patient-controlled sedation (PCS).
- Prior to any sedation administration, it is important that all patients be carefully interviewed and examined, particularly with regard to their cardiovascular function and airway risk.
- Training is absolutely crucial for all health professionals who are administering sedation/analgesia during gastrointestinal endoscopy.
- Training should include theoretical, practical and preceptorship components.
- Institutional/local guidelines should be established to guide NAAP.

Non-propofol-Based Sedation

There are numerous different medication options that can be used for procedural sedation instead of, or as an adjunct, to propofol. Multiple factors such as the patient, proceduralist and facilities available will dictate when and which of these options are utilized. It is important to note that sedation options are continuously evolving as newer medications and techniques come on to the market every year and the most common, widespread and well researched are detailed here.

Opioids

This class of medications act on multiple receptors within the CNS to provide analgesia and sedation [12]. There are multiple options and routes of administration, but typically intravenous fentanyl is used because of its rapid onset and short duration of action [13–15]. Other options, such as pethidine and morphine, have fallen out of favour due to their side effect profiles and longer half-lives [12–14]. Fentanyl also has a better cardiorespiratory toxicity profile when compared with morphine [12–14]. The therapeutic window is relatively consistent but can be affected by renal failure and opioid tolerance [12–14]. Side effects include respiratory depression and cough reflex suppression, which can have disastrous consequences [12–14]. Usually opiates are used in conjunction with another agent, such as propofol or a benzodiazepine, to provide analgesia, while the paired agent provides sedation.

Benzodiazepines

Benzodiazepines exert their class effect by binding to inhibitory receptors in the CNS, which potentiate gamma-aminobutyric acid (GABA) mediated chloride influx [12]. Through this mechanism, benzodiazepines can induce sedation, amnesia and provide an anticonvulsant effect but do not exert an analgesic effect [12]. As such, benzodiazepines are often combined with an analgesic medication such as an opioid like fentanyl. Unfortunately, the cardiopulmonary depressing effects of benzodiazepines are potentiated by opioids, and patients need to be closely monitored during and post-procedure [12–14]. Typically, midazolam is the medication of choice, due to its rapid onset, short half-life and relatively safe profile in most patient populations [12–14].

Ketamine

Ketamine induces a dissociative state and, by partial agonism of opiate receptors, analgesia, such that numerous procedures can be completed in relative patient comfort [15, 16]. The dissociative state may render patients unable to speak or follow commands but respiration and airway reflexes are left intact, although not necessarily protective, at procedural sedation doses, highlighting ketamine's utility in emergent situations where fasting is not assured and rapid sedation is required [15, 16]. However, ketamine does have a significant side effect profile including cardiovascular and respiratory stimulation, and should therefore be avoided in patients who are unable to accommodate acute hypertension [16]. It is also important to note that ketamine can cause an increase in oral secretions and appropriate facilities for monitoring and management of this are required. Yet the most important side effect of ketamine, which is observed in approximately 10–20% of adult patients, is emergent delirium, which is typified by confusion, hallucinations, excitement and irrational behaviour, and can last for several hours

[16]. Interestingly the emergent reaction is not commonly observed in the paediatric population, those under the age of 16, and it is therefore, commonly used for procedural sedation in this group [15, 16]. Intravenous use of ketamine has a rapid onset of action, approximately a minute, and lasts for 15 min. Intramuscularly use gives a longer duration of action, approximately 30 min, although it can be painful and takes 3–5 min for onset of action [15, 16].

Nitrous Oxide

Nitrous oxide (NO) is an inhaled gas that can be safely used for procedural sedation to manage pain and pre-procedure anxiety [17]. The mechanism of action of NO appears to be multifactorial with stimulation of release of endogenous opioids responsible for the analgesic effect, while activation of the GABA receptors in the CNS appears to cause the anxiolytic properties [17]. The gas is excreted from the lungs and, due to the risk of diffusion hypoxia from the high solubility of NO, it is important to administer oxygen following cessation of sedation [17, 18]. Nitrous oxide does cause a mild decrease in cardiac output but also results in an increase in peripheral resistance, which works to maintain the blood pressure [17, 18]. There is minimal impairment of airway reflexes but aspiration remains a risk with deeper sedation. NO is not commonly used for sedation in endoscopic studies but there is research supporting its use as an adjunct with other sedative medications. It remains popular for use in procedural sedation, particularly for paediatric patients, due to its ease of use, rapid onset of action, excellent side effect profile and rapid recovery time [17–21].

Practical considerations

- Opioids, benzodiazepines, ketamine and nitrous oxide are alternatives to propofol for gastrointestinal endoscopy sedation.
- Each has unique properties and health professionals must be trained appropriately for each drug.

Staffing

In general, there should be at least three appropriately trained staff present during the administration of procedural sedation and/or analgesia [1]. An exception is made for those instances using inhaled methoxyflurane/nitrous oxide, or low-dose oral sedation in low-risk patients [1]. In all other cases the team should consist of the proceduralist, the practitioner who will administer sedation and subsequently monitor the patient and a minimum of one staff member to assist either party as needed [1]. All members of the sedation team, nursing and physicians alike, should engage in training and have some previous experience in sedation [1]. In the case of a general anaesthetic, there must be a staff member to assist the anaesthetist at all times during the procedure [1]. As part of patient selection, as previously discussed, all those with ASA ≥3, Mallampati scores ≥3, other factors that predispose them to airway obstruction, along with those who chronically use narcotic analgesia warrant the presence of an anaesthetist [1, 2].

The practitioner administering the sedation and/or analgesia, NAAP or otherwise, should have sedation, and the monitoring of the patient, as their sole tasks during the procedure [1, 2]. They must be appropriately trained and credentialed by the relevant governing bodies [1, 2]. They must be trained to understand the mechanism of action of the drugs being administered and be able to adjust dosing and technique to patients of differing ages, possible drug interactions, or potentially confounding comorbidities [1]. They must be able to monitor a patient's level of consciousness, cardiac and respiratory function, while detecting and managing any deteriorations caused by the sedation [1]. In the absence of an anaesthetist, or other appropriately trained and credentialed medical specialist, deeper sedation and/or general anaesthesia should not be used [1]. A practitioner trained in airway management and cardiopulmonary resuscitation, to a level appropriate to the patient's age and condition, should be present during all forms of procedural sedation and/or analgesia [1].

Practical considerations

- All gastrointestinal endoscopy suits should be staffed by a proceduralist, the practitioner who will administer the sedation and a minimum of one staff member to assist either party as needed.
- The practitioner administering the sedation should have that and the monitoring of the patient as their sole tasks during the procedure.
  - They must be appropriately credentialed and trained as per local guidelines.

Monitoring

A patient must be monitored during a procedure to ensure that their response to sedation and the procedure is appropriate, allowing any complications to be quickly assessed and managed [2]. Typically, complications to sedation will be of cardiorespiratory origin and intra-procedural monitoring should therefore be aimed at early detection of changes in cardiorespiratory performance [2]. There are a number of different modalities available to perform this task and these

can be divided into two categories, invasive and noninvasive methods [2]. Various factors such as the patient's comorbidities, level and type of sedation, equipment available and the skills of the staff will dictate which form of monitoring is required [2]. While the vast majority of patients will be able to manage with noninvasive methods, a mix of both may be required for more medically complex patients [2].

Noninvasive monitoring is essential for safe endoscopy [1, 2]. Two simple and readily available forms of noninvasive monitoring include pulse oximetry, for real-time assessment of the patient's pulse and oxygen saturations, and a sphygmomanometer, for evaluation of the blood pressure [1, 2]. The oxygen saturation, heart rate and blood pressure should be continuously monitored at all times [1, 2]. When targeting conscious sedation, inadvertent progression to deep sedation is not an uncommon occurrence, highlighting the importance of continuous monitoring throughout the procedure [1, 2]. Capnographic and electrocardiogram (ECG) monitoring can be important in high risk patients, and with intended deeper sedation [2]. During prolonged procedures such as EUC and ERCP, it can be difficult to visually assess respiration and in these settings capnography has been demonstrated to significantly decrease the incidence of hypoxia and apnoea [2, 3]. Although not routinely needed, access to urgent ECG should be available at all times. At present, there is no evidence to support the routine use of bispectral index monitoring (BIS) during endoscopy [5].

There are numerous modalities for invasive monitoring and their use will be practitioner and patient dependent. Arterial lines provide real-time values for mean arterial pressure, heart rate and blood pressure, which can be useful for medically complex patients with little cardiorespiratory reserve and in whom a poor response to sedation may have significant consequences [1]. It is important to remember that by its very nature, invasive monitoring comes with risks and these need to be weighed against the benefits of the monitoring.

In assessing the depth of sedation, one can use the patient's response to verbal commands or stimulation [1, 11]. Loss of response to stimulation suggest a high likelihood of inadvertent loss of airway reflexes and/or cardiovascular depression, and sedation should be down-titrated accordingly [1, 2, 11].

Practical considerations

- All patients undergoing gastrointestinal endoscopy must be appropriately monitored based on their individual cardiovascular function, airway risk, and procedure length/complexity.
- Noninvasive monitoring:
  - Blood pressure
  - Pulse oximetry
  - Electrocardiogram
  - Bispectral index monitoring
  - Subjective clinical assessment
  - Capnography

Recovery

Post-procedure, the patients should be allowed to recover in a room that is properly equipped and staffed [1]. The facilities of the room and skills of the recovery staff should allow for the effective management of patients who have suffered complications of the procedure or who have been rendered unconscious [1]. While recovering, patients should be monitored by a practitioner aware of the potential adverse events of any drugs administered [1, 2]. Pulse oximetry and sphygmomanometry should continue during this time [2]. More serious post-sedation adverse events can occur up to 30 min after the use of benzodiazepines and opioids, but these are far less frequent with propofol [2]. In the event of a complication during recovery, a system to ensure the safe transfer of the patient to appropriate medical care must be in place [2].

Discharge of the patient must be authorized by the practitioner administering sedation and/or analgesia or another appropriately qualified practitioner [2]. The use of objective assessments, such as post-anaesthetic discharge scoring systems (PADSS) can be useful in evaluating a patient's readiness for discharge [2]. Patients must have a responsible adult to care for them and, where possible, should be provided with written instructions addressing dietary advice, resumption of normal activities and inability to make legally binding decisions and not drive a motor vehicle or operate heavy machinery [1, 2]. As psychomotor function remains significantly retarded following sedation, patients should refrain for 24 h from drinking alcohol, driving a motor vehicle, operating heavy machinery or making legally binding decisions [1, 2]. This advice should be provided to the patient both verbally and in written form, along with a 24-h contact phone number [2].

Practical considerations

- Post-procedure, monitoring should be continued until patients are stable.
- The recovery room should be staffed with health professionals trained in monitoring post-sedation patients and the identification of deterioration.
- Discharge of patients is best performed using an objective assessment such as post-anaesthetic discharge scoring systems (PADSS).

Documentation

Careful documentation with respect to sedation must be maintained throughout the procedure including vital signs assessed at regular intervals, including baseline levels prior to the procedure; drugs (name, dose), intravenous fluids (type, amount) and oxygen (rate, method); sedation-related complications and their management; predetermined discharge criteria; and the patient's achievement of them [2].

References

1. Australian and New Zealand College of Anaesthetists (ANZCA) PS09 Guidelines on sedation and/or analgesia for diagnostic and interventional medical, dental or surgical procedures. 2014. ANZCA Documents <http://www.anzca.edu.au/getattachment/resources/professional-documents/ps09-2014-guidelines-on-sedation-and-or-analgesia-for-diagnostic-and-interventional-medical-dental-or-surgical-procedures.pdf>
2. Dumonceau JM, et al. Non-anesthesiologist administration of propofol for gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates Guideline – Updated June 2015. Endoscopy. 2015;47(12):1175–89.
3. Vargo JJ, et al. Position statement: nonanesthesiologist administration of propofol for GI endoscopy. Gastrointest Endosc. 2009;70(6):1053–9.
4. Fanti L, et al. Target controlled infusion for non-anaesthesiologist propofol sedation during gastrointestinal endoscopy: the first double blind randomized controlled trial. Dig Liver Dis. 2015;47(7):566–71.
5. Lera dos Santos ME, et al. Deep sedation during gastrointestinal endoscopy: propofol-fentanyl and midazolam-fentanyl regimens. World J Gastroenterol. 2013;19(22):3439–46.
6. Redondo-Cerezo E, et al. Gastroenterologist-guided sedation with propofol for endoscopic ultrasonography in average-risk and high-risk patients: a prospective series. Eur J Gastroenterol Hepatol. 2012;24(5):506–12.
7. Rex DK, et al. Endoscopist-directed administration of propofol: a worldwide safety experience. Gastroenterology. 2009;137(4):1229–37. quiz 1518–1229
8. Jensen JT, et al. High efficacy with deep nurse-administered propofol sedation for advanced gastroenterologic endoscopic procedures. Endosc Int Open. 2016;4(1):E107–11.
9. Sienkiewicz E, et al. Propofol-alfentanyl versus midazolam-alfentanyl in inducing procedural amnesia of upper gastrointestinal endoscopy in children–blind randomised trial. Eur J Pediatr. 2015;174(11):1475–80.
10. Pambianco DJ, et al. 1053 a comparison of Propofol sedation by an anesthesiologist versus a gastroenterologist-led team using the SEDASYS® system. Gastrointest Endosc. 2015;81(5):AB192.
11. Slagelse C, et al. Nurse-administered propofol sedation for gastrointestinal endoscopic procedures: first Nordic results from implementation of a structured training program. Scand J Gastroenterol. 2011;46(12):1503–9.
12. Meyers JL, Chaudhuri S. Procedural sedation and analgesia: a practical review for non-anesthesiologists. J Surg Radiol. 2011;1:2(4).
13. Godwin SA, Caro DA, Wolf SJ, et al. Clinical policy: procedural sedation and analgesia in the emergency department. Ann Emerg Med. 2005;45(2):177–96.
14. Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology. 2002;96(4):1004–17.
15. Nejati A, Moharari RS, Ashraf H, Labaf A, Golshani K. Ketamine/Propofol versus midazolam/fentanyl for procedural sedation and analgesia in the emergency department: a randomized, prospective, double-blind trial. Acad Emerg Med. 2011;18(8):800–6.
16. Strayer RJ, Nelson LS. Adverse events associated with ketamine for procedural sedation in adults. Am J Emerg Med. 2008;26(9):985–1028.
17. Emmanouil DE, Quock RM. Advances in understanding the actions of nitrous oxide. Anesth Prog. 2007;54(1):9–18.
18. Paterson SA, Tahmassebi JF. Pediatric dentistry in the new millennium: use of inhalation sedation in pediatric dentistry. Dent Update. 2003;30(7):350–6. 358
19. Lan C, Shen X, Cui H, Liu H, Li P, Wan X, et al. Comparison of nitrous oxide to no sedation and deep sedation for diagnostic upper gastrointestinal endoscopy. J Gastrointest Surg. 2013;17(6):1066–72.
20. Aboumarzouk OM, Agarwal T, Syed Nong Chek SA, Milewski PJ, Nelson RL. Nitrous oxide for colonoscopy. Cochrane Database Syst Rev. 2011;(8):CD008506.
21. Patel R, Lenczyk M, Hannallah RS, McGill WA. Age and onset of desaturation in apnoeic children. Can J Anaesth. 1994;41(9):771–4.

The Roles and Responsibilities of Nurses in the Endoscopy Unit

46

George Tan, Theresa Thompson, and Amol Sharma

Introduction

Endoscopy requires well-coordinated team effort in order to provide the best care to patients. All healthcare providers in the endoscopy unit must work together cohesively to ensure that endoscopic procedure operations run safely and efficiently. Organizational structure is essential, and nurses play a pivotal role in the day-to-day processes of the unit. Their roles and responsibilities are diverse and range from addressing patient needs, assisting with procedures, maintaining clean equipment, replenishing depleted stock items, documenting in the electronic health record, and being cognizant of several other miscellaneous aspects of the facility including budgeting, staffing, training, auditing, and research [1].

In this chapter, we will discuss the roles and responsibilities of nurses in the endoscopy unit. At our medical center, we utilize an endoscopy nurse manager, a charge nurse, staff registered nurses (RNs), and licensed practice nurses (LPNs). Other key endoscopy personnel include our endoscopy technicians, patient care assistants, operating room assistants, inventory clerk, and endoscopy scheduler. We will discuss how the nurses at every level interact with the ancillary team members to provide the optimal patient experience and workflow. Figure 46.1 summarizes pictorially the hierarchical nursing organizational structure in the endoscopy unit.

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Endoscopy Nurse Manager

The endoscopy nurse manager (ENM) is an entry level position for nurses who are interested in nursing management. Not all endoscopy centers have an ENM, but their role is advantageous to running an efficient endoscopy unit. At our institution, the ENM oversees the daily operations of our endoscopy suite under the direct supervision of the GI chief, administrator of the center, and director of the center. He or she is responsible for assessing and allocating efficient use of resources, establishing and maintaining the staff schedule, and evaluating and training the center's personnel. This management position also involves developing a budget plan, monitoring staffing patterns, coordinating ancillary services, projecting equipment needs, researching technology needs, and being fiscally accountable for the department.

To be an ENM, several specific skills and abilities are required. This includes having extensive knowledge of professional nursing theory and practice acquired through graduation from an accredited school of nursing and the ability to apply these skills to an operational endoscopy unit. The ENM needs to have a BSN degree with a Master's degree preferred. He or she must be very organized, have the ability to plan and multitask, and be readily available to answer any questions or concerns that arise. The ENM needs to maintain effective working relationships with all fellow employees, physicians, patients, and their families. At times, if the endoscopy center is short staffed, the ENM may also assume patient care duties when necessary.

Charge Nurse

The charge nurse operates directly under the ENM. If the endoscopy center does not have an ENM, the charge nurse may assume both roles. Without an ENM, it may be necessary to rotate the charge nurse weekly to distribute managerial respon-

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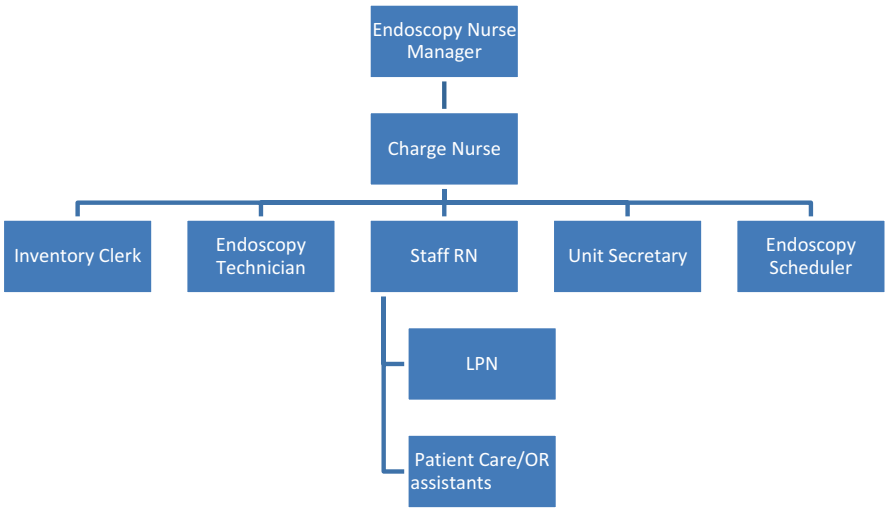

Fig. 46.1 Endoscopy unit hierarchical nursing organizational structure

sibilities effectively. The charge nurse is responsible for carrying out the endoscopy unit's protocols that are provided by the endoscopy nurse manager and to work in accordance with the hospital and endoscopy suite's mission statement and vision. The charge nurse assumes a leading role in the endoscopy unit, ensuring cases run in a timely manner. He or she is directly in charge of assigning the staff members to accomplish daily tasks according to their specific level of training; therefore, the charge nurse must be familiar with the qualifications of every nursing and non-nursing personnel in the endoscopy suite.

The charge nurse collaborates directly with the endoscopy schedulers to ensure that patients are allotted appropriate intervals of time for their procedures during appropriate periods of time during the day to match staff, physician, and anesthesia resources and that urgent or emergent cases get prioritized accordingly. At our Digestive Health Center, the charge nurse must also accommodate hospitalized inpatients needing urgent or emergent endoscopic procedures, which, during periods of limited staff availability, can be quite challenging. A registered nurse (RN) must be available on-site during all hours of operation of an endoscopy center, and at least one RN must be in the procedure room per Medicare guidelines [2]. If there is a shortage of endoscopy RNs, the charge nurse would temporarily assume the role of the endoscopy room nurse to help improve workflow. At all times, the charge nurse is constantly aware of minimum staffing requirements put forth by the Society of Gastroenterology Nurses and Associates, Inc. (SGNA) and must allocate RNs accordingly. This includes having at least one RN in the pre-procedure area, at least one RN per procedure room, and two RNs have to be in the post-procedure area. In certain complicated cases determined by the severity of the patient's condition or complexity and length of the procedure, such as endoscopic retrograde cholangiopancreatography (ERCP) or balloon enteroscopy, an additional RN or support staff such as the patient care or operating room assistant is recommended to be present in the procedure room [3, 4].

In addition to overseeing patient care and managing staff RNs in the endoscopy unit, the charge nurse also works closely with endoscopy technicians and the inventory clerk. The charge nurse ensures that every procedure room is also properly staffed with an endoscopy technician. The endoscopy technician gathers all necessary supplies before each endoscopic procedure. The charge nurse ensures that the endoscopy technician is able to demonstrate the skills and judgment required to provide direct care to patients under the direction of the physician and staff RN and can perform all aspects of endoscope reprocessing, which involves the decontamination and high-level disinfection of the endoscopy equipment. Any issues with the equipment or supplies must be communicated with the charge nurse, the nurse manager, and the inventory clerk.

The inventory clerk assists the charge nurse by being fiscally accountable for the storage and shelf life of endoscopic equipment and disposable supplies. He or she is responsible for the appropriate usage and efficient inventory management. The inventory clerk reports directly to the ENM or the charge nurse and must be aware of budgetary constraints.

The charge nurse also collaborates with the patient care assistant, unit secretary, and endoscopy schedulers after completion of endoscopic procedures to ensure continuity of patient care and adequate follow-up. At our Digestive Health Center, for instance, the charge nurse ensures the patient care assistant (PCA) transports all biopsy, brushing, and polypectomy specimens to the pathology lab. Under the supervision of the charge nurse, the PCA also helps with facility maintenance, making beds when patients arrive in the pre-procedure room, and escorting patients out of the endoscopy suite once they are stable for discharge. Unit secretaries assist the PCAs and also answer phone calls, arrange for ordered outpatient follow-up

labs and imaging studies, and participate in patient outreach at the charge nurse's request. The charge nurse will make sure patients speak directly with endoscopy schedulers to make appropriate follow-up appointments. The charge nurses confirm that urgent and emergent procedures for hospitalized inpatients are prioritized within the endoscopy schedule, appropriately prepared for endoscopy, and post-procedure sign-out is provided to the hospital RN.

In addition to running the day-to-day operations of the endoscopy unit, the charge nurse and the endoscopy center administrator are also responsible for hiring and training the new endoscopy RNs. While every endoscopy center will have their own criteria for hiring new employees, here at Augusta University, we use a competency-based endoscopy nursing orientation tool that highlights our required competency goals followed by a checklist of performance criteria to ensure that these goals are met. The charge nurse will assign a preceptor (senior staff RN) to train the new employees and will then initial and date each step on the orientation packet once the trainee has successfully fulfilled each requirement. The key competency objectives that the preceptor will emphasize include the demonstration of knowledge of the endoscopy unit and associated areas of the hospital, teamwork and patient-/family-centered care, effective infection control procedures, and knowledge of the scopes and equipment as well as the cleaning and disinfection process. The trainee must also demonstrate excellent patient care in the endoscopy room and do appropriate pre- and post-assessments, administer medications properly, document appropriately, possess effective communication skills, maintain a safe environment, and ensure a proper room is set up for each procedure. Several other competencies must be observed by the nursing preceptor, and these tasks and corresponding performance criteria are summarized in Fig. 46.2. These competencies are based on guidelines supported by standards of practice according to the Society of Gastroenterology Nurses and Associate Practice Committee Board of Directors [5].

Practical Considerations

- If an endoscopy unit does not have an endoscopy nurse manager, the charge nurse may assume this role. Due to substantial administrative burden, rotating charge nurses on a weekly basis may be considered.
- The charge nurse oversees and manages the entire endoscopy unit and needs to be able to prioritize patient cases as well accommodate endoscopic procedures for hospitalized inpatients.
- The charge nurse needs to be aware of SGNA minimum staffing requirements and be available to circulate into an endoscopy room if there is a shortage of nursing staff.

Staff Registered Nurses (RNs)

The staff registered nurses (RNs) practice in the endoscopy unit with the skills and techniques acquired through their training from an accredited school of nursing and prior nursing experience to provide ethically sound patient care. This position requires that nurses are able to assess patient and family needs and implement a medical plan that will be necessary in order to deliver safe, high-quality care. When the patient arrives to the endoscopy unit, the staff RNs play a critical role in the pre-procedure stage, the intra-procedure stage, and the post-procedure stage of patient care as outlined by the SGNA.

The SGNA highlights several responsibilities of the staff RN during the pre-procedure stage. This includes documenting the correct time and date, the type of procedure performed, the reason for procedure, and noting logistics such as patient arrival mode, who accompanied the patient, how the patient will be going home, pre-procedural contacts, and who will be available for pre-procedural instruction. The staff RN also identifies the patient and family's primary language and any potential barriers to effective pre-procedural instruction. Staff RNs also need to thoroughly review the patient's medical history. In particular, any previous problems with sedation analgesia, medication allergies, previous medical and orthopedic procedures, any significant family history of gastrointestinal (GI) diseases, any history of tobacco, alcohol, or drug use, and current medications with special attention to any anticoagulants and nonsteroidal anti-inflammatories (NSAIDs) need to be noted. The RN must document potential exposure to certain infectious diseases such as HIV, tuberculosis (TB), or viral hepatitis. If the patient has diabetes, the staff RN should inquire when the patient last took insulin and the most recent blood glucose reading [6] as well as obtain a pre-procedural blood glucose level.

After a thorough review of systems, the pre-procedure stage continues assessment of the patient's condition upon arrival by the staff RN. He or she documents the American Society of Anesthetists (ASA) score determined by the physician. The staff RN also calculates an Aldrete score to assess the patient's overall health status prior to undergoing endoscopy (Fig. 46.3). The pre-procedural Aldrete score is compared to a post-procedural score to assess patient's recovery after anesthesia and readiness for discharge. The staff RN assesses the patient's pain level, checks baseline vital signs, and reviews the sedation plan. The staff RN proceeds to perform a physical examination and establish intravenous (IV) access to administer IV fluids, medications, and transfusion of any blood products such as packed red blood cells, fresh frozen plasma, or platelets, as needed. An oral assessment is important to identify patients with dentures, loose teeth, or other oral abnormalities. Patients are also screened for

AU Health
Augusta University Health
Competency Based
ENDO RN Orientation Tool

Name: _____ Date of Hire: _____

Validator's Initials/Date	Competency Statement	Performance Criteria
	1. Demonstrates knowledge of the Endoscopy Unit and associated areas in the hospital.	☐ Locate the Code Cart. ☐ Locate the fire extinguisher, fire alarms, and O^2 shutoff valves. ☐ Locate the dirty utility room ☐ Locate the clean utility room. ☐ Locate Charge cards/stickers ☐ Locate the family area. ☐ Locate unit manuals: a. Safety b. EOP c. Unit Policy Manual d. Chemical Safety e. MSDS ☐ Locate on-line hospital manuals a. Hospital Policy Manual b. MSDS c. Infection Control Manual d. Formulary ☐ Locate the Time Clock ☐ Locate time schedule ☐ GRMC e-mail account ☐ Paging a. Via phone b. On-line ☐ Sending orders via OrderComm ☐ Fax Machine ☐ Personal e-mail account ☐ Demonstrate understanding of the assignment board.
	2. Demonstrates a spirit of teamwork and patient/family centered care.	☐ Demonstrates ability to communicate and use effective interpersonal skills with colleagues and other members of the medical center. ☐ Ensures customer satisfaction oriented environment for both patients and families. ☐ Fosters a positive work environment and encourages team work. ☐ Demonstrates appropriate time management skills. ☐ Verbalizes knowledge and understanding of patient and staff rights and responsibilities. ☐ Verbalizes PACU's mission, philosophy and scope of service. ☐ Ensures a safe environment for patients/families and staff, identifying health/safety risks & takes appropriate and immediate steps to alleviate risk
	3. Demonstrates effective infection control procedures.	☐ Correctly explains Standard Precautions. ☐ Identifies patients who are SI or VRE coded and verbalizes procedure. ☐ Able to verbalize and follows procedures for segregating/isolating patients on Transmission

Fig. 46.2 Endoscopy RN competency table

Validator's Initials/Date	Competency Statement	Performance Criteria
		Based Precautions. ☐ Uses proper technique for a. Blood safety devices b. Disposing of sharps, single use vials and glass vials c. Disposal of infectious and regulated waste d. Storing clean and sterile supplies e. Collecting and transporting lab specimens. ☐ States location of and indications for personal protective equipment. Demonstrates proper use of personal protective equipment. ☐ Demonstrates proper hand washing technique. ☐ Demonstrates proper cleaning and decontamination of medical equipment using appropriate cleaning agents. ☐ Describes procedures for managing a needle stick or blood borne pathogen exposure. ☐ Demonstrates correct use of the negative pressure room
	4. Demonstrates knowledge of equipment.	☐ Flexible scopes ☐ Immersible scopes ☐ Gastroscope ☐ Colonoscope ☐ Sigmoidoscope ☐ Duodenoscope ☐ Bronchoscope ☐ Fiber optic vs. Video equipment ☐ Endoscopic ultrasound ☐ Capsule endoscopy ☐ Accessories a. Snare b. Bronch Brush Holder c. Handles d. Syringes e. Hot biopsy i) Disposable and nondisposable biopsy forceps f. 3 prong retriever ☐ Basket retriever.
	5. Receives patient from the endoscopy room	☐ Connects appropriate equipment and monitoring devices. ☐ Receives verbal report from Anesthesia provider. ☐ Reviews paperwork for completeness.
	6. Assists with performance of initial postoperative assessment	☐ Obtains vital signs (pulse, BP, Temperature, RR, SaO2, and ETCO2) and recognizes normal and abnormal values. ☐ Assesses psychological status. ☐ Performs airway/ respiratory assessment. ☐ Performs cardiovascular assessment. ☐ Performs neurological/neurovascular assessment ☐ Assesses IV catheter site/patency ☐ Assesses and responds to patient's pain using appropriate pain scales. ☐ Obtains order for and applies warming blanket as needed for patient comfort. ☐ Assesses appearance of surgical dressing site. ☐ Documents all care as per policy.

Fig. 46.2 (continued)

Validator's Initials/Date	Competency Statement	Performance Criteria
	7. Follows appropriate procedures for medication administration	☐ Identifies location of medications and emergency drug box. ☐ Utilizes the Accudose to retrieve medications. ☐ Reconciles narcotic variances appropriately. ☐ Inventories medications per policy. ☐ Calculates and administers prescribed medication by appropriate route ☐ Documents narcotic wastes correctly. ☐ Verbalizes knowledge of procedural medications including dose, action, onset and duration. ☐ Verbalizes knowledge of reversal medications including dose, action, onset and duration. ☐ Verbalizes knowledge of sclerotherapy medications. ☐ Labels syringes when drawing up medications. ☐ Uses Hurricaine spray appropriately. Verbalizes the cause, signs and treatment of methemoglobinemia.
	8. Demonstrates the ability to document per GRMC policy/procedure and ensures patient meets discharge criteria from Endo PACU per hospital policy (according to ASPAN standards)	☐ Patient meets "Medically Fit for Discharge criteria" a. Patient is awake or easily aroused or back to baseline consciousness. b. Aldrete score ≥ 8 c. Adequately ventilated d. Temperature, heart rate and blood pressure within normal limits or at baseline. e. Pain controlled f. Vomiting controlled g. All laboratory and radiographic studies ordered for PACU completed and reviewed by ordering physician. h. Appropriate postoperative orders and prescriptions written. ☐ Completes the Outpatient Admission Form a. Plan of Care b. Patient/significant other education ☐ Discharge instructions including patient/significant other education. ☐ Post-procedure call back ☐ Admission assessment for patients admitted post-procedure ☐ Completes pathology/lab forms and documents or co-signs specimens in log. ☐ Documents charges appropriately. ☐ Calls report to receiving nurse ☐ Transports patient/equipment safely. ☐ Identifies personnel and equipment needed for transportation as determined by assessment data. ☐ Utilizes patient transfer equipment appropriately. ☐ Demonstrates good body mechanics when transferring patients.
	9. Demonstrates the ability to use and maintain equipment as appropriate.	☐ Video System/Light Source ☐ Cardiac monitor a. Set-up b. Alarm c. Recording ☐ Wall Suction ☐ Ambu bag ☐ Travel Cart

Fig. 46.2 (continued)

Validator's Initials/Date	Competency Statement	Performance Criteria
		☐ Electrocautery devices a. ERBE ☐ Valley Lab ☐ CLO test controls test and log. ☐ Code Care and Defibrillator
	10. Demonstrates the ability to clean and disinfect scopes/equipment	☐ Identifies enzymatic cleaner to be used during cleaning. ☐ Demonstrates appropriate use of personal protective equipment. ☐ Demonstrates cleaning/disinfection for the following scopes: a. Upper and lower endoscopes b. Double channel endoscopes c. ERCP scope d. EUS scope ☐ Demonstrates leak testing. ☐ Demonstrates cleaning of a scope with an air leak. ☐ Demonstrates positioning of scopes in washer and attaching appropriate tubing. ☐ Demonstrates use of scope reprocessor. ☐ Demonstrates testing of gluteraldehyde with test strips. ☐ Demonstrates.cleaning/disinfection process for: a. Reusable biopsy/retrieval forceps b. Heater probe c. ERBE cable d. Savary dilators, wires e. Water bottles ☐ Can verbalize the spill containment procedure. ☐ Stores scopes correctly.
	11. Demonstrates effective communication skills appropriate to the Unit environment	☐ Provides report to other staff when handing off patients using PAMPER format. ☐ Demonstrates appropriate use of telephone/paging system a. Use of audio and text pages b. Overhead pages c. Transfer a call d. Activate Codes i) Code RED ii) Code BLUE ☐ Code Grey ☐ Maintains confidentiality of all patient/hospital related communication/ documents. ☐
	12. Demonstrates an appropriate safe patient, staff and unit environment	☐ Describes the procedure for activating the fire alarm. ☐ Maintains fall precautions. ☐ Positions patients correctly for procedures. ☐ Demonstrates the ability to transfer and transport patients safely. Disposes of sharps and biomedical waste appropriately.
	13. Demonstrates the ability to set up the rooms as appropriate for each procedure.	☐ Correct endoscope. ☐ Light source with water bottle ☐ Sterile water ☐ Mouth piece ☐ Accessories: ☐ Biopsy forceps ☐ Graspers ☐ Snare with basin

Fig. 46.2 (continued)

Validator's Initials/Date	Competency Statement	Performance Criteria
		☐ Electrodes ☐ 0^2 set up ☐ Monitor ☐ Suction with tubing ☐ Specimen container, slides, fixative, labels ☐ Cytology brush. ☐ Lubricant, gauze pads, washcloths, disposable gloves. ☐ Cardiac monitor ☐ Wet towel ☐ Syringe with blunt needle ☐ Water and simethicone ☐ Enzymatic detergent
	14. Demonstrates the ability to breakdown and clean the room post-procedure	☐ Cleans equipment and vertical surfaces in room with appropriate disinfectant. ☐ Checks supplies and restocks as appropriate. ☐ Runs equipment diagnostics as appropriate. ☐ Replaces suction equipment Uses Isolyzer appropriately.
	15. Demonstrates the ability to obtain vital signs appropriately.	☐ Able to accurately measure and document: a. Weight b. Height c. Temperature d. Pulse e. Respirations f. Blood pressure ☐ Demonstrates use of pulse oximeter a. Ensures proper placement b. Documents spO^2 ☐ Troubleshoots appropriately.
	16. Demonstrates appropriate use of oxygen equipment	☐ Sets up wall oxygen. ☐ Sets up portable oxygen E cylinder. ☐ Demonstrates correct placement of existing oxygen device on patient. a. Nasal cannula b. Face mask ☐ Trach collar
	17. Demonstrates the ability to use effective Infection Control measures	☐ Follows Standard Precautions procedures. ☐ Washes hands between patients. ☐ Follows category-specific precautions procedures. ☐ Describes procedure for handling needle sticks. ☐ Uses sterile/aseptic technique appropriately
	18. Demonstrates Clutter Control.	☐ Ensures only necessary equipment remains in patient areas/hallway/ breakroom/utility room. ☐ Returns unused equipment to appropriate storage area. ☐ Maintains lead aprons on the stand (nothing touching floor).
	19. Participates in off unit procedures	☐ ICUs ☐ ER, ER Obs ☐ Adult OR ☐ CMC OR
	20. Prepares for and assists with a variety of procedures	☐ EGD/Colonoscopy ☐ Banding ☐ Biopsies for pathology (hot and cold) and CLO. ☐ Polypectomy by snare ☐ Brushings for cytology (on slides) ☐ Obtaining aspirates ☐ Foreign Body Removal

Fig. 46.2 (continued)

Validator's Initials/Date	Competency Statement	Performance Criteria
		☐ Sclerotherapy ☐ Esophageal Dilation with: a. Savary b. Balloons c. Pneumatic Dilation ☐ EGD with PEG/PEJ placement a. Nutrition consult ☐ Placement clips ☐ Endoscopic Mucosal Resection (EMR) ☐ Endoloop ☐ Liver Biopsy ☐ Paracentesis ☐ Endoscopic Ultrasound a. Fine Needle Aspiration b. Blocks ☐ ERCP ☐ Placement of Blakemore tube. ☐ Metal Stent Placement a. EGD b. Colon c. ERCP ☐ pH monitoring ☐ Manometry ☐ Bravo capsule placement ☐ Given capsule endoscopy and ESO cam ☐ Implants
	21. Demonstrates familiarity with and properly identifies unit clerk's role in GRMCI programs.	☐ Demonstrates familiarity with and ability to complete any associated forms: ☐ Needlestick protocol ☐ PSN Variance Report System ☐ OOPS program ☐ Culturally and Linguistically Appropriate Services (CLAS) ☐ Bloodless Medicine Program ☐ National Patient Safety Goals ☐ EMTALA ☐ Witnessing consents ☐ Demonstrates ability to access and complete. assigned on-line learning. ☐ Verbalizes understanding of Patient/Family Centered Care

Fig. 46.2 (continued)

Fig. 46.3 Aldrete score: assessment for postanesthesia recovery and readiness for discharge

Aldrete Score					
Points	**Activity**	**Respiration**	**Circulation**	**Consciousness**	**Color**
2	Able to move all 4 extremities	Deeply breaths, coughs freely	SBP +/- 20mmHg pre-procedure level	Fully awake	Pink
1	Able to move 2 extremities	Dyspnea or limited breathing	BP + 20-50mmHg pre-procedure level	Arises on calling	Pale, dusky, blotched, jaundiced
0	Able to move 0 extremeties	Apneic	BP +/- 50mmHg pre-procedure level	Unresponsive	Cyanotic

Fig. 46.4 Endoscopy room personnel showing the patient undergoing an upper endoscopy performed by the postdoctoral gastroenterology fellow, supervised by the gastroenterology attending (*left*). The anesthesiologist and endoscopy technician are at the head of the bed. The staff RN (circulator) is at the computer recording the events of the procedure

pregnancy and whether they are at risk for any types of physical, mental, emotional, or sexual abuse. In preparation for the procedure, the RN also confirms that the patient has taken all of his or her appropriate medications and completed a bowel prep for colonoscopy. Finally, pre-procedural staff RNs review lab results and advance directives, document any belongings removed, and advise the patient and family on the subsequent steps during and after the procedure [6].

In the endoscopy room, staff RNs are relied upon to perform a variety of intra-procedure duties. They identify the patient, verify the procedure being performed, and patient allergies during a time-out prior to the procedure. The staff RNs also confirm the sedation plan and ensure that all of the consent forms have been appropriately completed and signed. The staff RN also verifies and documents all personnel and providers present in the endoscopy room (Fig. 46.4). Next, the staff RN in the endoscopy room, also known as the circulator, documents endoscope serial numbers and equipment used during the procedure, pathology specimens obtained, procedure start and end times, any adverse events or occurrences, and patient vital signs. The circulator also documents the name and quantity of all medications, IV fluids, and verified blood bank products administered during the procedure. Sedation is administered by anesthesia personnel, and the patient is monitored continuously by the anesthesia and RN staff throughout the procedure.

After the endoscopic procedure is completed, the patient is escorted to the postanesthesia care unit (PACU) for recovery. During the post-procedure stage, staff RNs assess the patient prior to discharge, document PACU admission time and endoscopic procedure performed, and check the patient's vital signs. Additional tests such as an EKG, blood glucose level, or basic post-procedure labs and imaging tests can be obtained at this time. The staff RN reviews discharge instructions, assembled as outlined by Joint Commission on Accreditation of Healthcare Organizations (JCAHO) [6], with patient and accompanying family members. Discharge instructions typically include post-procedure diet, medication changes, and any other limitations such as if bedrest or driving restrictions. Staff RNs may also review any other discharge instructions and post-procedure teaching such as routine care after percutaneous endoscopic gastrostomy (PEG) tube placement. Staff RNs ensure appropriate follow-up appointments are in place. He or she also discusses potential signs and symptoms that may warrant emergency medical attention. The staff RN must also document any procedure devices placed or removed during the procedure, any significant occurrences, and whether the patient will be discharged home, admitted to the hospital, or transferred to another facility. Prior to discharge, the staff RNs perform their final assessment, including a repeat Aldrete score to assess postanesthesia recovery and discharge readiness, pain assessment, removal of peripheral IV access, and return of personal belongings such as dentures, glasses, or hearing aids.

Licensed Practical Nurses (LPNs)

The licensed practical nurse (LPN) functions under the direct supervision of the GI physician or staff RN in the endoscopy unit. He or she is responsible for planning, implementing, and

evaluating nursing care for assigned patients. LPNs may administer pharmacological and other treatment regimens or perform certain diagnostic studies as ordered by a physician so long as this falls within the limitations of licensure and institutional policy. The LPN also assists the RNs with patient follow-up care and collaborates with other interprofessional healthcare members to deliver high-quality patient care in the endoscopy center [5, 7].

Practical Considerations

- RNs need to be adequately trained in the pre-procedure, intra-procedure, and post-procedure stages of endoscopy in order to deliver safe, high-quality patient care.
- Under the supervision of the GI physician or staff RN, LPNs can be a useful adjunct to patient care in the endoscopy suite.

Continuous Quality and Process Improvement

After the patient has been discharged from the endoscopy suite, the nursing staff will call the patient the next day for a post-procedure follow-up. This allows the patient to discuss any problems or concerns they may be experiencing from the procedure or provide feedback from their overall experience in the endoscopy unit. Patients are also mailed random surveys to solicit their feedback, which may be used to improve the quality of patient care and service for the future. Endoscopy team meetings and group discussions review any pitfalls in patient care to determine areas in need of improvement. For instance, if a procedure was aborted because anticoagulation was not appropriately held, could this have been prevented by identification during an additional pre-procedure phone call or a patient text message? Indeed, this is just one aspect of continuous quality and process improvement.

Another aspect of continuous quality improvement for endoscopy nurses includes participating in continuing medical education (CME) courses and maintaining their certification and licensure [5]. In addition, all endoscopy unit nurses are encouraged to contribute to evidence-based practice by participating in research activities, integrating evidence and research findings into nursing practice. RNs and LPNs should also participate in self-evaluation reflective of professional practice standards and engage in performance improvement activities, where feasible [5]. Lastly, both endoscopy RNs and LPNs are recommended to participate as active members in their respective professional and consumer organizations, contribute to professional publications, and present at professional meetings to improve the field of gastrointestinal endoscopy [5].

Conclusion

Endoscopy is a collaborative effort, in which nurses play an integral role. The endoscopy nurse manager oversees the daily operations of the endoscopy center, and its protocols are carried out by the charge nurse. The charge nurse directly manages and interacts with every member of the endoscopy team to ensure that safe, efficient, and high-quality patient care is achieved. The charge nurse ensures that all procedure rooms meet the minimum nursing staff requirements as outlined by the SGNA and communicates with the patient care/operating room assistants, endoscopy technicians, inventory clerk, unit secretary, and endoscopy schedulers to ensure that all patients receive the best care and have adequate follow-up. The staff registered nurses (RNs) also play a critical role in the pre-procedure, the intra-procedure, and the post-procedure stages of patient care. Licensed practical nurses (LPNs) can be a helpful adjunct in the endoscopy unit. Continuous quality and process improvement is best achieved with involvement of all endoscopy nurses and ancillary staff in order to continually provide the best care to patients.

References

1. Canard JM, Letard JC, Palazzo L, Penman I, Lennon AM. Gastrointestinal endoscopy in practice. Edinburgh: Elsevier Chuchill Livingstone; 2011.
2. Ginsberg GG, Gostout CJ, Kochman ML, Norton ID. Clinical gastrointestinal endoscopy. 2nd ed. London: Elsevier Saunders; 2005.
3. Minimum Registered Nurse Staffing for Patient Care in the Gastrointestinal Endoscopy Unit [Position Statement]. Society of Gastrointestinal Nurses and Associates, Inc.; 2012.
4. Jain R, et al. Minimum staffing requirements for the performance of GI endoscopy. Gastrointestinal Endoscopy. 72(3):469–70.
5. Standards of Clinical Practice & Role Delineations [Position Statement]. Society of Gastrointestinal Nurses and Associates, Inc.; 2013.
6. Guidelines for Nursing Documentation in Gastrointestinal Endoscopy [Position Statement]. Society of Gastrointestinal Nurses and Associates, Inc.; 2013.
7. National Association for Practical Nurse Education and Service, Inc. (2007). Standards of practice and educational competencies of graduates of practical/vocational nursing programs. Alexandria.

Quality and Efficiency in Gastrointestinal Endoscopy Units

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Introduction

Both quality and efficiency have had varied definitions over the years. At its core, quality is defined as a measure of excellence or a state of being free from defects, deficiencies, and significant variations [1]. On the other hand, efficiency is defined as the use of resources in such a way as to maximize the production of goods and services [2]. While both have been the cornerstone of many industries, it has not been until recently that they have been at the forefront for driving improvements in care within gastrointestinal (GI) endoscopy units. This focus on improving both quality and efficiency in GI has been spurred by the dramatic rise in the demand for endoscopic procedures as well as the rising number of insured patients in the United States (USA) requiring GI care. Moreover, as reimbursements in the USA become more intertwined with performance and quality indicators, both for procedures and endoscopy units, gastroenterologists, governing organizations, payers, and patients are demanding improvements in these two areas.

This chapter will focus on several aspects of quality and efficiency within endoscopy units. First, the importance of value, in relation to both quality and efficiency, in GI endoscopy will be discussed. Second, the literature surrounding quality measures in GI endoscopy units will be reviewed with a particular focus on interventions that have been demonstrated to improve the quality of care for patients receiving services in endoscopy units. Third, the history and study of efficiency in endoscopy units will be examined; first we will look at other healthcare industries that have extensively studied and improved efficiency in their fields, then we will examine a number of proposed efficiency metrics and benchmarks in endoscopy units, and finally we will discuss opportunities where endoscopy units could improve their efficiency.

Importance of Value (Quality and Efficiency) in GI Endoscopy

Healthcare expenditures in the USA grew from 5.1% of gross domestic product in 1960 to over 17% in 2013; it is estimated to further rise to over 19% in the next 10 years [3]. Continued growth at this rate is unsustainable, and the focus of healthcare reform has shifted from improving quality alone to optimizing value [4].

In healthcare, value represents the health outcomes achieved per dollar spent [5]. Quality and efficiency are key components of value in that they impact both health outcomes and cost. As such, by improving quality and efficiency, we can positively impact the value of care provided to patients. This concept holds true for care provided in clinics as it does for procedures such as endoscopy where a high-value endoscopy, for example, is one provided with maximal quality at the lowest cost.

As gastrointestinal procedures make up the largest percentage of ambulatory surgical center claims in Medicare, value-based purchasing will especially impact GI endoscopy units [6]. Evidence for this impact is already accumulating. Several cases are illustrative, including value-based reimbursement programs, tiered provider networks, bundled pay-

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ments, and reference pricing. Each of these programs will be addressed separately.

First is value-based reimbursement. Congress, in passing the Affordable Care Act in 2010, extended CMS' mandate around value-based reimbursement to ambulatory surgical centers [7]. As a result, CMS is developing a value-based purchasing plan for ambulatory surgical centers that includes measures of all dimensions of quality and efficiency. The value-based payment adjustment for ASCs will reflect how well an ASC performs in these dimensions relative to its peers. Similar programs from CMS currently exist for hospital-based payment and physician reimbursement.

Second, similar to value-based reimbursement programs, in which the government is trying to incentivize high-value care, tiered provider networks illustrate the private insurance industry's attempt at the same goal. In these programs, insurers use quality metrics and cost-efficiency measures to distinguish "high-value" providers in their network [8]. Patients may be incentivized to choose top tier providers through copayment or coinsurance benefit design. However, evaluations of the impact of these tiering programs are not publically available.

Third, bundled payments are an alternative payment model that again attempts to incentivize high-value care prospectively by encouraging more coordinated patient care with attention to quality and cost. In this model, a negotiated price (between payer and provider) is set for services related to a specific condition or procedure. The American Gastroenterological Association recently proposed a model for bundled payments for colonoscopy [9]. Bundled payments encourage high-value care through a variety of mechanisms. For example, in the colonoscopy model, bundled payments may encourage providers to treat patients in a cost-efficient facility (i.e., ASC) as opposed to a hospital-based unit. Similarly, bundled payments may also encourage providers to use anesthesiologists for sedation when clinically warranted as opposed to all colonoscopies.

Finally, reference pricing is another alternative payment model that seeks to incentivize high-value care by fixing a set price for a specific episode of care. In contrast to bundled payments, there is no negotiation between provider and payer. In addition, the provider of services has no financial risk in the provision of care. Instead, patients are given a set amount of money with which to purchase services. Patients can choose to receive services from any provider, but they are responsible for costs above that reimbursed by the payer or employer. As such, the consumer is made a more active purchaser of healthcare services. The experience by the California Public Employees Retirement System (CalPERS) with reference pricing for colonoscopy was recently reported [10]. CalPERS saved $7million on spending for colonoscopy for their beneficiaries in the first 2 years of the program, representing a 28% savings compared to matched controls. These savings were driven in large part from a choice by patients to have their colonoscopy performed in low-cost settings; indeed, the use of ambulatory surgery centers increased approximately 18% as a result of the reference price program.

As these examples illustrate, demonstrating high quality and low costs in GI endoscopy is critical for successfully competing in the value-based healthcare marketplace. The next sections of this chapter will review ways in which to measure quality and efficiency of the endoscopy unit. Quality measures for procedures are discussed in a separate chapter.

Practical Considerations

- GI procedures make up the largest percentage of ambulatory surgical center Medicare claims.
- GI endoscopy practices will be subject to federal and private value-based purchasing programs.
- Measuring quality and efficiency metrics can help GI endoscopy practices compete in this value-based healthcare marketplace by demonstrating high quality and low costs.

Quality Measures in GI Endoscopy Units

There has been a dramatic rise in the request for GI specialty care in the USA and in particular endoscopic services over the last three decades [11–13]. In parallel, several quality indicators for a number of endoscopic procedures have been identified [14–18] to help provide standards and benchmarks for practicing providers, reduce practice variation, and improve overall quality of care in endoscopy; however, these indicators have been focused on providers and procedure documentation. An essential component of high-quality endoscopy services must also focus on the endoscopy unit itself. Unlike procedure-associated quality indicators, evidenced-based indicators used to measure quality of endoscopy units are lacking.

Outside of the USA, there has been some effort to develop performance indicators for endoscopy units with the aims of enhancing quality while developing uniformity in endoscopy unit processes and operations. Along these lines, the United Kingdom's (UK) National Health Services developed the Global Rating Scale (GRS) in 2004 [19]. This web-based scoring system was the first to assess service at the level of the endoscopy unit. This system extensively examines and rates endoscopy units in the domains of clinical quality (appropriateness, information/consent, safety, comfort, quality, timely results) and quality of the patient experience (equality, timeliness, choice, privacy and dignity, aftercare, ability to provide feedback) in an ongoing process with publication of the scores. Since its inception, the GRS has been

Table 47.1 Selected endoscopy unit quality measurements and specific interventions to improve them

Quality	
Measurements	Interventions for improvement
Procedure related	
Tracking quality indicators identified for specific endoscopic procedures (e.g., adenoma detection rate, cecal intubation rate)	Report cards (with provider performance and benchmarks/targets identified)
Patient pause/time-out performed before procedures	Checklist of patient pause/time-out process for staff Identify staff member for leading the process
Documentation and periodic review of informed consent process	
Documented and recommended indications for endoscopic procedures	
Endoscopy reports communicated to referring providers and patients	
Formalized discharge criteria in place	Validated discharge criteria (e.g., Aldrete) utilized
Infection control and safety	
Documented disinfection policy and process in place for endoscope reprocessing	Checklists for all steps involved in reprocessing endoscopes Staff document completion of reprocessing steps over a given timeframe (i.e., week, month)
Outlining safety policy and procedures in endoscopy unit	Orientation for staff on infection control Focused training in the form of in-services or hands-on training for new equipment and frequently used equipment
Frequency of adverse events post procedure	Report cards (with provider performance and benchmarks/targets identified)
Staff experience	
Staff satisfaction survey	Annual performance evaluations and ongoing feedback for staff Continual hands-on/in-service training for staff Employee recognition program Ongoing, regular staff meeting/daily team huddles
Employee turnover rate	
Patient experience	
Patient satisfaction survey	Educational handouts/multimedia that review preparation/instructions for endoscopic procedures Pre-consultation with endoscopist performing the procedure Decrease endoscopy appointment wait times
Monitoring patient comfort both during and after an endoscopic procedure	Endoscopist technique (e.g., water exchange, patient position, air insufflation with carbon dioxide) Environment (e.g., playing music during a procedure)

instrumental in identifying service gaps, increasing patient satisfaction, reducing wait times, reducing adverse events, and driving performance improvement projects within endoscopy units throughout the UK [20]. Furthermore, a modified GRS has been adopted across Europe [21, 22] and Canada [23, 24]. However, much of the work for developing these endoscopy unit measures has been limited to expert opinion and/or consensus, and evidence to support the majority of outlined measures is scarce. Presently, no such endoscopy unit measures have been published in the USA.

While evidence may be lacking in the area of endoscopy unit measurement, there is some literature to help guide us. The literature describes a number of common elements for measuring quality in GI endoscopy units that span across four key domains: (1) procedure-related aspects, (2) infection control and safety, (3) staff experience, and (4) patient experience. Table 47.1 highlights notable endoscopy unit quality measures and interventions demonstrated to improve them.

Practical Considerations

- No endoscopy unit quality measures have been endorsed in the USA.
- Important areas to evaluate include procedural quality, infection control and safety, staff experience, and patient experience.
- Procedural quality can be improved with pre-procedure checklists and physician audit and feedback.
- Infection control and safety is dependent on appropriate staff training and use of endoscopy reprocessing checklists.
- Staff experience is improved with staff empowerment, continuous training, and regular performance assessments.
- Patient experience improvements focus on staff and provider communication, access, and comfort.

Procedure Related

Performing high-quality and safe endoscopic procedures (throughout all aspects of the procedure) is essential to the quality of an endoscopy unit. Much of the literature on procedure-related quality indicators has focused on aspects of the pre- and post-procedure process in endoscopy units. There have been few studies available that have examined procedure-related quality indicators for endoscopy units. For instance, documenting and performing endoscopic procedures for an appropriate indication are valuable indicators

because it is associated with an increase in the diagnostic yield of findings during endoscopy [25–28]. Similarly, improved safety outcomes have been demonstrated for performing a patient pause/time-out immediately before the beginning of a procedure [29–33] and utilizing validated, standardized discharge criteria [34–37]. Likewise, intra-procedural quality indicators have been enumerated [14–18]; monitoring quality indicators for providers performing specific endoscopic procedures has resulted in improved quality and reduced practice variation among providers. Furthermore, performance targets for many of these procedure quality indicators have been established and recommended for endoscopists performing such procedures [14–16, 18]. These indicators are further described in another chapter within the book.

Several interventions have been proposed to improve performance with regard to procedure-related measurements in endoscopy units. Much of this work has focused on improving performance with regard to specific quality indicators established for endoscopic procedures. For instance, sharing and communicating data on quality indicators can help reduce practice variation among staff/endoscopists as well as can improve the individual performance of endoscopists who underperform on some indicators [38]. For example, using report cards that measure a few key quality indicators with minimal standards of practice established for each, ensuring individual endoscopists are blinded to data that is shared, and that such information is administered regularly and frequently to endoscopists can help drive improvement in performance on quality indicators over time [39]. Many clinics and hospital departments have also found that posting and regularly updating metrics in a place easily seen by all staff are helpful. Performance boards alert staff to trends and can highlight important issues [40]. They augment report cards and are an excellent place to hold daily huddles and to stimulate discussion about performance and upcoming issues [41]. Finally, a number of quality improvement projects aimed at improving procedure-related quality indicators have been reported in the literature [39, 42–46]. Examples of these projects include the use of quarterly report cards for endoscopists, dedicated educational interventions for underperforming providers, monthly journal clubs for providers, establishing policies and standards within the endoscopy unit on specific quality metrics, and providing feedback to endoscopists about their performance.

Additionally, the implementation of standard work around some of these performance improvement measures has had demonstrated successes. This has been well documented in areas such as the patient pause/time-out. Essential to a successful patient pause/time-out is to consistently have one individual lead it (i.e., provider or nurse), use a checklist that captures all essential elements, employ active communication of all team members, and to briefly document it after it is complete. The implementation of such checklists for the patient pause/time-out can minimize morbidity and mortality for patients, strengthens teamwork and communication among team members involved in the procedure, and improves compliance with safety measures [29–33]. While application of these same principles has not been demonstrated in other areas of procedure-related processes (i.e., around pre-procedure or discharge operations), these same doctrines would undoubtedly be beneficial in these areas and help to increase the quality of the endoscopy unit.

Infection Control and Safety

Infection control and safety play an integral role in the quality of an endoscopy unit. There does exist a risk, albeit small, for transmission of some infectious agents through endoscopy [47]. The majority of this risk is due to lapses in established protocols for endoscope handling and reprocessing. Significant practice variation with regard to infection control has been reported in endoscopy units across the USA; gaps in both infection control and safety have been noted in over a fifth of the US Ambulatory Endoscopy units surveyed in areas such as hand hygiene and personnel protective equipment, injection safety and medication handling, and equipment processing [48]. Moreover, infection outbreaks that have been directly linked to specific endoscopy units [49] or equipment [50] have been prominent in the media over the years; this media coverage has heightened the public's concern around infection and the performing of endoscopic procedures. Such variation highlights the need for continued work toward training and standardization in this area. It is also important to note that a number of guidelines have been established in the area of infection control and safety by both medical societies [47, 51–54] and regulatory agencies [55, 56]. These guidelines have focused on reprocessing of endoscopes, antibiotic prophylaxis before procedures, safe medication administration practices, and general infection control. However, it should be noted that much of this work is based more on expert opinion rather than outcome data.

Specific interventions aimed at improving infection control and safety in the endoscopy unit have centered on following and monitoring standard guidelines and policies and have been outlined in several documents [47, 51, 52]. In terms of infection control, cleaning of endoscopes first with pre-cleaning in the procedure room and then by manual cleaning with detergent solution and brushes [57, 58], followed by high-level disinfection and then proper rinsing, drying, and hanging of the endoscopes, helps to significantly reduce the number of microorganisms detected in an endoscope, thereby reducing transmission rates to patients. Newer evidence has suggested that periodic monitoring of endoscopes with microbiological cultures [59], bioburden test

kits, or adenosine triphosphate bioluminescence testing [60–62] can further aid in reducing the burden of microorganisms in endoscopes. In addition to outlining the process for reprocessing endoscopes, ensuring that staff are properly trained and competent in these steps is equally important in maintaining sound infection control practices in the endoscopy unit. National practice guidelines are in place mandating that all personnel who reprocess endoscopes be provided with device-specific reprocessing instructions annually and that at a minimum, annual competency testing be performed on all staff who reprocess endoscopes [63]. Interventions recommended to help reinforce these guidelines include developing checklists for all steps involved in reprocessing endoscopes, documentation of completing these steps by each staff member within a specific timeframe (i.e., over a week/month), orientation for staff on infection control, and focused training in the form of in-services or hands-on training [64]. Also, an infection prevention plan that is directed by a qualified person is recommended for each endoscopy unit [52]. In terms of safety, standard precautions are advocated for all staff in order to reduce transmission of infections from patients to endoscopy unit staff [47]. A common element for ensuring adequate infection control and safety within an endoscopy unit is extensive training, monitoring, and reassessment of all staff on these core principles.

Staff Experience

Staff satisfaction is a well-recognized and central element to many business sectors, and improved staff engagement has historically been positively correlated with patient satisfaction [65–67]. In regard to staff experience and healthcare, much of the literature has focused on nursing staff where promoting high-level leadership practices [68]; having a relationship with and support from their manager; organizational commitment [69, 70]; work content; environment [71] such as adequate staffing, resources, and workload [72]; and salary [68] are all strongly linked to overall higher job satisfaction. Furthermore, improvements in each of these areas led to improved staff retention, less absenteeism, improved team communication, and greater patient satisfaction. Limited literature in this area echoes previous research in other healthcare sectors and that the presence of strong leadership [73], shared governance with active participation by employees [74], guidance and feedback about performance [75], and developing and reassessing career goals [76] are strongly tied to greater staff satisfaction in the endoscopy unit. Similar results have been found for physicians, but other areas such as the changing healthcare environment, autonomy, and relationships with patients and colleagues [77] are also notable contributors to provider satisfaction in the workplace.

Few interventions have proven efficacy in specifically enhancing endoscopy unit staff satisfaction, but effective tools have been reported within the wider healthcare field. First, recognizing the value and work of staff through employee recognition programs can lead to improvement in staff satisfaction [67]. Second, it is essential to foster an environment that promotes staff development and promotion through both internal and external training and educational curriculum [78]. Third, conducting performance evaluations and providing meaningful and ongoing employee feedback are well-established mechanisms for empowering staff and improving the work environment. Other critical areas that can better the staff experience are ensuring adequate staffing levels in the organization, having an easily identified and strong leadership, and ensuring robust and clear communication from frontline managers [79, 80]. Finally, it is important to hear the voice of the endoscopy unit staff which can be accomplished through implementation of staff satisfaction surveys and then using the results to develop countermeasures [67] in areas scored low by staff.

Patient Experience

The final domain of endoscopy unit measurement should pertain to patient experience. Patient experience has always been a cornerstone of high-quality healthcare, but it was not until 1991 that is was selected as a major quality indicator for healthcare. Currently, patient indicators have been adopted by a number of regulatory agencies; in some cases, physician and hospital payments are now linked to the results from patient experience surveys. Along these lines, several patient experience surveys have been developed for endoscopy units. For example, the American Society for Gastrointestinal Endoscopy (ASGE) has developed and validated a modified Group Health Association of America-9 survey (mGHAA-9) [81]. Similarly, Press-Ganey recently released a Consumer Assessment of Healthcare Providers and Systems (CAHPS) survey that concentrates on the ambulatory surgery/endoscopy environment [82]. Both surveys share similar themes in that they assess a number of elements about care a patient may receive at an endoscopy unit: aspects of care before the procedure, about the facility and staff, communications about the procedure, recovery, and overall experience.

Much investigation has been undertaken examining the relationship between improved patient experience and the performance of an endoscopic procedure. Several factors have been associated with higher patient experience scores for patients undergoing an endoscopic procedure; these factors include the endoscopists' and nurses' personal manner, technical skill of the endoscopist, physical environment of the endoscopy unit, adequate explanation of the procedure and results after the procedure, shorter wait times, and prompt access to endoscopic services [83, 84]. Additionally, adequate control of patients' pain during the procedure has been strongly correlated with higher patient experience scores and has been demonstrated to be a priority for patients

undergoing endoscopy [81, 83, 85, 86]. Interestingly, the majority of the patient experience measures used for GI endoscopy are derived from a clinician perspective, and to date there are no patient-derived experience measures [87]. While it is essential to ensure that patients have a positive experience when utilizing the healthcare system, it does remain unclear if higher patient experience scores result in better outcomes for patients; in fact, recent data has suggested that higher patient satisfaction was associated with greater inpatient admissions, higher overall healthcare and prescription drug expenditures, and increased mortality [88].

Many of the interventions highlighted for improving patient satisfaction with endoscopy revolve around communication. The use of educational videos [89] and educational handouts [90] and pre-consultation with a provider [91] are effective methods for improving communication with patients prior to endoscopy and can lead to a better patient experience. Pain control and reducing anxiety are also critical elements to address when improving patient satisfaction. Several predictors have been found to correlate with decreased tolerability when undergoing endoscopy and include female gender, younger age, first procedure, and patient use of psychotropic medications or alcohol [92]. Strategies aimed at improving patient comfort, and thus satisfaction, have focused on addressing some of these predictors and have included increased sedation, insufflation with carbon dioxide [93] rather than air, water immersion during insertion of a colonoscope [94], patient position during the procedure (i.e., supine), and playing music during a colonoscopy [95, 96]. Equally important to improving the patient experience is to ensure that a robust sample of patients from the endoscopy unit are surveyed in order to understand patient concerns and identify systemic problems. A number of methods, including mailing, calling, or emailing, can be used for distributing patient satisfaction surveys [97], but in order to improve response rates, it is necessary to ask patients ahead of time their preferred method for receiving such a survey and to distribute the survey after the patient leaves the endoscopy unit. Overall, concrete methods for improving patient experience in endoscopy focus on personal manner and etiquette of the endoscopist and staff, minimizing procedural discomfort, prompt consultation with the patient both before and after the procedure, and easy access with shortened appointment wait times for endoscopy.

Efficiency Measures in GI Endoscopy Units

Equally important as measuring quality in endoscopy units, it is essential to understand how improving and measuring efficiency can enhance endoscopy unit operations. While the study of efficiency has been the focus of management in many industries, it has not been until recently that incorporating efficiency models into healthcare, and in particular the endoscopy unit, has occurred. The focus and rise of improving efficiency within endoscopy units has been prompted by a number of challenges in GI healthcare, including a rising demand for procedures with limited resources and a large, expanding patient population. Simultaneously, efficiency has now been recognized by several medical societies and regulatory agencies as a critical element of healthcare; for example, the Institute of Medicine has identified efficiency and timeliness as key dimensions of healthcare quality [98].

While the rigorous application and study of efficiency is a relatively new concept to endoscopy units, other areas of the healthcare sector have been more proactive in this area. In the field of healthcare efficiency, anesthesia has been the clear leader for the last four decades. In particular, there has been a tremendous amount of research focused on improving efficiency in ambulatory surgery centers and hospital operating rooms (OR). Three key steps have emerged on how to improve efficiency within a healthcare setting from this literature and offer tremendous insight for endoscopy units on how to begin this process. These three steps center on (1) measurement and monitoring of processes through the use of metrics, (2) observing the processes and operations of the organization and then modeling proposed changes in order to improve it, and (3) finally implementing these proposed changes in a systematic way.

First, metrics need to be developed so that improvement work can be measured and monitored. For instance, clearly defined efficiency metrics for the operating room have been established by the Association of Anesthesia Clinical Directors which have been utilized and validated in several studies [99]. Once metrics have been clearly defined and data gathered on them, it is then essential to begin establishing benchmarks/targets for them. In doing so, this is where performance gaps can be identified and quality improvement projects can be developed. However, accepted and rigorously studied efficiency metrics/benchmarks are lacking for endoscopy units.

Second, it is necessary to better understand areas where performance improvement work is needed and where it can be successfully implemented. Pivotal to this success is the employment of time and motion studies (i.e., direct and continuous observation of a task) or work sampling (i.e., observing work at various instants of time) in order to determine the time required for various tasks. This approach allows one to assess and determine where improvements in the overall process of an operation can be improved. In conjunction with information gained from either of these two approaches, discrete event simulation modeling (i.e., modeling the operations of a system) can then be used to study proposed changes to a system in order to predict its performance in the real world. In addition to anesthesia [100–106], a number of other healthcare specialties have successfully employed sim-

ulation modeling to improve efficiency, such as primary care [107–110], emergency rooms [111–113], and pediatrics [114, 115]. As an example, anesthesia simulation modeling has demonstrated that duration of a surgical procedure is not a rate-limiting step in OR efficiency, but rather factors that occur prior to and subsequently after the procedure (e.g., patient pre-procedure requirements and room turnover time) are more critical factors to efficiency [100]. Similar findings have been reported for GI endoscopy units [116–118].

Thirdly, the implementation of performance improvement projects using a systematic and consistent process, in most cases modeled after the PDSA (Plan-Do-Study-Act) method, is needed. A key element of PDSA is to incrementally implement changes so as to determine if a new procedure/process is having the expected positive effects before a full implementation and to study if changes need to be made to the design. On this topic, one important element that has emerged from the anesthesia literature with regard to implementing improvement projects is that clearly studying and identifying process inefficiencies and instituting multidisciplinary education programs with clear goals to address them [103, 104] can led to a dramatic improvement in operating room efficiency. In summary, these three consistent steps have been instrumental in improving efficiency in the operating room and have allowed for the enhancement of quality and patient care for surgical patients. Given the vast number of similarities between the operating theater and endoscopy units, these same steps are also applicable to the field of GI.

Practical Considerations

- Endoscopy unit efficiency metrics measure the structure, process, and outcomes of the endoscopy unit.
- Measurement and monitoring of these metrics is a necessary step toward improved productivity.
- Endoscopy unit efficiency can be improved by focusing on several key areas, including personnel utilization, patient scheduling, procedure delays, procedure room turnover, and recovery room time.

Endoscopy Unit Efficiency Metrics and Benchmarks

In order to begin enhancing efficiency within an endoscopy unit, one of the first steps is to clearly define the metrics that will be used to initially assess the organization and to eventually measure its success. In an attempt to study efficiency within endoscopy units, several authors have proposed endoscopy unit metrics (Table 47.2 provides a comprehensive list of all reported efficiency metrics from the literature). These metrics are modeled after the ones developed by anesthesia where each aspect from when a patient arrives at the endoscopy unit to the moment when they are discharged is separated into its constituent parts and measured with respect to time. The most exhaustive research in the area of endoscopy unit metrics has been performed by only a few groups [118, 119] who examined a number of time factors involved in patient flow through an endoscopy unit. However, efficiency measurements used in these studies, while comprehensive and potentially useful in assessing overall flow and utilization of the endoscopy unit, were labor intensive, cumbersome, and difficult to practically employ into most endoscopy units. A more global approach was recently proposed whereby endoscopy unit efficiency metrics were divided into three distinct categories, (1) structural, (2) process, and (3) outcome measures; unfortunately very little data has validated many of these proposed measures, and again the practical implementation of them has been questioned [120]. Presently, no set of efficiency metrics has been adopted nor accepted by the GI societies. While it is not practical to measure all of the proposed endoscopy unit efficiency metrics from the literature, it is essential to select a few of them to begin the process of systematically collecting, tracking, and monitoring the data and then using it to improve your own organization. Table 47.3 highlights a select few efficiency metrics that correlate strongly with an endoscopy unit's efficiency and provides a starting point for where many endoscopy units can begin their measurements.

Once an endoscopy unit has determined which set of metrics to utilize and measure, it is critical to have benchmarks (i.e., standard or point of reference in measuring or judging the current value or success of an organization in order to determine its success or overall performance in comparison to the performance of other similar organizations). Initially, one may not need benchmarks because internal metrics can be used to monitor the success or failure of implementing process or technology changes. However, benchmarks serve to help guide the organization in accordance with accepted industry standards and best practices. Yet, as with metrics, few published benchmarks are available for endoscopy units. Scant data is available for some measurements that are used in research, but again it is unclear if these measurements/ranges represent the "optimal" assessment. Additionally, of the few published benchmarks, there is considerable heterogeneity in their numbers with a multitude of confounding factors such as type of sedation utilized for each procedure, procedure type, and type of endoscopy unit where the data was collected (outpatient ambulatory center, tertiary hospital, academic hospitals) that may impact the interpretation of their results (Table 47.4). Much of the remaining literature is less rigorous and focuses mostly on "expert opinion" with respect to suggested personnel, equipment, and facility

Table 47.2 Existing endoscopy unit metrics as published in the literature

Operational metrics
Waiting room time (time between patient check-in and transport to pre-procedure room)
Pre-procedure room time (time between patient entering pre-procedure room and transport to procedure room)
Procedure room time (time between patient entering procedure room and patient transported out of procedure room)
Sedation time (time of initial dose of sedating medication to beginning of procedure)
Recovery room time (time between patient returning to recovery room and discharged from endoscopy center)
Procedure room turnover time (time of when patient is transported to recovery room and procedure room is ready to accept the next patient)
Number of cancelations and no-shows/procedure room/day
Total duration of patient in endoscopy center (time of when patient checks in and when patient is discharged)
Total facility time (time of when first patient checks in to when last patient is discharged)
Productivity metrics
Number of procedures/procedure room/day
Number of patients/physician/day
Number of procedures/physician/day
Number of patients/procedure room/day
Physician utilization (proportion of the time physician is engaged in procedure and completing procedure-related paperwork)
Nursing utilization (proportion of the time nurse is engaged in procedure and completing procedure-related paperwork)
Personnel metrics
Number of physicians assigned to an endoscopy room/endoscopy unit
Number of nurses assigned to an endoscopy room/endoscopy unit
Number of nurses assigned to a pre-procedure or recovery room/endoscopy unit
Number of ancillary staff/endoscopy unit
Facility metrics
Number of endoscopy rooms
Number of endoscope reprocessing rooms
Number of pre-procedure beds/endoscopy room
Number of recovery beds/endoscopy room
Equipment metrics
Number of colonoscopes/endoscopy room
Number of upper endoscopes/endoscopy room
Number of advanced endoscopic equipment/endoscopy room
Time required to reprocess one endoscope
Number of automatic reprocessing machines/endoscopy room
Patient satisfaction metrics
Appointment lead time (length of time from scheduling of endoscopic procedure to day of procedure)
On-time start of performing an endoscopic procedure
Patient satisfaction surveys (e.g., Press-Ganey, OAS-CAHPS)

requirements of endoscopy units with no clear evidence to support such recommendations [130, 131] (Table 47.5). Consequently, there is minimal data on accepted metrics and benchmarks, and available information is fraught with bias, inconsistencies, and lack of evidence.

Interventions to Improve Endoscopy Unit Efficiency

With an emphasis on cost containment and improving efficiency in healthcare, a number of methods, such as time and motion studies and discrete event simulation modeling, have been successfully advocated and performed to help attain these goals [134]. Promising work has been conducted using these two tools to help fully examine a number of factors that impact endoscopy unit efficiency [118, 119]. Using information learned from these two methods, a number of changes have then been implemented in endoscopy units resulting in improved efficiency and productivity. What is evident from the current literature is the power that intense observation and simulation modeling can offer in better understanding the operations and how potential changes can affect the efficiency of an endoscopy unit. Such a systematic approach has been essential in developing interventions aimed at improving endoscopy unit efficiency.

In assessing efficiency within endoscopy units, several elements have emerged as potential areas where process improvements can be executed. These areas include personnel utilization, patient scheduling, delays, room turnover time, and recovery room time. A framework for how and where to make improvement changes in each of these areas is discussed below (Fig. 47.1 and Table 47.3).

Personnel Utilization

A crucial factor within an endoscopy unit is the staff and how to best utilize staffing resources. A tremendous amount of work has been conducted in this arena and can serve as a useful resource for endoscopy units. In general staffing guidelines are affected by state regulations and whether or not anesthesia services are involved. With respect to nursing, some GI societies have proposed nursing staff models, with one nurse per procedure room to perform sedation and another staff member recommended to help assist the endoscopist. While helpful it should be noted that no data exist to support or refute these recommendations [135]. Likewise, proposed models for utilizing endoscopists have been put forth. Some have proposed that if there is an abundance of endoscopy rooms, then it is more efficient to employ a "one-endoscopist-two-room" model [130]. This model has been studied further; however, its results with respect to efficiency are inconclusive and conflicting. For example, using such a model has been shown to increase efficiency nearly 50% [118] and procedure volume by 11% [133], but some studies

have shown that it comes at a cost to the endoscopy unit being suboptimized with patient length of stays increasing and non-physician staff utilization decreasing [118]. Another proposed endoscopist model is the incorporation of non-physicians (nurse practitioner/physician assistants) into the endoscopy unit who can perform endoscopy. Numerous data have shown that non-physicians can safely perform endoscopic procedures with similar quality as physicians [136–140]. Expanding the role of non-physicians into performing endoscopy would allow endoscopy units to increase services and access and allow gastroenterologists to focus their attention on more complex and demanding procedures/cases. Nurse practitioners/physician assistants are generally less costly than physicians, but their productivity may also be less [141], and thus this needs to be considered. Other considerations for staffing include utilizing endoscope technicians in the room turnover process, ensuring that one staff member (whether it be a nurse or technician) serves as a "floater" throughout the day to assist in areas where bottlenecks may be occurring in endoscopy unit patient flow, and identifying both a nursing and physician leader of the day who can help with patient flow and to address challenges as they occur.

Table 47.3 Selected endoscopy unit efficiency measurements and specific interventions to improve them

Efficiency	
Measurements	Interventions for improvement
Number of patients/procedure room/day	Reduce room turnover time Sedation selection (fentanyl/midazolam for moderate sedation) Endoscopist not performing sedation Minimize/eliminate post-procedure paperwork
Sedation time (i.e., time to induction)	Sedation selection (fentanyl/midazolam or propofol for moderate sedation)
Room turnover time	Parallel processing of staff Clear signaling of when a procedure is completed and standard work for staff in the room turnover process Minimizing procedure delays
Recovery room time	Sedation selection (fentanyl/midazolam or propofol for moderate sedation)
Schedule utilization	Block scheduling Incorporating no-show rate into number of patients scheduled per provider
Procedure delays	Clear instructions for patients (how to prepare for procedure, logistics for getting to unit) Establish performance expectations for endoscopists

Table 47.4 Reported ranges of endoscopy unit efficiency measurements from the literature

Operational benchmarks	EGD	Colonoscopy
On-time procedure start (%) [119, 121]	53.3–75.0	55.0–75.0
Pre-procedure time (min) [64, 118, 119]	6.0–20.9	3.0–61.0
Procedure duration (min) [64, 118, 119, 122, 123]	3.0–31.1	14.0–42.0
Sedation time (min)		
Moderate sedation[a] [118, 119, 122–124]	5.0–10.0	2.1–11.2
Propofol [124–126]	2.1–3.6	2.1
Room turnover time(min) [118, 119, 123, 127]	3.0–26.6	2.0–26.6
Recovery room time (min)		
Moderate sedation[a] [64, 118, 119, 123, 124]	9.1–50.2	14.0–61.0
Propofol [123–125, 128, 129]	3.4–15.0	14.3–18.0
Endoscopist completing paperwork after procedure (min) [118]	2.0	3.0

[a]Moderate sedation includes midazolam/fentanyl, midazolam/meperidine, opioid alone

Patient Scheduling

Within ambulatory surgery centers, several studies have demonstrated that shortening procedure time does not improve overall efficiency, but rather other factors such as scheduling and operational improvements are more instrumental [116]. One potential efficiency improvement may relate to the initial scheduling of patients. A proposed method

Table 47.5 Reported endoscopy unit benchmarks based on expert opinion

Productivity benchmarks	
Number of procedures/room/day [132]	14–16
Number of patients/room/half-day	6
Personnel/staff benchmarks	
Number of physicians/room	1
Number of nurses/room [131]	1.5–2
Number of reprocessors per endoscopy unit	1–2
Equipment benchmarks	
Number of endoscopes: endoscopy room	2 upper endoscopes and 2 colonoscopes:1
Mean time of reprocessing endoscopes (min)	30
Number of automatic endoscope reprocessors: procedure room [133]	1.5–2:1
Facility benchmarks	
Size of endoscopy room [131]	220/300 square feet
Number of recovery beds: procedure room [130, 133]	2–3:1
Number of pre-procedure beds: procedure room [130, 133]	2:1

for scheduling procedures focuses on utilizing open access endoscopy (i.e., scheduling and performing endoscopic procedures without a formal GI consultation/office visit). Such a method can improve patient access to both clinic and endoscopy, but some limitations may exist. For example, some studies suggest that open access yields more inappropriate indications for procedures with a reported 10–28% prevalence of incorrectly scheduled procedures [131]. A second approach to scheduling patients is the utilization of block time (i.e., scheduling a provider for a defined, set period of time each day to perform procedures, usually in half-days) for providers and has been recommended as the most efficient use of creating an endoscopy schedule [142]; however, data for this recommendation only hails from the anesthesia literature [143, 144]. Additionally, mathematical models have been developed to help improve use rate, utilize waiting time characteristics and patient no-show rates, and incorporate overbooking into endoscopy unit schedules, but the implementation of these scheduling models into practice has not been reported [145]. While it is not clear which method would improve efficiency, what is evident from the literature is that through observation of workflow and understanding endoscopy unit patterns, one can better align the endoscopy unit schedule to better improve throughput and utilization [119].

Procedure Delays

Equally important as scheduling factors are minimizing delays within the endoscopy unit. There are two types of endoscopy unit delays: patient and procedure related. With regard to patient-related delays, there are number of interventions the endoscopy unit can employ. These include ensuring patient instructions and expectations are clear, providing simple and easy directions to the endoscopy unit, an advance call to patients to review preparatory instructions/medications, and ensuring an efficient check-in process once the patient arrives at the endoscopy unit. A number of modalities have been shown to improve patient adherence to instructions and reduce patient-related delays including multimedia, interactive computer programs, and education classes [146]. On the other hand, procedure-related delays are similarly important to minimize. In this area physicians are overwhelming responsible for such delays [147]. These delays have a significant impact on workflow processes, add to patient waiting time, and increase room turnover time. Physician-related delays are usually the result of two factors: (1) multitasking and performing other tasks not related to endoscopy or (2) consistently exceeding their scheduled procedure times. It is crucial to address these issues with providers, monitor and share this data with physicians, and have mechanisms in place to deal with physician behavior.

Sedation

While reducing endoscopic procedure time does not appear to increase efficiency of an endoscopy unit [127], other factors that occur within the procedure room can improve efficiency. In particular, induction/sedation time can be reduced based on the type of sedation utilized leading to less overall time in a procedure room and thus greater efficiency. Alternating the type of moderate sedation has demonstrated some benefits in improving the efficiency within the endoscopy unit. Recently, the use of midazolam/fentanyl was shown to reduce total procedure time (due to shorter induction-to-intubation time) for patients undergoing upper endoscopies with overall efficiency rising 22% compared with midazolam/meperidine use for the same procedure [122]. Likewise, significant attention has been focused on the use of propofol which has demonstrated benefits on endoscopy unit efficiency in a number of areas [125]. However, controversy surrounds the administration of propofol by endoscopists/nurses, and the addition of an anesthesiologist to the care team to provide such a service, while increasing overall efficiency, does so at a dramatic financial

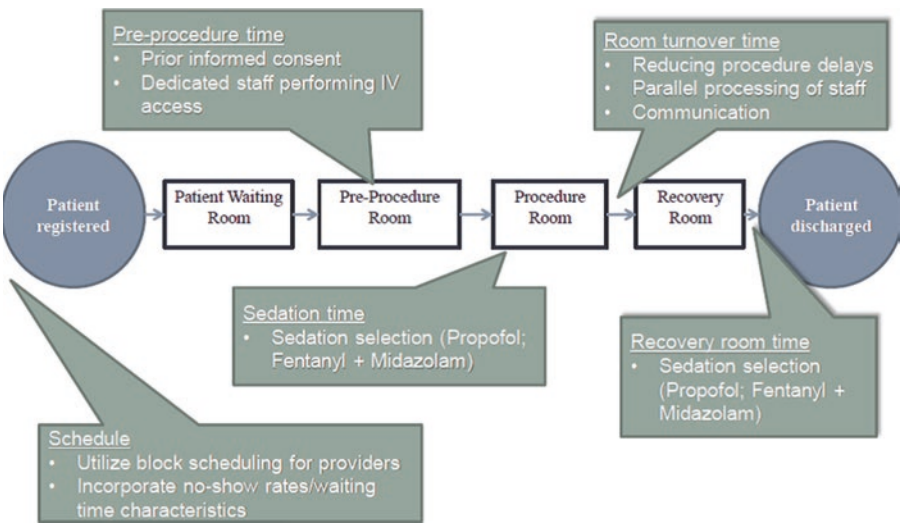

Fig. 47.1 Factors that can streamline endoscopy unit workflow processes and improve efficiency

cost. Nonetheless, the sedation type administered should be examined as it has an impact on several components of endoscopy center efficiency.

Room Turnover Time

One area that has been used as a marker for improving efficiency is reducing endoscopy room turnover time once a procedure is completed. For example, a clear inverse relationship between procedure volume and shorter room turnover times exists [116]. Yet, the majority of tasks associated with room turnover time are fixed and can be difficult to streamline. However, previous work in the operating room has realized this challenge, and some work has demonstrated that parallel processing of tasks among staff members (i.e., simultaneously performing several patient-related tasks at the same time) can lead to a dramatic reduction in operating room turnover time [101, 102]. Furthermore, clear and easy communication/signaling of when a procedure is completed (in order to begin the room turnover process) and clearly identifying staff roles are critical elements at minimizing this time.

Recovery Room

Lastly, reducing recovery room time can help increase endoscopy unit efficiency. With regard to recovery room time, Grossman modeled an ambulatory surgery center and demonstrated that recovery time was the main bottleneck. In fact, a 50% reduction in recovery room time increased the number of patients per room per day and shortened the overall length of stay of patients [148]. However, how to address this bottleneck has been less well studied and is a challenging problem. Aside from increasing the physical space of the recovery area, the only specific intervention proposed to reduce this time has been sedation related. The use of propofol in some endoscopy units [125], using one sedating medication compared with two medications [123] or using midazolam/fentanyl for moderate sedation [122], all reduces recovery room time and increases overall procedure volume in endoscopy units, thereby enhancing the overall efficiency of the endoscopy unit.

Conclusion

Improving quality and efficiency in endoscopy units has been an increasingly important topic. The development and measurement of quality measures within endoscopy units is a fairly new development in GI, with some parts of the world much farther along than the US. Central to endoscopy unit quality measures are four key areas that center on procedure-related aspects, infection control and safety, staff experience, and patient experience. Within each of these areas, a number of proposed indicators have been put forth, but what is clear from the literature is that clear outcome measures with a robust literature supporting them are lacking. Equally lacking are proven interventions within endoscopy unit settings to help improve these four key areas.

At the same time, incorporating efficiency measurements can significantly improve the quality of the endoscopy unit. There are three key steps to consider when beginning the journey of improving endoscopy unit efficiency. The first step in improving efficiency within an endoscopy unit is to determine which metrics would be the most relevant and feasible to measure within one's organization. At the same time, it is crucial to remember that metrics help identify where to improve but do not directly cause improvements to take place. Secondly, an initial assessment of potential areas where inefficiencies may exist in an endoscopy unit should be conducted with particular focuses on patient flow, staffing, facility, and equipment. Lastly, a number of areas exist where endoscopy units can focus in order to begin improvement work in efficiency. Examining endoscopist models, minimizing patient- and procedure-related delays, utilizing block scheduling, reducing room turnover time through clear communication and role definition, and considering the types of sedation administered are factors that have been demonstrated to impact efficiency and increase procedure volume in endoscopy units.

References

1. Definition of quality. http://www.merriam-webster.com/dictionary/quality. Accessed 2 Jan 2016.
2. Origen of efficiency. http://dictionary.reference.com. Accessed 2 Jan 2016.
3. Sisko AM, Keehan SP, Cuckler GA, et al. National Health Expenditure Projections, 2013–23: faster growth expected with expanded coverage and improving economy. Health Aff. 2014;33:1841–50.
4. Dulai PS, Fisher ES, Rothstein RI. How may the transition to value-based payment influence gastroenterology: threat or opportunity? Clin Gastro Hep. 2012;10:609–11.
5. Porter ME. What is value in health care? N Engl J Med. 2010;363:2477–81.
6. From: U.S. Department of Health and Human Services Report to Congress: Medicare Ambulatory Surgical Center Value-Based Purchasing Implementation Plan. https://www.cms.gov/ASCPayment. Accessed 3 Nov 2011.
7. From: U.S. Department of Health and Human Services Report to Congress. http://www.cms.gov/Medicare/Medicare-Fee-for-service-Payment/ASCPayment/index.html. Accessed 24 Feb 2015.
8. Gellad ZF, Brill JV. Toward a learning healthcare system: use of colorectal cancer quality measures for physician evaluation. In: Shaukat a, Allen J, editors. Quality and benchmarks in colorectal cancer screening. Clin Gastroenterol Hepatol. 2016:14(5):644–7

9. Brill JV, Jain R, Margolis PS, et al. A bundled payment framework for colonoscopy performed for colorectal cancer screening or surveillance. Gastroenterology. 2014;146:849–853.e9.
10. Robinson JC, Brown TT, Whaley C, et al. ASsociation of reference payment for colonoscopy with consumer choices, insurer spending, and procedural complications. JAMA Intern Med. 2015;175:1783–9.
11. Bohra S, Byrne MF, Manning D, et al. A prospective analysis of inpatient consultations to a gastroenterology service. Ir Med J. 2003;96:263–5.
12. Cai Q, Bruno CJ, Hagedorn CH, et al. Temporal trends over ten years in formal inpatient gastroenterology consultations at an inner city hospital. J Clin Gastroenterol. 2003;36:34–8.
13. Jordan MR, Conley J, Ghali WA. Consultation patterns and clinical correlates of consultation in a tertiary care setting. BMC Res Notes. 2008;1:96.
14. Adler DG, Lieb JG 2nd, Cohen J, et al. Quality indicators for ERCP. Am J Gastroenterol. 2015;110:91–101.
15. Park WG, Shaheen NJ, Cohen J, et al. Quality indicators for EGD. Gastrointest Endosc. 2015;81:17–30.
16. Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. Am J Gastroenterol. 2015;110:72–90.
17. Rizk MK, Sawhney MS, Cohen J, et al. Quality indicators common to all GI endoscopic procedures. Am J Gastroenterol. 2015;110:48–59.
18. Wani S, Wallace MB, Cohen J, et al. Quality indicators for EUS. Gastrointest Endosc. 2015;81:67–80.
19. Global Rating Scale. http://www.globalratingscale.com. Accessed 2 Jan 2016.
20. Williams T, Ross A, Stirling C, et al. Validation of the Global Rating Scale for endoscopy. Scott Med J. 2013;58:20–1.
21. Sint Nicolaas J, de Jonge V, de Man RA, et al. The Global Rating Scale in clinical practice: a comprehensive quality assurance programme for endoscopy departments. Dig Liver Dis. 2012;44:919–24.
22. Sint Nicolaas J, de Jonge V, Korfage IJ, et al. Benchmarking patient experiences in colonoscopy using the Global Rating Scale. Endoscopy. 2012;44:462–72.
23. MacIntosh D, Dube C, Hollingworth R, et al. The endoscopy Global Rating Scale-Canada: development and implementation of a quality improvement tool. Can J Gastroenterol. 2013;27:74–82.
24. Armstrong D, Barkun A, Bridges R, et al. Canadian Association of Gastroenterology consensus guidelines on safety and quality indicators in endoscopy. Can J Gastroenterol. 2012;26:17–31.
25. Bersani G, Rossi A, Ricci G, et al. Do ASGE guidelines for the appropriate use of colonoscopy enhance the probability of finding relevant pathologies in an open access service? Dig Liver Dis. 2005;37:609–14.
26. ASGE Standards of Practice Committee, Early DS, Ben-Menachem T, et al. Appropriate use of GI endoscopy. Gastrointest Endosc. 2012;75:1127–31.
27. de Bosset V, Froehlich F, Rey JP, et al. Do explicit appropriateness criteria enhance the diagnostic yield of colonoscopy? Endoscopy. 2002;34:360–8.
28. Froehlich F, Repond C, Mullhaupt B, et al. Is the diagnostic yield of upper GI endoscopy improved by the use of explicit panel-based appropriateness criteria? Gastrointest Endosc. 2000;52:333–41.
29. Haynes AB, Weiser TG, Berry WR, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med. 2009;360:491–9.
30. Howell AM, Panesar SS, Burns EM, et al. Reducing the burden of surgical harm: a systematic review of the interventions used to reduce adverse events in surgery. Ann Surg. 2014;259:630–41.
31. Lepanluoma M, Takala R, Kotkansalo A, et al. Surgical safety checklist is associated with improved operating room safety culture, reduced wound complications, and unplanned readmissions in a pilot study in neurosurgery. Scand J Surg. 2014;103:66–72.
32. Lyons VE, Popejoy LL. Meta-analysis of surgical safety checklist effects on teamwork, communication, morbidity, mortality, and safety. West J Nurs Res. 2014;36:245–61.
33. Pugel AE, Simianu VV, Flum DR, et al. Use of the surgical safety checklist to improve communication and reduce complications. J Infect Public Health. 2015;8:219–25.
34. Aldrete JA. The post-anesthesia recovery score revisited. J Clin Anesth. 1995;7:89–91.
35. Chernik DA, Gillings D, Laine H, et al. Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: study with intravenous midazolam. J Clin Psychopharmacol. 1990;10:244–51.
36. Trevisani L, Cifala V, Gilli G, et al. Post-Anaesthetic Discharge Scoring System to assess patient recovery and discharge after colonoscopy. World J Gastrointest Endosc. 2013;5:502–7.
37. White PF, Song D. New criteria for fast-tracking after outpatient anesthesia: a comparison with the modified Aldrete's scoring system. Anesth Analg. 1999;88:1069–72.
38. de Jonge V, Sint Nicolaas J, Cahen DL, et al. Quality evaluation of colonoscopy reporting and colonoscopy performance in daily clinical practice. Gastrointest Endosc. 2012;75:98–106.
39. Kahi CJ, Ballard D, Shah AS, et al. Impact of a quarterly report card on colonoscopy quality measures. Gastrointest Endosc. 2013;77:925–31.
40. Bloodworth K. The productive ward and the productive operating theatre. J Perioper Pract. 2011;21:97–103.
41. Rodriguez HP, Ivey SL, Raffetto BJ, et al. As good as it gets? Managing risks of cardiovascular disease in California's top-performing physician organizations. Jt Comm J Qual Patient Saf. 2014;40:148–58.
42. Coe SG, Crook JE, Diehl NN, et al. An endoscopic quality improvement program improves detection of colorectal adenomas. Am J Gastroenterol. 2013;108:219–26. quiz 227
43. Corley DA, Jensen CD, Marks AR. Can we improve adenoma detection rates? A systematic review of intervention studies. Gastrointest Endosc. 2011;74:656–65.
44. Coe SG, Panjala C, Heckman MG, et al. Quality in colonoscopy reporting: an assessment of compliance and performance improvement. Dig Liver Dis. 2012;44:660–4.
45. Hande KA. Measuring endoscopic performance for colorectal cancer prevention quality improvement in a gastroenterology practice. Nurs Clin North Am. 2014;49:15–27.
46. Pike IM, Vicari J. Incorporating quality measurement and improvement into a gastroenterology practice. Am J Gastroenterol. 2010;105:252–4.
47. ASGE Standards of Practice Committee, Banerjee S, Shen B, et al. Infection control during GI endoscopy. Gastrointest Endosc. 2008;67:781–90.
48. Schaefer MK, Jhung M, Dahl M, et al. Infection control assessment of ambulatory surgical centers. JAMA. 2010;303:2273–9.
49. Fischer GE, Schaefer MK, Labus BJ, et al. Hepatitis C virus infections from unsafe injection practices at an endoscopy clinic in Las Vegas, Nevada, 2007-2008. Clin Infect Dis. 2010;51:267–73.
50. Muscarella LF. Risk of transmission of carbapenem-resistant Enterobacteriaceae and related "superbugs" during gastrointestinal endoscopy. World J Gastrointest Endosc. 2014;6:457–74.
51. ASGE Quality Assurance Committee, Petersen BT, Chennat J, et al. Multisociety guideline on reprocessing flexible gastrointestinal endoscopes: 2011. Gastrointest Endosc. 2011;73:1075–84.
52. ASGE Ensuring Safety in the Gastrointestinal Endoscopy Unit Task Force, Calderwood AH, Chapman FJ, et al. Guidelines for safety in the gastrointestinal endoscopy unit. Gastrointest Endosc 2014;79:363–372.

53. ASGE Technology Committee, Pedrosa MC, Farraye FA, et al. Minimizing occupational hazards in endoscopy: personal protective equipment, radiation safety, and ergonomics. Gastrointest Endosc. 2010;72:227–35.
54. Martin MA, Reichelderfer M. APIC guidelines for infection prevention and control in flexible endoscopy. Association for Professionals in Infection Control and Epidemiology, Inc. 1991, 1992, and 1993 APIC Guidelines Committee. Am J Infect Control. 1994;22:19–38.
55. Standard practice for cleaning and disinfection of flexible fibreoptic and video endoscopes used in the examination of hollow viscera. ASTM Standard F1518-94. Philadelphia: American Society for Testing and Materials.
56. Food and Drug Administration ICD, Branch Division of General and Restorative Devices, Office of Device Evaluation. Guidance on the content and format of premarket notification [510 (k)] submissions for liquid chemical germicides. Rockville: FDA; 1992.
57. Ishino Y, Ido K, Koiwai H, et al. Pitfalls in endoscope reprocessing: brushing of air and water channels is mandatory for high-level disinfection. Gastrointest Endosc. 2001;53:165–8.
58. Nelson DB. Infectious disease complications of GI endoscopy: part II, exogenous infections. Gastrointest Endosc. 2003;57:695–711.
59. Beilenhoff U, Neumann CS, Rey JF, et al. ESGE-ESGENA guideline for quality assurance in reprocessing: microbiological surveillance testing in endoscopy. Endoscopy. 2007;39:175–81.
60. Alfa MJ, Fatima I, Olson N. Validation of adenosine triphosphate to audit manual cleaning of flexible endoscope channels. Am J Infect Control. 2013;41:245–8.
61. Alfa MJ, Fatima I, Olson N. The adenosine triphosphate test is a rapid and reliable audit tool to assess manual cleaning adequacy of flexible endoscope channels. Am J Infect Control. 2013;41:249–53.
62. Alfa MJ, Olson N, Degagne P, et al. Development and validation of rapid use scope test strips to determine the efficacy of manual cleaning for flexible endoscope channels. Am J Infect Control. 2012;40:860–5.
63. The Joint Commission. Comprehensive accreditation manual for hospitals. Oakbrook Terrace ITJCAAfAHAhfahW: 2006.
64. Colonoscopy July–December 2014 report: performance measurement and benchmarking in ambulatory care organizations. AAAHC Institute for Quality Improvement. http://www.aaahc.org/institute/. Accessed 20 Dec 2015.
65. Collins KS, Collins SK, McKinnies R, et al. Employee satisfaction and employee retention: catalysts to patient satisfaction. Health Care Manag (Frederick). 2008;27:245–51.
66. Harter JK, Schmidt FL, Hayes TL. Business-unit-level relationship between employee satisfaction, employee engagement, and business outcomes: a meta-analysis. J Appl Psychol. 2002;87:268–79.
67. Pund LEaPS. Linking quality assurance to human resources: improving patient satisfaction by improving employee satisfaction. https://spea.indiana.edu/doc/undergraduate/ugrd_thesis2012_hmp_pund.pdf. Accessed 1 May 2015.
68. Coomber B, Barriball KL. Impact of job satisfaction components on intent to leave and turnover for hospital-based nurses: a review of the research literature. Int J Nurs Stud. 2007;44:297–314.
69. Moneke N, Umeh OJ. Factors influencing critical care nurses' perception of their overall job satisfaction: an empirical study. J Nurs Adm. 2013;43:201–7.
70. Moneke N, Umeh OJ. How leadership behaviors impact critical care nurse job satisfaction. Nurs Manag. 2013;44:53–5.
71. Irvine DM, Evans MG. Job satisfaction and turnover among nurses: integrating research findings across studies. Nurs Res. 1995;44:246–53.
72. Atefi N, Abdullah KL, Wong LP, et al. Factors influencing registered nurses perception of their overall job satisfaction: a qualitative study. Int Nurs Rev. 2014;61:352–60.
73. Hobgood E. Leading the way: walking in a nurse's shoes. Gastroenterol Nurs. 2003;26:215–8.
74. Metcalf R, Tate R. Shared governance in the endoscopy department. Gastroenterol Nurs. 1995;18:96–9.
75. Salmore R. Praise as a means to increase job satisfaction. Gastroenterol Nurs. 1990;13:98–100.
76. Greenwald B. How the gastroenterology nurse can establish and meet career goals. Gastroenterol Nurs. 2006;29:291–4.
77. Gerrity MS, Pathman DE, Linzer M, et al. Career satisfaction and clinician-educators. The rewards and challenges of teaching. The Society of General Internal Medicine Career Satisfaction Study Group. J Gen Intern Med. 1997;12 Suppl 2:S90–7.
78. Burston AS, Tuckett AG. Moral distress in nursing: contributing factors, outcomes and interventions. Nurs Ethics. 2013;20:312–24.
79. Andrews DR, Dziegielewski SF. The nurse manager: job satisfaction, the nursing shortage and retention. J Nurs Manag. 2005;13:286–95.
80. Awa WL, Plaumann M, Walter U. Burnout prevention: a review of intervention programs. Patient Educ Couns. 2010;78:184–90.
81. Yacavone RF, Locke GR 3rd, Gostout CJ, et al. Factors influencing patient satisfaction with GI endoscopy. Gastrointest Endosc. 2001;53:703–10.
82. OAS CAHPS Regulatory Survey. http://www.pressganey.com/solutions/service-a-to-z/oas-cahps-regulatory-survey. Accessed 19 Dec 2015.
83. Ko HH, Zhang H, Telford JJ, et al. Factors influencing patient satisfaction when undergoing endoscopic procedures. Gastrointest Endosc. 2009;69:883–91. quiz 891.e1
84. Sewitch MJ, Gong S, Dube C, et al. A literature review of quality in lower gastrointestinal endoscopy from the patient perspective. Can J Gastroenterol. 2011;25:681–5.
85. de Jonge V, Sint Nicolaas J, Lalor EA, et al. A prospective audit of patient experiences in colonoscopy using the Global Rating Scale: a cohort of 1,187 patients. Can J Gastroenterol. 2010;24:607–13.
86. Maslekar S, Hughes M, Gardiner A, et al. Patient satisfaction with lower gastrointestinal endoscopy: doctors, nurse and nonmedical endoscopists. Color Dis. 2010;12:1033–8.
87. Brown S, Bevan R, Rubin G, et al. Patient-derived measures of GI endoscopy: a meta-narrative review of the literature. Gastrointest Endosc. 2015;81:1130–40.e1–9.
88. Fenton JJ, Jerant AF, Bertakis KD, et al. The cost of satisfaction: a national study of patient satisfaction, health care utilization, expenditures, and mortality. Arch Intern Med. 2012;172:405–11.
89. Arabul M, Kandemir A, Celik M, et al. Impact of an information video before colonoscopy on patient satisfaction and anxiety. Turk J Gastroenterol. 2012;23:523–9.
90. Galaal K, Bryant A, Deane KH, et al. Interventions for reducing anxiety in women undergoing colposcopy. Cochrane Database Syst Rev. 2011:CD006013.
91. Vignally P, Gentile S, Grimaud F, et al. Pertinence of a pre-colonoscopy consultation for routine information delivery. Gastroenterol Clin Biol. 2007;31:1055–61.
92. Pena LR, Mardini HE, Nickl NJ. Development of an instrument to assess and predict satisfaction and poor tolerance among patients undergoing endoscopic procedures. Dig Dis Sci. 2005;50:1860–71.
93. Wu J, Hu B. The role of carbon dioxide insufflation in colonoscopy: a systematic review and meta-analysis. Endoscopy. 2012;44:128–36.
94. Hsieh YH, Koo M, Leung FW. A patient-blinded randomized, controlled trial comparing air insufflation, water immersion, and water exchange during minimally sedated colonoscopy. Am J Gastroenterol. 2014;109:1390–400.
95. Bechtold ML, Perez RA, Puli SR, et al. Effect of music on patients undergoing outpatient colonoscopy. World J Gastroenterol. 2006;12:7309–12.

96. Bechtold ML, Puli SR, Othman MO, et al. Effect of music on patients undergoing colonoscopy: a meta-analysis of randomized controlled trials. Dig Dis Sci. 2009;54:19–24.
97. Harewood GC, Yacavone RF, Locke GR 3rd, et al. Prospective comparison of endoscopy patient satisfaction surveys: e-mail versus standard mail versus telephone. Am J Gastroenterol. 2001;96:3312–7.
98. National Research Council (2001). Crossing the quality chasm: a new health system for the 21st century. The National Academies Press. Accessed at http://www.nationalacademies.org/hmd/~/media/Files/ReportFiles/2001/Crossing-the-Quality-Chasm/QualityChasm2001reportbrief.pdf. on September 18, 2017.
99. Zhang BPM, Dessouky M, Belson D. A mixed integer programming approach for allocating operating room capacity. J Oper Res Soc. 2009;60(5):663–73.
100. Dexter F, Macario A. Decrease in case duration required to complete an additional case during regularly scheduled hours in an operating room suite: a computer simulation study. Anesth Analg. 1999;88:72–6.
101. Friedman DM, Sokal SM, Chang Y, et al. Increasing operating room efficiency through parallel processing. Ann Surg. 2006;243:10–4.
102. Olmstead J, Coxon P, Falcone D, et al. World-class OR turnaround times: secrets uncovered. AORN J. 2007;85:942–5. 947–9
103. Overdyk FJ, Harvey SC, Fishman RL, et al. Successful strategies for improving operating room efficiency at academic institutions. Anesth Analg. 1998;86:896–906.
104. Weinbroum AA, Ekstein P, Ezri T. Efficiency of the operating room suite. Am J Surg. 2003;185:244–50.
105. Van Houdenhoven M, van Oostrum JM, Hans EW, et al. Improving operating room efficiency by applying bin-packing and portfolio techniques to surgical case scheduling. Anesth Analg. 2007;105:707–14.
106. van Oostrum JM, Van Houdenhoven M, Vrielink MM, et al. A simulation model for determining the optimal size of emergency teams on call in the operating room at night. Anesth Analg. 2008;107:1655–62.
107. Edwards RH, Clague JE, Barlow J, et al. Operations research survey and computer simulation of waiting times in two medical outpatient clinic structures. Health Care Anal. 1994;2:164–9.
108. Penneys NS. A comparison of hourly block appointments with sequential patient scheduling in a dermatology practice. J Am Acad Dermatol. 2000;43:809–13.
109. Stahl JE, Roberts MS, Gazelle S. Optimizing management and financial performance of the teaching ambulatory care clinic. J Gen Intern Med. 2003;18:266–74.
110. Parks JK, Engblom P, Hamrock E, et al. Designed to fail: how computer simulation can detect fundamental flaws in clinic flow. J Healthc Manag. 2011;56:135–44. discussion 145–6
111. Connelly LG, Bair AE. Discrete event simulation of emergency department activity: a platform for system-level operations research. Acad Emerg Med. 2004;11:1177–85.
112. Saunders CE, Makens PK, Leblanc LJ. Modeling emergency department operations using advanced computer simulation systems. Ann Emerg Med. 1989;18:134–40.
113. Storrow AB, Zhou C, Gaddis G, et al. Decreasing lab turnaround time improves emergency department throughput and decreases emergency medical services diversion: a simulation model. Acad Emerg Med. 2008;15:1130–5.
114. Hung GR, Whitehouse SR, O'Neill C, et al. Computer modeling of patient flow in a pediatric emergency department using discrete event simulation. Pediatr Emerg Care. 2007;23:5–10.
115. Racine AD, Davidson AG. Use of a time-flow study to improve patient waiting times at an inner-city academic pediatric practice. Arch Pediatr Adolesc Med. 2002;156:1203–9.
116. Zamir S, Rex DK. An initial investigation of efficiency in endoscopy delivery. Am J Gastroenterol. 2002;97:1968–72.
117. Day LW, Belson D, Dessouky M, et al. Optimizing efficiency and operations at a California safety-net endoscopy center: a modeling and simulation approach. Gastrointest Endosc. 2014;80:762–73.
118. Harewood GC, Chrysostomou K, Himy N, et al. A "time-and-motion" study of endoscopic practice: strategies to enhance efficiency. Gastrointest Endosc. 2008;68:1043–50.
119. Day LW, Belson D, Dessouky M, et al. Optimizing efficiency and operations at a California safety-net endoscopy center: a modeling and simulation approach. Gastrointest Endosc. 2014;
120. Gellad ZF, Thompson CP, Taheri J. Endoscopy unit efficiency: quality redefined. Clin Gastroenterol Hepatol. 2013;11:1046–1049.e1.
121. Allen JI. A performance improvement program for community-based gastroenterology. Gastrointest Endosc Clin N Am. 2008;18:753–71. ix
122. Dzeletovic I, Harrison ME, Crowell MD, et al. Impact of fentanyl in lieu of meperidine on endoscopy unit efficiency: a prospective comparative study in patients undergoing EGD. Gastrointest Endosc. 2013;77:883–7.
123. McQuaid KR, Laine L. A systematic review and meta-analysis of randomized, controlled trials of moderate sedation for routine endoscopic procedures. Gastrointest Endosc. 2008;67:910–23.
124. Tsai HC, Lin YC, Ko CL, et al. Propofol versus midazolam for upper gastrointestinal endoscopy in cirrhotic patients: a meta-analysis of randomized controlled trials. PLoS One. 2015;10:e0117585.
125. Sipe BW, Rex DK, Latinovich D, et al. Propofol versus midazolam/meperidine for outpatient colonoscopy: administration by nurses supervised by endoscopists. Gastrointest Endosc. 2002;55:815–25.
126. Lera dos Santos ME, Maluf-Filho F, Chaves DM, et al. Deep sedation during gastrointestinal endoscopy: propofol-fentanyl and midazolam-fentanyl regimens. World J Gastroenterol. 2013;19:3439–46.
127. Rex DK, Lahue BJ, Dronzek RW. Impact of two procedure rooms per physician on productivity: computer simulation examines the impact of process change in the hospital gastroenterology department [abstract]. Gastrointest Endosc. 2005;61:AB154.
128. Walker JA, McIntyre RD, Schleinitz PF, et al. Nurse-administered propofol sedation without anesthesia specialists in 9152 endoscopic cases in an ambulatory surgery center. Am J Gastroenterol. 2003;98:1744–50.
129. Levitzky BE, Lopez R, Dumot JA, et al. Moderate sedation for elective upper endoscopy with balanced propofol versus fentanyl and midazolam alone: a randomized clinical trial. Endoscopy. 2012;44:13–20.
130. Marasco JA, Marasco RF. Designing the ambulatory endoscopy center. Gastrointest Endosc Clin N Am. 2002;12:185–204. v
131. Petersen BT. Promoting efficiency in gastrointestinal endoscopy. Gastrointest Endosc Clin N Am. 2006;16:671–85.
132. Overholt BF. Improving efficiencies in the GI practice of endoscopic ambulatory surgery center. J Clin Gastroenterol. 2007;41:352–5.
133. Kowalski T, Edmundowicz S, Vacante N. Endoscopy unit form and function. Gastrointest Endosc Clin N Am. 2004;14:657–66. viii
134. Jacobson SH, Hall SN, Swisher JR. Discrete-event simulation of health care systems. Patient flow: reducing delay in healthcare delivery. Springer; 2006. p. 211–52.
135. ASGE Standards of Practice Committee, Jain R, Ikenberry SO, et al. Minimum staffing requirements for the performance of GI endoscopy. Gastrointest Endosc. 2010;72:469–70.
136. DiSario JA, Sanowski RA. Sigmoidoscopy training for nurses and resident physicians. Gastrointest Endosc. 1993;39:29–32.

137. Schoenfeld P, Lipscomb S, Crook J, et al. Accuracy of polyp detection by gastroenterologists and nurse endoscopists during flexible sigmoidoscopy: a randomized trial. Gastroenterology. 1999;117:312–8.
138. Schroy PC, Wiggins T, Winawer SJ, et al. Video endoscopy by nurse practitioners: a model for colorectal cancer screening. Gastrointest Endosc. 1988;34:390–4.
139. Maule WF. Screening for colorectal cancer by nurse endoscopists. N Engl J Med. 1994;330:183–7.
140. Day LW, Siao D, Inadomi JM, et al. Non-physician performance of lower and upper endoscopy: a systematic review and meta-analysis. Endoscopy. 2014;46:401–10.
141. McGrath S. The cost-effectiveness of nurse practitioners. Nurse Pract. 1990;15:40–2.
142. Popa K. Modified block scheduling: an approach to the efficient use of procedure time. Gastroenterol Nurs. 1993;16:27–9.
143. Dexter F, Epstein RH. Operating room efficiency and scheduling. Curr Opin Anaesthesiol. 2005;18:195–8.
144. Marjamaa R, Vakkuri A, Kirvela O. Operating room management: why, how and by whom? Acta Anaesthesiol Scand. 2008;52:596–600.
145. Sonnenberg A. How to overbook procedures in the endoscopy unit. Gastrointest Endosc. 2009;69:710–5.
146. Siao D, Sewell JL, Day LW. Assessment of delivery methods used in the informed consent process at a safety-net hospital. Gastrointest Endosc. 2014;80:61–8.
147. Yong E, Zenkova O, Saibil F, et al. Efficiency of an endoscopy suite in a teaching hospital: delays, prolonged procedures, and hospital waiting times. Gastrointest Endosc. 2006;64:760–4.
148. Grossman P, Lahue BJ, Dronzek R. Where are ambulatory surgery center (ASC) bottlenecks? Use of computer simulation modeling to evaluate efficiency targets [abstract]. Gastrointest Endosc. 2005;61:AB150.

Quality Measures in Gastrointestinal Endoscopy

48

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Introduction

Quality improvement in healthcare has emerged as an increasingly central focus of public discourse. The death of Libby Zion in 1984 introduced the fallibility of healthcare providers and potential for error inherent in the practice of medicine into the public consciousness. The Institute of Medicine's 1999 landmark report "To Err is Human" crystallized awareness of the widespread prevalence of medical errors, capturing the attention of lawmakers and the general public with its estimate of up to 98,000 deaths attributable to medical errors annually [1] and serving as a call to action to advance the cause of patient safety. The report prompted legislation such as the "Healthcare Research and Quality Act of 1999", which renamed the Agency for Health Care Policy and Research to the Agency for Healthcare Research and Quality and funded agency projects to address these new priorities. The Institute of Medicine followed up with its 2001 report "Crossing the Quality Chasm" which expanded its focus from error and patient safety to the health system organization and more explicitly emphasized aligning payment methods with quality improvement goals and empowerment of consumers and payers [2]. The Medicare Prescription Drug, Improvement, and Modernization Act in 2003 enacted these recommendations and linked hospital payment to quality. The combined forces of public interest, regulatory emphasis, and financial inducements have contributed to the burgeoning attention to quality improvement.

Legislation has also codified the role of reporting programs. PQRS is a pay-for-reporting program that uses payment adjustments to promote healthcare quality reporting for patients covered by Medicare Part B Fee-for-Service (FFS). It initially came into being in the 2006 Tax Relief and Health Care Act as PQRI and became permanent as PQRS in 2010 with passage of the Affordable Care Act (ACA). The ACA also shifted the payment adjustment from incentives to penalties starting in 2015 and shifted from pay for reporting to pay for value by introducing a value-based modifier. More recently, the Medicare Access and CHIP Reauthorization Act of 2015 aims to incorporate electronic health record incentives, PQRS, and the value-based modifier into a single Merit-based Incentive Payment System (MIPS) beginning in 2019.

The private sector has similarly begun to use quality metrics to improve healthcare value and to promote the practice of high-quality care. For example, both United Healthcare and Blue Cross Blue Shield have introduced Physician Tiering programs to incentivize high value care. These programs use many of the same quality metrics as federal programs. Similarly, the Core Measures Collaborative is an initiative of CMS and America's Health Insurance Plans (AHIP) to better align public and private quality metrics [3]. Table 48.1 provides examples of the use of colonoscopy quality metrics across public and private programs in one North Carolina Market.

Quality improvement is particularly important to gastroenterology as a specialty with a strong procedural base and readily measurable outcomes. Colonoscopy plays an important role in prevention and early identification of colorectal cancer. For example, a study of 2602 patients in the national polyp surveillance study found that compared to the general population, the standardized incidence-based mortality ratio for individuals undergoing colonoscopic polypectomy was 0.47 (95% confidence interval [CI], 0.26–0.80), suggesting a 53% reduction in mortality [4]. However, the protective effect of colonoscopy is not uniform, and there are gaps in care attributable to provider variation in colonoscopy quality.

The gravest outcome of these gaps is interval cancer, which is a colon cancer that is found after a screening or surveillance colonoscopy before the date of the recommended

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Table 48.1 Utilization of quality metrics across public and private programs

Measure	PQRS	BCBS	ASC
Colonoscopy interval for patients with history of adenomatous polyps—avoidance of inappropriate use	Yes	Yes	Yes
Colonoscopy interval normal colonoscopy in average-risk patients	Yes	Yes	Yes
Colonoscopy complication rate	No	Yes	No
Adenoma detection rate	Yes	Yes	No
Cecal intubation rate	Yes	No	No
Withdrawal time	No	No	No
Polyp detection rate	No	No	No
Colonoscopy bowel preparation	No	No	No

Measures currently utilized by PQRS, Blue Cross Blue Shield Physician Tiering Program, and the CMS Ambulatory Surgery Center Quality Reporting Program

next exam. Cooper et al. found a sobering 7.2% interval cancer rate in review of over 57,000 patients in the Surveillance, Epidemiology, and End Results (SEER) Medicare database using a definition using colonoscopy performed 6–36 months prior to cancer diagnosis as a proxy for interval cancer [5]. This study identified higher risk of interval cancer with proximal cancers, non-gastroenterologists performing the procedure, lower proceduralist polypectomy rate, presence of diverticulosis, and increased comorbidities [5]. Le Clercq et al. examined all patients diagnosed with colorectal cancer over a 10-year period and identified patients who had undergone screening colonoscopy in 5 years prior to diagnosis [6]. This study confirmed the finding that interval cancers were more frequently located in the proximal colon, were smaller in size, and more often had a flat macroscopic appearance. The authors also found that the majority (86%) of identified interval cancers would have been preventable; 58% were attributed to missed lesions, 20% to inadequate examination (incomplete colon intubation or poor bowel preparation) or inadequate surveillance (failure to follow national guidelines), and 9% to incomplete resection of cancer in the same segment as previously diagnosed advanced adenoma [6]. This is an important finding because it highlights some modifiable targets for intervention that may decrease the rate of this serious adverse clinical outcome.

The possibility of a missed cancer or advanced adenoma is also dependent on the competence of the physician performing the colonoscopy. The ACG/ASGE guideline on competence endoscopy defines competence as having "gone through a period of training to develop requisite endoscopic skills and acquire the knowledge base required to safely perform, interpret, and correctly manage findings of endoscopic procedures" in order to "assure that a safe and technically successful procedure is performed and that the observations and results are accurate" [7]. While clear procedural volume targets are set for training programs, it is acknowledged that measuring the procedural competence of physicians in practice is challenging.

Perhaps as a result of this challenge, wide variations exist in the performance of colonoscopy. The adenoma detection rate (ADR), which is a commonly utilized assessment of individual physician quality, varies widely. Chen et al. found that ADRs range from 15% to 41%, with the individual endoscopist performing the procedure being a stronger predictor of ADR than age or sex [8]. Studies have also identified marked variation in detection rates of proximal serrated polyps, with 20-fold variations between endoscopists and a range of 1–18% detection rate [9]. In a study in which patients underwent repeat colonoscopy the same day, Rex et al. found a sobering overall miss rate for adenomas of 24% (27% for adenomas <5 mm, 13% for adenomas 6–9 mm, and 6% for adenomas >1 cm) [10]. These findings of significant variation in ADR as well as a substantial miss rate underline the disquieting finding that not every colonoscopy is equal. This variation in quality, however, is also an opportunity for improvement.

This chapter will review quality metrics in endoscopy, review the challenges in defining and implementing these measures, and provide an overview of current endoscopy quality prior indicators. It will also discuss the impact of quality measurement on practice and review gaps in care and opportunities for improvement in endoscopic care.

Measuring Quality Metrics in Endoscopy

Definitions and Conceptual Framework

With the rapid emergence of quality as an academic field and focus in shaping healthcare policy, it is important to establish the conceptual framework and terminology.

Defined, quantitative parameters that can be used to measure quality and help to standardize the care provided are called *quality indicators*. These are often more formally defined as a ratio between the incidence of correct performance and the opportunity for correct performance. In other words a quality indicator is the proportion of interventions that achieve a predefined goal [11].

Quality indicators are typically divided into three categories based on the Donabedian framework [12]:

1. *Structural measures*: These measures assess the characteristics of the healthcare environment. For example, these measures can refer to resources available in an endoscopy unit, access to procedural scheduling or staff training. These measures are advantageous because they are more often easily modifiable; however, their link to clinical outcomes is not always clear.

2. *Process measures*: These measures assess performance during the delivery of care according to evidence-based standards of care. For example, these measures can assess the frequency with which endoscopy is performed for an appropriate indication or with which a plan for management of antithrombotic therapy is formulated and documented prior to the procedure. Process measures are the most common type of quality indicator. These are more readily, directly, and immediately measured. These measures are advantageous because they identify the enabling mechanisms by which structural measures mediate outcome; however, the estimates of quality are less final than those derived from outcomes.
3. *Outcome measures*: These measures assess the results of the care that was provided. This can include procedural adverse events or interval cancers diagnosed after colonoscopy. Outcome measures, while attractive as the most patient-centered and often clinically significant targets, are also beset by important limitations. Many occur years after the episode of care and are difficult to consistently capture and measure in a fragmented healthcare system. Additionally, adjustments for case-mix or social and medical complexity of a patient population are challenging, and there are rarely well-established and validated methods of accomplishing such adjustments. With the advent of widespread electronic health records and initiatives to promote more integrated, accessible health information, these may become more feasible targets.

With movement toward greater transparency in the healthcare system, quality measures are being reviewed and used for decision-making by important stakeholders such as government, insurers, the Joint Commission, and patients. *Accountability* refers to positive or negative incentives for performance in quality measures. This can include, for instance, accreditation or pay-for-performance programs.

Chassin et al. proposed the general following criteria for assessing accountability measures; these criteria will inform our assessment of evolving measures in gastroenterology:

1. *There is a strong evidence base showing that the care process leads to improved outcomes.* Aspirin after myocardial infarction is commonly cited as an intervention with an indisputably strong evidence base, the implementation of which has greatly improved since it began to be measured and reported.
2. *The measure accurately captures whether the evidence-based care process has, in fact, been provided.* Checkboxes in medical records to satisfy a requirement for documentation of an intervention of smoking cessation are examples in which a tidy medical chart may not reflect meaningful changes in the process of care.
3. *The measure addresses a process that has few intervening care processes that must occur before the outcome is realized.* If a measure is too tenuously connected to a meaningful clinical outcome or principle, it is a poor target for quality improvement, and imposition of measurement and accountability runs the risk of increasing health system costs without consequential impact on clinical outcomes.
4. *Implementing the measure has little or no chance of inducing unintended adverse consequences.* The widespread criticism of the quality metric evaluating antibiotics within 6 h for pneumonia for generating inappropriate administration and overuse of antibiotics for nonspecific radiographic abnormalities exemplifies this principle [13].

Review of Current Endoscopy Quality Priority Indicators

Quality endoscopy has been defined in the most recent American College of Gastroenterology (ACG) and American Society for Gastrointestinal Endoscopy (ASGE) guidelines as "an examination in which patients receive an indicated procedure, correct and relevant diagnoses are recognized or excluded, any therapy provided is appropriate, and all steps that minimize risk have been taken" [11].

Quality indicators common to all endoscopic procedures can be divided into time periods for endoscopy: pre-procedure, intra-procedure, and post-procedure. Priority indicators have been identified by the major society task force based on their clinical relevance, their variability in practice, and feasibility of their measurement. This serves to focus the efforts of individual endoscopists on these indicators as a starting point (Table 48.2) with priority indicators emphasized in bold. The task force acknowledges that not every indicator should immediately be implemented in every practice setting, and most require further validation prior to universal adoption.

Practical Points

The Donabedian framework: Types of quality indicators

- *Structural measures*: Features of healthcare environment
  Example: Access to procedural scheduling
- *Process measures*: Performance during delivery of care
  Example: Endoscopy performed for appropriate indication
- *Outcome measures*: Results of care delivered
  Example: Procedure complication rate

Table 48.2 ACG/ASGE proposed quality indicators common to all procedures

Quality indicator	Measure type	Performance target
Pre-procedure		
Frequency with which endoscopy is performed for an indication that is included in a published standard list of appropriate indications, and the indication is documented	Process	>80%
Frequency with which informed consent is obtained and fully documented	Process	>98%
Frequency with which pre-procedure history and directed physical examination are performed and documented	Process	>98%
Frequency with which risk for adverse events is assessed and documented before sedation is started	Process	>98%
Frequency with which prophylactic antibiotics are administered for appropriate indication	Process	>98%
Frequency with which a sedation plan is documented	Process	>98%
Frequency with which management of antithrombotic therapy is formulated and documented before the procedure	Process	N/A
Frequency with which a team pause is conducted and documented	Process	>98%
Frequency with which endoscopy is performed by an individual who is fully trained and credentialed to perform that particular procedure	Process	>98%
Intra-procedure		
Frequency with which photo-documentation is performed	Process	N/A
Frequency with which patient monitoring during sedation is performed and documented	Process	>98%
Frequency with which the doses and routes of administration of all medications used during the procedure are documented	Process	>98%
Frequency with which use of reversal agents is documented	Process	>98%
Frequency with which procedure interruption and premature termination because of sedation-related issues are documented	Process	>98%
Post-procedure		
Frequency with which discharge from the endoscopy unit according to predetermined discharge criteria is documented	Process	>98%
Frequency with which patient instructions are provided	Process	>98%
Frequency with which the plan for pathology follow-up is specified and documented	Process	>98%
Frequency with which a complete procedure report is created	Process	>98%
Frequency with which adverse events are documented	Process	>98%
Frequency with which adverse events occur	Outcome	N/A
Frequency with which post-procedure and late adverse events occur and are documented	Outcome	N/A
Frequency with which patient satisfaction data are obtained	Process	N/A
Frequency with which communication with referring providers is documented	Process	N/A

Priority Indicators for Colonoscopy

The ACG/ASGE task force also identified a series of quality indicators for colonoscopy (Table 48.3). This section will review the evidence informing identified priority indicators, as well as other suggested quality indicators which are gaining more attention in the literature.

Appropriate Surveillance Intervals

The first priority quality indicator is the frequency with which colonoscopies follow recommended post-polypectomy and post-cancer resection surveillance intervals as well as 10-year intervals between screening colonoscopies in average-risk patients who have negative examination results and adequate bowel cleansing. Performance of this indicator is known to vary in clinical practice, and physician adherence to recommended surveillance intervals is low [14–16]. Measuring adherence to this principle is becoming increasingly important in the current healthcare environment of increasing costs and concomitant increasing public, governmental, and payer attention to cost-effectiveness. As open access to endoscopy proliferates within health systems, gastroenterologists are challenged not only to know published indications and utilize these in their clinical practice but also to educate referring physicians who are also able to order endoscopic procedures.

There are many cited reasons for divergence from surveillance guidelines, including concern about potential missed lesions, financial incentives to perform procedure, concern about borderline adequate bowel preparations, unfamiliarity with practice guidelines, fear of malpractice litigation, and uncertainty about quality of evidence behind guidelines [14, 15]. Recent data suggests that this problem exists even in the VA system, which lacks the financial incentives speculated to contribute to this problem. In a study of over 1400 colonoscopies in the VA system, over a third (36%) did not adhere to recommended intervals, with over 94% of these

Table 48.3 ACG/ASGE proposed quality indicators for colonoscopy

Quality indicator	Measure type	Performance target
Pre-procedure		
Frequency with which colonoscopy is performed for an indication that is included in a published standard list of appropriate indications, and the indication is documented	Process	>80%
Frequency with which informed consent is obtained, including specific discussions of risks associated with colonoscopy, and fully documented	Process	>98%
Frequency with which colonoscopies follow recommended post-polypectomy and post-cancer resection surveillance intervals and 10-year intervals between screening colonoscopies in average-risk patients who have negative examination results and adequate bowel cleansing	Process	>90%
Frequency with which ulcerative colitis and Crohn's colitis surveillance is recommended within proper intervals	Process	>90%
Intra-procedure		
Frequency with which the procedure note documents the quality of preparation	Process	>98%
Frequency with which bowel preparation is adequate to allow the use of recommended surveillance or screening intervals in outpatient exams	Process	>85%
Frequency with which visualization of the cecum by notation of landmarks and photo-documentation of landmarks is documented in every procedure	Process	>90% (all) >95% (screening)
Frequency with which adenomas are detected in asymptomatic average-risk individuals (screening)	Outcome	
Adenoma detection rate (male and female)		>25%
Adenoma detection rate for male patients		>30%
Adenoma detection rate for female patients		>20%
Frequency with which withdrawal time is measured	Process	>98%
Average withdrawal time in negative-result screening colonoscopies	Process	>6 min
Frequency with which biopsy specimens are obtained when colonoscopy is performed for an indication of chronic diarrhea	Process	>98%
Frequency of recommended tissue sampling when colonoscopy is performed for surveillance in ulcerative colitis and Crohn's colitis	Process	>98%
Frequency with which endoscopic removal of pedunculated polyps and sessile polyps is attempted before surgical referral	Outcome	>98%
Post-procedure		
Incidence of perforation for all examinations	Outcome	<1:500
Incidence of perforation for screening colonoscopies	Outcome	<1:1000
Incidence of post-polypectomy bleeding	Outcome	<1%
Frequency with which post-polypectomy bleeding is managed without surgery	Outcome	>90%
Frequency with which appropriate recommendation for timing of repeat colonoscopy is documented and provided to the patient after histologic findings are reviewed	Process	>90%

instances involving recommendation for earlier colonoscopy than guidelines would suggest. Nonadherence was associated with detection of hyperplastic or high-risk adenomatous polyps, less than optimal bowel preparation quality, and Northeast region [16].

Cecal Intubation/Visualization of the Cecum

Complete examination of the colon and documentation that this was performed is a prima facie fundamental evaluation of examination quality. The multi-society task force has set a cecal intubation rate goal of >90% for all exams and >95% for screening exams. There is some data to support this intuitive measure. In a retrospective review using administrative data from over 14,000 patients in Ontario, completion rate of colonoscopy was associated with a lower risk of interval cancer. After authors controlled for patient and endoscopy factors, patients undergoing colonoscopy performed by an endoscopist with a completion rate of greater than or equal to 95% were less likely to develop interval cancer than if performed by an endoscopist with an 80% completion rate for both proximal cancer (OR, 0.72; 95% CI, 0.53–0.97) and distal cancer (OR, 0.73; 95% CI, 0.54–0.97) [17]. Other studies have failed to identify this metric as a risk factor for development of interval cancer. For instance, in Kaminski et al.'s retrospective analysis of 45,026 patients undergoing screening colonoscopies with 42 interval colorectal cancers identified in a national cancer registry during a period of 188,788 person-years, the endoscopist's rate of cecal intubation was not significantly associated with interval cancer risk ($P = 0.50$) [18]. With improvement in endoscopic techniques over time and very high cecal intubation rates in most recent published studies, even very large-scale studies may not be adequately powered to detect the impact of small variations in cecal intubation rates on interval cancer risk. There is certainly high biological plausibility that a complete inspection

of the colon would lead to a lower risk of missed lesions that could result in interval cancers. This may be why a higher percentage of gastroenterologists agreed with using cecal intubation rate as a quality metric completion rate (90%) than with using adenoma detection rate (83%) despite the latter's more robust accumulated evidence [19].

Adenoma Detection Rate (ADR)

Adenoma detection rate has increasingly emerged as one of the foremost metrics in assessing quality of individual endoscopists. It is defined as the frequency with which adenomas are detected in asymptomatic, average-risk individuals in screening colonoscopy. The major society task force has targeted adenoma detection rates of >30% for men, >20% for women, and >25% overall. The guideline suggests that while individual endoscopists with ADRs below 25% should endeavor to improve their performance, the targeted ADR should not be considered a standard of care and should be utilized instead as a target in quality improvement.

Adenoma detection rate has accumulated an increasing body of evidence showing that increasing ADR predicts a decreased interval risk of colon cancer—an indisputably important and clinically relevant outcome. In Kaminski et al.'s retrospective analysis of 45,026 patients undergoing screening colonoscopies involving 186 endoscopists, the endoscopist's rate of detection of adenomas was significantly associated with a decrease in the risk of interval colorectal cancer ($P = 0.008$) [18].

Corley et al. extended the findings of Kaminski et al. by examining the relationship between ADR and interval cancer in physicians with ADRs well above 20%. In their study of over 250,000 colonoscopies by 136 gastroenterologists, each 1.0% increase in the physician's adenoma detection rate was associated with a 3% decrease in the risk of cancer (HR 0.97; 95% CI, 0.96–0.98) as well as a 5% decrease in cancer mortality. In addition, physicians with ADRs in the highest quintile (ADR of 33.5–52.5%) compared to physicians with ADRs in the lowest quintile (ADR of 7.4–19%) had a decreased interval cancer hazard ratio of 0.52 (95% CI, 0.39–0.69). Higher ADR was also predictive of decreased risks of advanced-stage disease, fatal interval cancer, early and delayed interval cancers, and both cancers in both the proximal and distal colons [20].

Despite this compelling data, there are limitations of ADR as a quality metric. The adenoma detection rate has been criticized for susceptibility to a "one-and-done" approach to examinations with less meticulous approach to examination after one adenoma is identified; this undesirable behavior is actually incentivized by some reimbursement structures which effectively pay only for the first polyp resected. In spite of this concerning possibility, no evidence has emerged of this type of practice. Alternative metrics—such as mean number of adenomas per procedure or adenoma per colonoscopy—have been proposed and are starting to be evaluated in some studies [21, 22]. It has been argued that because each adenoma carries some risk of malignancy, endoscopists who are finding and removing more adenomas per colonoscopy (even if they are not detecting adenomas in a higher number of colonoscopies) would naturally provide a greater level of protection against interval colorectal cancer. While this argument certainly has strong biological plausibility, this alternative measure needs further evaluation and validation before it can be recommended [22].

With the prominence of adenoma detection rate in the literature, there has been attention to what clinically significant factors it fails to capture in addition to sheer number of adenomas identified. The prospect of right-sided ADR has been raised since this is a common area for missed lesions [9]. In addition, an advanced adenoma detection rate or stratification by size to capture higher risk, more clinically significant lesions, has also been discussed [22]. Finally, concerns have been raised about failing to incorporate the detection rate of sessile serrated polyps in the ADR metric or current quality indicators since there is marked variability between endoscopists in identifying these lesions [9, 23]. Heterogeneity in pathology assessments, in particular blurring of distinctions between sessile serrated polyps and hyperplastic polyps, currently limits the utility of this as a separate target or measure for incorporation into ADR.

Another limitation of the ADR involves pragmatic considerations about feasibility and burden of recording. Since pathology reports are not available at the time of the procedure, capturing this metric requires the endoscopist or other staff to capture pathology after the time of the procedure. The polyp detection rate, which in contrast could be readily tracked at the time of the procedure or even by review of claims data, has been proposed as an alternative to address the concerns about feasibility. Polyp detection rate has been shown to correlate with ADR and, however, is even more subject to concerns about "gaming" the measure with the potential to meet targets by removal of distal diminutive hyperplastic polyps which are often not removed or are removed and discarded in clinical practice [24, 25].

Interventions to Improve ADR

Targeted educational interventions have been found to improve endoscopists' ADR. The EQUIP study randomized half of the endoscopists in an academic endoscopy unit to receive an educational intervention as well as monthly feedback on their ADRs after completion of the education

and found that the intervention group increased ADR to 47% (p = 0.0013), whereas the control group ADR remained unchanged at 35% [26]. This intervention consisted of two training sessions: the first reviewed methods and techniques found to improve ADR (withdrawal time, working the folds, washing, careful inspection) and focused on recognition of subtle characteristics of flat lesions (color, friability, vascular changes, and wall deformity); the second session utilized a narrow band imaging learning module to train the endoscopists on surface and vascular patterns predictive of neoplasia. The EQUIP-2 study went on to assess the durability of the ADR increase in the 5 months following the original study and found that the educational intervention group preserved their increase in ADR group from 36% at baseline to 47% in the prior study and 46% in the following 5 months. The ADR in the prior control group which had remained unchanged from 36% at baseline to 35% was found to have increased only marginally in this follow-up evaluation to 39% [27]. In a separate study in the community practice setting, Barclay et al. found improvement in ADR from 23.5% at baseline to 34.7% with an educational intervention, although this was coupled with mandated 8-minute withdrawal time using an audible timer [28].

Another intervention that has shown promise in improving ADR is engaging experienced endoscopy nurses as second observers during withdrawal. Lee et al. conducted a multicenter prospective randomized trial in which endoscopy nurse participation significantly increased the PDR and ADR compared with observation by a colonoscopist alone (adjusted OR of 1.58 for PDR and adjusted OR of 1.47 for ADR), although this effect was largely driven by procedures involving fellows [29]. Aslanian et al. performed a single-center randomized prospective study to evaluate the effect of endoscopy nurse participation in procedures involving only experienced colonoscopists without trainees. This study found significantly more polyps per colonoscopy in the nurse observation group (1.32 polyps vs. 1.03, $p = 0.0024$) and significantly more adenomas per colonoscopy in the nurse observation group (0.82 vs. 0.64, $p = 0.02$). There was also a nonsignificant trend toward improved ADR in the nurse observation group [30].

Strategies to mitigate fatigue also may help to improve ADR. Sanaka et al. first noted that morning colonoscopies were associated with a significantly higher ADR than afternoon colonoscopies (29.3% compared with 25.3% in the afternoon, p = 0.008) as well as a trend toward declining ADR for each subsequent hour of the day (p = 0.01) [31]. Gurudu et al. found that this effect could be counteracted by performing colonoscopies in half-day blocks, with no significant difference in ADR between afternoon and morning procedures (27.6 vs. 26.6%; OR = 1.05; 95% CI 0.88, 1.26; P = 0.56) [32].

Other studies of interventions have been less successful in impacting ADR. In a study of community gastroenterologists, Shaukat et al. did not find an effect on ADR by informing practice members of their ADR rates, expected ADR rates, and mandated 6-min withdrawal time in >95% of colonoscopy examinations with 1% of total compensation at risk if this last measure was not achieved [33].

Practical Points

Interventions to improve ADR

- Targeted educational interventions
- Experienced endoscopy nurses as second observers during withdrawal
- Fatigue mitigation: half-day endoscopy sessions
- Mandated withdrawal time with audible timer
- Less impactful based on current data: financial incentives, making endoscopists aware of their own ADRs, education on expected ADRs, new equipment

Withdrawal Time

Withdrawal time is not a priority quality indicator, but as a concrete variable readily measurable at the time of the procedure, it has been a target of a number of quality improvement efforts in the recent literature. A study by Barclay et al. reported that physicians with mean withdrawal times of 6 min or more had higher adenoma detection rates (28.3% vs. 11.8%, $P < 0.001$) and higher detection rates of advanced neoplasia (6.4% vs. 2.6%, $P = 0.005$) [34].

A recent systematic review by Corley et al. focusing on interventions targeting withdrawal time, with or without feedback, identified four studies and five abstracts which did not show a significant impact on polyp or adenoma detection rate, even when significant improvements were made in adhering to a greater than 6-min withdrawal time [35]. However, one intervention which did show a marked and measurable increase in ADR was targeting an 8-min withdrawal time (2 min per major colonic segment using an audible timer), coupled with training on enhanced inspection techniques (adequate insufflation, repetitive examination of colonic segments, examination of flexures and proximal sides of folds, use of torqueing to flatten folds, and suctioning of liquid). In this small study of 12 gastroenterologists in a community-based practice performing screening colonoscopies, withdrawal times increased from 6.3 min at baseline to 9.8 min during the intervention, and mean adenoma detection rate increased from 23.5% at baseline to 34.7% ($P < 0.0001$) [28].

These promising results call for replication in larger studies and potential wider-scale implementation.

More recently, withdrawal time has been associated with a hard outcome of meaningful import in a large retrospective study of 76,000 screening colonoscopies performed in Minnesota between 2004 and 2009 with 78 interval cancers identified. This study found that mean withdrawal times were inversely associated with interval cancer incidence ($p < 0.0001$), with withdrawal times <6 min associated with adjusted incidence rate ratio of 2.3 (95% confidence interval, 1.53.4; $P < 0.0001$) [36].

Bowel Preparation

Bowel preparation is critical to performing high-quality colonoscopy as it enables completion of the procedure, efficiency in cecal intubation, and careful inspection of the colonic mucosa. Multi-society task force guidelines set a goal of >85% bowel prep adequacy. Adequate bowel prep is defined as one which permits detection of polyps >5 mm in size and is a prerequisite for utilization of published surveillance intervals; if inadequate bowel prep is noted, colonoscopy should be repeated within 1 year [10]. Rex et al. estimated that poor bowel preparation increases costs associated with colonoscopy by 12–20%, driven largely by shortened screening intervals than would otherwise be recommended but also by longer procedure times [37]. Poor bowel preparation also exposes patients to the discomfort and risks associated with earlier repeat of bowel preparation and colonoscopy than their health status might have otherwise warranted. This indicator may gain more widespread policy interest given current health system priorities, cost, patient safety implications, and potential decrements in patient satisfaction with need for repeat procedures.

This proposed indicator challenges the entire system of care, requiring not only a good choice of bowel prep to prescribe but also the strength and efficacy of patient education and identification of at-risk patients who may need more in-depth engagement. Medicaid patients and patients seen at university- and teaching hospital-affiliated practices are at higher risk [38], and social support is also an important factor in good bowel prep with married patients found to have better bowel preps [39]. In a large series of over 12,000 colonoscopies performed at a university-affiliated medical center, Medicaid patients had a 34% rate of suboptimal bowel preparations, nearly doubling the rate of non-Medicaid patients [39]. This readily identifiable factor may be of utility in targeting more intensive educational interventions to at-risk populations.

One of the most important factors determining bowel preparation quality is the interval between the end of the prep and start of the procedure, with diminishing quality particularly limiting visualization of the right side of the colon with increasing intervals [40]. A treatise on different bowel preparations is beyond the scope of this chapter; however one readily implementable intervention with significant impact on bowel prep quality is a split preparation. A meta-analysis of randomized controlled trials comparing single-dose PEG to split-dose PEG in over 1200 patients found that split dose increased the number of satisfactory preps markedly (OR 3.70) as well as patient willingness to repeat the same bowel prep for future procedures (OR 1.76) and that it decreased the number of preparation discontinuations (OR 0.53) [40].

Practical Points

Key performance measures for colonoscopy

- Procedure performed for appropriate indication
- Adherence to post-polypectomy surveillance guidelines
- Rate of adequate bowel preparation
- Cecal intubation rate
- Adenoma detection rate:
  >25% for men and women
  >30% for men
  >20% for women
- Average withdrawal time:
  >6 min
- Perforation rate
- Post-polypectomy bleeding rate
- Documentation of recommendation for appropriate repeat colonoscopy timing

Upper Endoscopy

The ACG/ASGE task force has formulated a series of quality indicators for upper endoscopy as well [41]. These are detailed in Table 48.4 below, which emphasizes priority quality indicators in bold. The priority indicators, and evidence informing them, will be discussed in greater detail in this section.

Cirrhosis and Upper GI Bleeding

Administration of prophylactic antibiotics to prevent bacterial translocation in patients with cirrhosis has become standard clinical practice, and the multi-society task force has set a target of >98% in enacting this measure. A Cochrane review summarizes the large weight of accumulated evidence for this practice combining 12 trials evaluating over 1200 patients who received antibiotic prophylaxis or pla-

Table 48.4 ACG/ASGE proposed quality indicators for upper endoscopy

Quality indicator	Measure type	Performance target
Pre-procedure		
Frequency with which EGD is performed for an indication that is included in a published standard list of appropriate indications, and the indication is documented	Process	>80%
Frequency with which informed consent is obtained, including specific discussions of risks associated with EGD, and fully documented	Process	>98%
Frequency with which appropriate prophylactic antibiotics are given in patients with cirrhosis with acute upper GI bleeding before EGD	Process	>98%
Frequency with which appropriate prophylactic antibiotics are given before placement of a PEG tube	Process	>98%
Frequency with which a PPI is used for suspected peptic ulcer bleeding	Process	>98%
Frequency with which vasoactive drugs are initiated before EGD for suspected variceal bleeding	Process	>98%
Intra-procedure		
Frequency with which a complete examination of the esophagus, stomach, and duodenum, including retroflexion in the stomach, is conducted and documented	Process	>98%
Among those with nonbleeding gastric ulcers, frequency with which gastric biopsies are done to exclude malignancy	Process	>80%
Frequency with which Barrett's esophagus is appropriately measured when present	Process	>98%
Frequency with which biopsies are obtained in cases of suspected Barrett's esophagus	Process	>90%
Frequency with which type of upper GI bleeding lesion is described, and the location is documented	Process	>80%
Frequency with which, during EGD examination revealing peptic ulcers, at least one of the following stigmata is noted: active bleeding, nonbleeding visible vessels (pigmented protuberance), adherent clot, flat spot, and clean-based	Process	>98%
Frequency with which, unless contraindicated, endoscopic treatment is given to ulcers with active bleeding or with nonbleeding visible vessels	Process	>98%
Frequency with which achievement of primary hemostasis in cases of attempted hemostasis of upper GI bleeding lesions is documented	Process	>98%
Frequency with which a second treatment modality is used (e.g., coagulation or clipping) when epinephrine injection is used to treat actively bleeding or nonbleeding visible vessels in patients with bleeding peptic ulcers	Process	>98%
Frequency with which variceal ligation is used as the first modality of treatment for the endoscopic treatment of esophageal varices	Process	>98%
Frequency with which at least four intestinal biopsies are done from patients in whom celiac disease is suspected	Process	>90%
Post-procedure		
Frequency with which PPI therapy is recommended for patients who underwent dilation for peptic esophageal strictures	Process	>98%
Frequency with which patients diagnosed with gastric or duodenal ulcers are instructed to take PPI medication or an H2 antagonist	Process	>98%
Frequency with which plans to test for H pylori infection are documented for patients diagnosed with gastric or duodenal ulcers	Process	>98%
Frequency with which patients with evidence of rebleeding from peptic ulcer disease after endoscopic treatment undergo repeat upper endoscopy	Process	>98%
Frequency with which patients are contacted to document the occurrence of adverse events after EGD	Process	N/A

cebo. This review found that administration of antibiotic prophylaxis was associated with reduced mortality (RR 0.79), reduced mortality from bacterial infections (RR 0.43), reduced bacterial infections (RR 0.35), as well as reduced rebleeding (RR 0.53) and reduced length of stay (mean decrease of 1.91 days) [42].

Peptic Ulcer Bleeding

Peptic ulcer disease is the most common cause of upper GI bleeding, and intravenous PPI therapy is fundamental to initial management, with a set target of >98% PPI use in the setting of suspected peptic ulcer disease. A Cochrane review demonstrated that PPI treatment significantly reduced the proportion of patients with high-risk stigmata for rebleeding at the time of endoscopy to 37.2% from 46.5% (OR 0.67) as well as the need for endoscopic therapy to 8.6% from 11.7% (OR 0.68). Mortality and rebleeding rates were not significantly impacted [43]. More recently, conventional wisdom

regarding method of PPI administration has been challenged by Sachar et al.'s systematic review and meta-analysis which showed no significant difference in several outcomes, including rebleeding within 30 and 3 days, mortality, urgent interventions, blood transfusion requirements, and hospital length of stay, when comparing intermittent IV PPI therapy to continuous IV PPI infusion [44]. Guidelines have not been revised to incorporate this finding and still recommend IV PPI bolus followed by PPI infusion, but as concerns about cost-effectiveness drive revisions in clinical practice, practice may adapt in response to this new evidence.

Given that actively bleeding ulcers and ulcers with visible vessels are at very high risk of rebleeding—with 55% and 43% rebleeding rates, respectively [45]—treatment unless contraindicated in at least 98% of cases is a quality indicator target. Meta-analysis data supports this principle, showing endoscopic therapy reduces risk of rebleeding with very low numbers needed to treat. Endoscopic therapy reduced the risk of rebleeding for ulcers with active bleeding (RR, 0.29; 95% CI 0.20–0.43) with a NNT of just 2; for ulcers with a non-bleeding visible vessel (RR, 0.49; 95% CI 0.40–0.59), a meta-analysis of 74 trials found a NNT of just 5 [46]. There is not adequate data to make blanket recommendations regarding treatment modality, except that epinephrine should not be used alone without a more definitive and durable therapy.

Diagnosis of either gastric ulcer or duodenal ulcer is associated with a high risk of *H. pylori* infection; 70% of gastric ulcers and 95% of duodenal ulcers are associated with *H. pylori*. Therefore, the quality indicator targets a high rate (>98%) of documentation of plans to test for *H. pylori* infection. Moreover, not only is there a high likelihood that *H. pylori* can be identified, eradication is also associated with superior duodenal ulcer healing compared to acid suppressive therapy. Relative risk of duodenal ulcer persistence was 0.66 in favor of eradication compared to acid suppressive therapy in a Cochrane review, although this effect was not found with gastric ulcers [47]. Eradication of *H. pylori* also has the benefit of reducing the risk of gastric MALT lymphoma.

Practical Points

Key performance measures for upper endoscopy

- Antibiotic administration rate in cirrhotic patients with upper GI bleeding
- PPI use for suspected peptic ulcer bleeding
- *H. pylori* testing rate when gastric or duodenal ulcers are found

Endoscopic Retrograde Cholangiopancreatography (ERCP)

Appropriate indication for ERCP is heavily emphasized in the ACG/ASGE guidelines, which set a higher performance target for this measure than for other procedures [48]. This reflects the higher risk of complications following ERCP, which warrants a more stringent patient selection process. In addition, because there are higher risks associated with the procedure, prioritized quality indicators focus more heavily on procedural outcomes—essentially on ensuring that the benefits of undergoing ERCP outweigh the risk. Because ERCP constitutes a lower proportion of procedural volume than colonoscopy or upper endoscopy in clinical practice, only priority indicators will be reviewed (Table 48.5).

A performance target of over 90% is set for several measures, including deep cannulation of ducts of interest in patients with native papillae, successful extraction of common bile duct stones <1 cm in patients with normal bile duct anatomy, and successful stent placement for patients with biliary obstruction below the bifurcation with normal bile duct anatomy. These targets are in line with the best available data on reported procedural success in the literature. A recent meta-analysis of procedural success rates in ERCP found that cumulative, weighted bile duct cannulation success rate was 89.3% (95% CI 0.866–0.919), common bile duct stone extraction rate was 88.3% (95% CI 0.825–0.941), and the rate of successful biliary stenting below the common bile duct bifurcation was 97.5% (95% CI 0.967–0.984) [49].

Although pancreatitis is one of the most common recognized complications of ERCP, there is not a performance target set for the rate of post-ERCP pancreatitis. This is likely in large part due to the marked variability in rates by procedural indication. Pancreatitis is often quoted as complicating 2–10% of procedures [50]; however in procedures done to evaluate for the possibility of sphincter of Oddi dysfunction, pancreatitis has been found to complicate over 20% of ERCPs [51]. Therefore, while pancreatitis is an important clinical outcome, the patient population has a disproportionate impact on measured rates; as such, it is challenging to set a meaningful universal target. Nonetheless, this metric remains an important quality indicator to track.

Endoscopic Ultrasound

Evidence guiding formulation of quality measures in endoscopic ultrasound is still emerging [52]. The multi-society task force priority indicators emphasize interpretability of reports, efficacy as a diagnostic test in assessing for pancreatic malignancy and limiting adverse events. Because EUS constitutes a lower proportion of procedural volume than colonoscopy or upper endoscopy in clinical practice, only priority indicators will be reviewed (Table 48.6).

Table 48.5 ACG/ASGE proposed priority quality indicators for ERCP

Priority quality indicator	Measure type	Performance target
Frequency with which ERCP is performed for an appropriate indication and documented	Process	>90%
Rate of deep cannulation of the ducts of interest in patients with native papillae without surgically altered anatomy	Process	>90%
Success rate of extraction of common bile duct stones <1 cm in patients with normal bile duct anatomy	Outcome	>90%
Success rate for stent placement for biliary obstruction for patients with biliary obstruction below the bifurcation in patients with normal anatomy	Outcome	>90%
Rate of post-ERCP pancreatitis	Outcome	N/A

Table 48.6 ACG/ASGE proposed priority quality indicators for EUS

Priority quality indicator	Measure type	Performance target
Frequency with which all GI cancers are staged with the AJCC/UICC TNM staging system	Process	>98%
Diagnostic rates and sensitivity for malignancy in patients undergoing EUS-guided FNA of pancreatic masses	Outcome	
Diagnostic rate		>70%
Sensitivity		>85%
The incidence of adverse events after EUS-guided FNA	Outcome	
Acute pancreatitis		<2%
Bleeding		<0.5%
Perforation		<1%

Although limited evidence supports the recommendation for staging system, standardization clearly facilitates communication between disciplines and the interpretation of reports. This is an easily assessed and readily accomplished measure with targeted performance of a greater than 98% frequency with which all GI cancers are staged with the AJCC/UICC TNM staging system.

Diagnostic rate and sensitivity for malignancy are outcome measures with immediate clinical relevance and potentially grave consequences to individual patients if performance is not excellent. Targets set are a diagnostic rate >=70% and sensitivity >=85%. These goals were informed by a multicenter retrospective review of the diagnostic yield of EUS-FNA of pancreatic masses at 21 centers (81% academic) that found an overall diagnostic rate of malignancy of 71% [53]. A more recent meta-analysis of 33 studies with nearly 5000 patients found a pooled sensitivity for malignancy cytology of 85% and specificity of 98%; if atypical and suspicious cytology results were included, the sensitivity increased to 91% and the specificity fell to 94% [54].

The outcome measure of adverse event rate after EUS also has immediate and self-evident clinical relevance. The ACG/ASGE task force set as a target an acute pancreatitis rate < 2%, a perforation rate < 0.5%, and a clinically significant bleeding rate < 1%. The largest data source available is a systematic review of EUS complications by Wang et al. which found an overall morbidity rate of 0.98%, pancreatitis rate of 0.44%, and bleeding rate of 0.13%. Perforation was exceedingly rare, representing just 1.9% of all complications (or a perforation rate of 0.019%). However, the rates of morbidity in prospective studies (2.44%) significantly exceeded those in retrospective studies (0.35%) suggesting the preponderance of retrospective studies may skew the overall results to an underestimate of complication rates [55]. These targets are thus within range of the best available estimates of complication rates in current practice in the literature.

Choosing Wisely

Many of the priority indicators in the ACG/ASGE Proposed Quality Indicators are process measures, especially those for colonoscopy and upper endoscopy. One such example, namely, procedure done for appropriate indication, addresses the important issue of overutilization of resources and unnecessary testing which has come to increasing prominence, and national efforts have coalesced to approach this problem. The American Board of Internal Medicine (ABIM) Foundation's Choosing Wisely campaign is a leader in this endeavor, partnering with Consumer Reports and Medical Specialty Societies with the stated goal of "advancing a national dialogue on avoiding wasteful or unnecessary medical tests, treatments and procedures." This multidisciplinary effort maintains resources online at http://www.choosingwisely.org/. The American Gastroenterological Association (AGA) has proposed several Choosing Wisely recommendations relevant to gastrointestinal endoscopy: first, they recommend against colonoscopy for at least 5 years for patients who have one or two small (<1 cm) adenomatous polyps, without high-grade dysplasia, completely removed via a high-quality colonoscopy; secondly, they recommend against repeat colorectal cancer screening (by any method) for 10 years after a high-quality negative colonoscopy in average-risk individuals; and finally, they have recommended against a follow-up surveillance examination earlier than 3 years in patients diagnosed with Barrett's esophagus with a second endoscopy confirming the absence of dysplasia on biopsy. Similarly, the American College of Surgeons recommend avoidance of colorectal screening tests in asymptomatic patients with a life expectancy less than 10 years and no family or personal his-

tory of colorectal neoplasia. The American Academy of Hospice and Palliative Medicine and American Geriatric Society both recommend against feeding tube placement in patients with advanced dementia.

Patient Reported Outcomes (PROs)

The increasing value placed on patient-centered healthcare is evident in payers incorporating patient satisfaction into compensation and a shift toward public reporting of patient satisfaction metrics. Understanding and improving the patient experience of care are thus imperative for high-quality care. The National Institute of Health launched an initiative, PROMIS (patient reported outcome measurement information system), to build and validate a set of publically available measures that can be implemented electronically in practice and establish clinical thresholds for action and meaningful improvement or decline [56]. More recently, an online database of PROs in gastroenterology has been developed and is available at http://www.researchcore.org/gipro/ [57]. Despite a surfeit of inventories and questionnaires, incorporation into clinical practice has been limited given time concerns and questions about whether results are actionable. More research is still needed to validate available PROs and translate these to a useful role in clinical practice, but the PROMIS initiative and GI PRO database are important strides toward giving clinicians the tools needed to systematically understand the patient experience.

Conclusions

While the quality measurement landscape continues to evolve, measuring and reporting on quality has become an expectation for clinical practice. Systematic assessment of quality is now fundamental to the healthcare environment and an important domain of clinical practice for individual physicians, practices, and institutions to understand. Significant progress has been made in defining and refining quality indicators which allow clinicians and institutions to objectively evaluate their individual and health system performance and identify concrete areas for improvement as well as objectively measure improvement efforts. Clinical research is beginning to substantiate the basis for quality indicators, linking some process measures such as adenoma detection rate to important clinical outcomes like mortality and risk of interval colorectal cancer. This data allows prioritization of quality metrics to those with indisputably important clinical results.

Despite significant advancements, sensitivity to the potential unintended consequences of quality measurement is critical, and many opportunities exist to improve the science and practice of healthcare quality measurement [58]. Similarly, in gastroenterology, more research is warranted to validate and prioritize proposed quality indicators and build an evidence base to support benchmarks. Benchmarks will also be important in assessing the healthcare system's responsiveness to patient perceptions of care and will be an important area of focus for future quality improvement. Although the era of personalized medicine is in its infancy, as research progresses, a patient-centered approach can be expected to be increasingly individualized. More robust electronic health record systems will be needed to allow clinically seamless reporting of quality metrics. While these quality measurement challenges are being addressed, there remain substantial gaps in patient access to even widely available, validated interventions such as colonoscopy for colorectal cancer screening. As such, improving accessibility to screening must remain a quality metric in and of itself.

References

1. Kohn LT, Corrigan J, Donaldson MS. To err is human: building a safer health system. Washington, D.C.: National Academy Press; 2000.
2. Institute of Medicine. Crossing the quality chasm: a new health system for the 21st century. Washington, D.C.: National Academy Press; 2001.
3. Conway PH. The core quality measures collaborative: a rationale and framework for public-private quality measure alignment. Web blog post. Health Affairs Blog. 23 June 2015. Available at: http://healthaffairs.org/blog/2015/06/23/the-core-quality-measures-collaborative-a-rationale-and-framework-for-public-private-quality-measure-alignment/
4. Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med. 2012;366:687–96.
5. Cooper GS, Xu F, Barnholtz Sloan JS, et al. Prevalence and predictors of interval colorectal cancers in medicare beneficiaries. Cancer. 2012;118:3044–52.
6. le Clercq CMC. Postcolonoscopy colorectal cancers are preventable: a population-based study. Gut. 2014;63:957–63.
7. Faigel DO, Baron TH, Lewis B, et al. Ensuring competence in endoscopy. ASGE Policy and Procedures Manual for Gastrointestinal Endoscopy: Guidelines for Training and Practice Available at http://gi.org/physician-resources/competencies-in-endoscopy/
8. Chen SC, Rex DK. Endoscopist can be more powerful than age and male gender in predicting adenoma detection at colonoscopy. Am J Gastroenterol. 2007;102:856–61.
9. Kahi CJ, Hewett DG, Norton DL, et al. Prevalence and variable detection of proximal colon serrated polyps during screening colonoscopy. Clin Gastroenterol Hepatol. 2011;9:42–6.
10. Rex DK, Cutler CS, Lemmel GT, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. Gastroenterology. 1997;112:24–8.
11. Rizk MK, Sawhney MS, Cohen J, et al. Quality indicators common to all GI endoscopic procedures. Am J Gastroenterol. 2015;110:48–59.
12. Donabedian A. Evaluating the quality of medical care. Milbank Q. 1966;44(3):166–203.
13. Chassin MR, Loeb JM, Schmaltz SP, Wachter RM. Accountability measures – using measurement to promote quality improvement. N Engl J Med. 2012;363(7):683–8.
14. Mysliwiec PA, Brown ML, Klabunde CN, et al. Are physicians doing too much colonoscopy? A national survey of colorectal surveillance after polypectomy. Ann Intern Med. 2004;141(4):264–71.
15. Kruse GR, Khan SM, Zaslavsky AM, et al. Overuse of colonoscopy for colorectal cancer screening and surveillance. J Gen Intern Med. 2014;30(3):277–83.

16. Johnson MR, Grubber J, Grambow SC, et al. Physician non-adherence to colonoscopy interval guidelines in the veterans affairs healthcare system. Gastroenterology. 2015;149:938–51.
17. Baxter NN, Sutradhar R, Forbes SS, et al. Analysis of administrative data finds endoscopist quality measures associated with post-colonoscopy colorectal cancer. Gastroenterology. 2011;140:65–72.
18. Kaminski MF, Regula J, Kraszewska E, et al. Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med. 2010;362(19):1795–803.
19. Gellad ZF, Voils CI, Lin L, Provenzale D. Physician perceptions on colonoscopy quality: results of a national survey of gastroenterologists. Gastroenterol Res Pract. 2014;2014:1–10.
20. Corley DA, Jensen CD, Marks AR, et al. Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med. 2014;370(14):1298–306.
21. Denis B, Sauleau EA, Gendre I, et al. The mean number of adenomas per procedure should become the gold standard to measure the neoplasia yield of colonoscopy: a population-based cohort study. Dig Liver Dis. 2014;46:176–81.
22. Wang HS, Pisegna J, Modi R, et al. Adenoma detection rate is necessary but insufficient for distinguishing high versus low endoscopist performance. Gastrointest Endosc. 2013;77(1):71–8.
23. Hetzel J, Huang CS, Coukos JA, et al. Variation in the detection of serrated polyps in an average risk colorectal cancer screening cohort. Am J Gastroenterol. 2010;105:2656–64.
24. Patel NC, Islam RS, Wu Q, et al. Measurement of polypectomy rate by using administrative claims data with validation against the adenoma detection rate. Gastrointest Endosc. 2013;77:390–4.
25. Williams JE, Holub JL, Faigel DO. Polypectomy rate is a valid quality measure for colonoscopy: results from a national endoscopy database. Gastrointest Endosc. 2012;75:576–82.
26. Coe SG, Crook JE, Diehl NN, Wallace MB. An endoscopic quality improvement program improves detection of colorectal adenomas. Am J Gastroenterol. 2013;108:219–26.
27. Ussui V, Coe S, Rizk C, et al. Stability of increased adenoma detection at colonoscopy. Follow-up of an endoscopic quality improvement program-EQUIP-II. Am J Gastroenterol. 2015;110:489–96.
28. Barclay RL, Vicari JJ, Greenlaw RL. Effect of a time-dependent colonoscopic withdrawal protocol on adenoma detection during screening colonoscopy. Clin Gastroenterol Hepatol. 2008;6:1091–8.
29. Lee CK, Park DI, Lee S, et al. Participation by experienced endoscopy nurses increases the detection rate of colon polyps during a screening colonoscopy: a multicenter, prospective, randomized study. Gastrointest Endosc. 2011;74:1094–102.
30. Aslanian HR, Shieh FK, Chan FW, Ciarleglio MM, et al. Nurse observation during colonoscopy increases polyp detection: a randomized prospective study. Am J Gastroenterol. 2013;108:166–72.
31. Sanaka MR, Deepinder F, Thota PN, Lopez R, Burke CA. Adenomas are detected more often in morning than in afternoon colonoscopy. Am J Gastroenterol. 2009;104:1659–64.
32. Gurudu SR, Ratuapli SK, Leighton JA, Heigh RI, Crowell MD. Adenoma detection rate is not influenced by the timing of colonoscopy when performed in half-day blocks. Am J Gastroenterol. 2011;106:1466–71.
33. Shaukat A, Oancea C, Bond JH, et al. Variation in detection of adenomas and polyps by colonoscopy and change over time with a performance improvement program. Clin Gastroenterol Hepatol. 2009;7:1335–40.
34. Barclay RL, Vicari JJ, Doughty AS, et al. Colonoscopic withdrawal times and adenoma detection during screening colonoscopy. N Engl J Med. 2006;355:2533–41.
35. Corley DA, Jensen CD, Marks AR. Can we improve adenoma detection rates? A systematic review of intervention studies. Gastrointest Endosc. 2011;74(3):656–65.
36. Shaukat A, Rector TS, Church TR, et al. Longer withdrawal time is associated with a reduced incidence of interval cancer after screening colonoscopy. Gastroenterology. 2015;149:952–7.
37. Rex DK, Imperiale TF, Latinovich DR, Bratcher LL. Impact of bowel preparation on efficiency and cost of colonoscopy. Am J Gastroenterol. 2002;97:1696–700.
38. Hillyer GC, Basch CH, Lebwohl B, et al. Shortened surveillance intervals following suboptimal bowel preparation for colonoscopy: results of a national survey. Int J Color Dis. 2013;28:73–81.
39. Lebwohl B, Wang TC, Neugut AI. Socioeconomic and other predictors of colonoscopy preparation quality. Dig Dis Sci. 2010;55:2014–20.
40. Kilgore TW, Abdinoor AA, Szary NM, et al. Bowel preparation with split-dose polyethylene glycol before colonoscopy: a meta-analysis of randomized controlled trials. Gastrointest Endosc. 2011;73:1240–5.
41. Park WG, Shaheen NJ, Cohen J, et al. Quality indicators for EGD. Gastrointest Endosc. 2015;81(1):17–30.
42. Chavez-Tapia NC, Barrientos-Gutierrez T, Tellez-Avila F, et al. Meta-analysis: antibiotic prophylaxis for cirrhotic patients with upper gastrointestinal bleeding – an updated Cochrane review. Aliment Pharmacol Ther. 2011;34:509–18.
43. Sreedharan A, Martin J, Leontiadis GI, et al. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. Cochrane Database Syst Rev 2010;(7)::CD005415.
44. Sachar H, Vaidya K, Laine L. Intermittent vs continuous proton pump inhibitor therapy for high-risk bleeding ulcers: a systematic review and meta-analysis. JAMA Intern Med. 2014;174(11): 1755–62.
45. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107:345–60.
46. Laine L, McQuaid KR. Endoscopic therapy for bleeding ulcers: an evidence-based approach based on meta-analyses of randomized controlled trials. Clin Gastroenterol Hepatol. 2009;7:33–47.
47. Ford AC, Delaney B, Forman D and P Moayyedi. Eradication therapy for peptic ulcer disease in Helicobacter pylori positive patients. Cochrane Database Syst Rev 2006;(2): CD003840.
48. Adler DA, Lieb JG, Cohen J, et al. Quality indicators for ERCP. Am J Gastroenterol. 2015;110:91–101.
49. DeBenedet AT, Elmunzer BJ, McCarthy ST, et al. Intraprocedural quality in endoscopic retrograde cholangiopancreatography: a meta-analysis. Am J Gastroenterol. 2013;108:1696–704.
50. Kubiliun NM, Elmunzer BJ. Preventing pancreatitis after endoscopic retrograde cholangiopancreatography. Gastrointest Endosc Clin N Am. 2013;23:769–86.
51. Freeman ML, DiSario JA, Nelson DB, et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. Gastrointest Endosc. 2001;54:425–34.
52. Wani S, Wallace MB, Cohen J, et al. Quality indicators for EUS. Am J Gastroenterol. 2015;110:102–13.
53. Savides TJ, Donohue M, Hunt G, et al. EUS-guided FNA diagnostic yield of malignancy in solid pancreatic masses: a benchmark for quality performance measurement. Gastrointest Endosc. 2007;66:277–82.
54. Hewitt MJ, McPhail MJW, Possamai L. EUS-guided FNA for diagnosis of solid pancreatic neoplasms: a meta-analysis. Gastrointest Endosc. 2012;75:319–31.
55. Wang K-X, Ben Q-W, Jin Z-D, et al. Assessment of morbidity and mortality associated with EUS-guided FNA: a systematic review. Gastrointest Endosc. 2011;73:283–90.
56. Spiegel BMR. Patient-reported outcomes in gastroenterology: clinical and research applications. J Neurogastroenterol Motil. 2013;19(2):137–48.
57. Khanna P, Agarwal N, Khanna D, et al. Development of an online library of patient-reported outcome measures in gastroenterology: the GI-PRO database. Am J Gastroenterol. 2014;109: 234–48.
58. Cassel CK, Conway PH, Delblanco SF, et al. Getting more performance from performance measurement. N Engl J Med. 2014; 371(23):2145–7.

Documentation and Description of Endoscopic Procedures

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Introduction

Quality assurance in endoscopic practice has become a standard requirement in most countries. In an era of liability and malpractice, ensuring quality in endoscopic practice is the only dependable strategy to reduce risk of litigation. One of the measures of quality of endoscopic procedures is appropriate documentation of lesions and completeness of the procedure. To maintain higher standards of practice and to train junior gastroenterologists, a physician should make every attempt to complete a thorough endoscopic examination, document the procedure with accurate vocabulary, take appropriate photographs of every step of the procedure, and specifically describe the presence or lack of abnormalities. This stepwise approach is helpful for comparison with follow-up examinations and serves to guide referring physicians for subsequent patient care. An endoscopist should note whether the given procedure was complete and if not, the reason for its incompleteness, i.e., noncooperative patient, inadequate sedation, retained food in the stomach, suboptimal or poor preparation, stricture, loop formation, etc.

Photographic documentation of endoscopic procedures may be evolving from still photographs to video recording. All examination findings at endoscopy and subsequent recommendations are based on images, which are created during the procedure. This allows a physician to maintain an accurate record for future use, comparison purposes, and research.

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The Endoscopy Reporting Standards

Documentation and description of endoscopic procedures is one of the most important parts of quality assurance in endoscopic practice. Quality documentation provides informative communication and clear understanding between physicians, health-care providers, patients, and billing personnel. Quality documentation is the key to demonstrate the good quality endoscopy, which can improve the patient's outcome. Furthermore, ensuring quality in endoscopic documentation is the only dependable strategy to reduce risk of litigation in an era of liability and malpractice. Standardized reporting format will ensure quality documentation which is essential for monitoring and benchmarking quality endoscopy. The format of endoscopic reporting is outlined in Table 49.1.

Practical Considerations

- Endoscopic procedural documentation is one of the most important parts of quality assurance in endoscopic practice.
- Standardized reporting format will ensure quality documentation.
- Table 49.1. proposed standardized endoscopic reporting format.

Photodocumentation of Endoscopic Procedures

In order to obtain the most helpful photographs, physicians must make every attempt to:

1. Identify endoscopic landmark and important endoscopic finding of the patient, endoscopists, and other health-care providers.

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Table 49.1 Documentation and description of endoscopic procedures

Format	Comment
Date of the procedure	
Patient demographic data	
Endoscopist (s)	
Assistant(s)	Including trainee participation in procedure
Documentation of relevant patient history and physical examination	
Confirmation of informed consent	
Endoscopic procedure	
Indication(s)	One may use symptoms, diseases for assessment of a condition or diagnostic sampling of a particular organ, etc.
Type of endoscopic instrument	
Medications used (anesthesia, analgesia, sedation)	Should include dose and route of administration. May also state "per anesthesia" if an anesthesiologist was involved and kept separate records of sedation
Anatomical extent of the examination	Include identifying anatomical landmark feature, e.g., cecum, verified by cecal strap, ileocecal valve, and appendiceal orifice
Ease of examination	Degree of difficulty in passing the scope. External pressure used or patient position changed
Patient toleration	
Limitation (s) of the examination	Document the quality of the patient's colon prep
Withdrawal time	Document adequate time for examination of colonoscopy
Findings	Use specific terminology as referenced elsewhere in this chapter
Specimens obtained and anatomical location	Document whether lesions were completely or only partially removed
Therapeutic intervention	
Images taken	Include images with the report
Complications	
Diagnostic impression	This is not a final diagnosis. This may mean conclusion, negative or positive
Discharge plan and follow-up	Guide referring physicians with specific recommendations
Copy(s) to the referring doctor	Communication of the findings to the referring doctor

Modified from Crespi et al. [1] and Lieberman et al. [2]

2. Clean the lens of endoscopes and remove any view-obscuring fluid, bubble, and debris of the region of interest before taking a photo.
3. Adequately inflate the lumen of the organ.
4. Avoid close lateral proximity with the mucosa to avoid over illumination of the area of interest.
5. Obtain images of the baseline lesion, endoscopic therapy image in action, and post-intervention appearance and surrounding mucosa.

Table 49.2 Recommended landmarks for photography in EGD and colonoscopy [5]

Procedure	Recommended landmarks for photography
EGD	Esophageal introitus, proximal, mid, and distal esophagus, gastroesophageal junction, gastric cardia and fundus on retroflexed view, gastric body on either retroflexed or retroflexed view, gastric angularis or incisura on retroflexed view, antrum and pylorus, duodenal bulb, and second or third portion of the duodenum
Colonoscopy	Cecum, appendiceal orifice, ileocecal valve, terminal ileum if terminal ileal intubation is achieved, ascending colon, transverse colon, descending colon, sigmoid colon, and the rectum in both forward and retroflexed views. Anal canal and perianal area if they are relevant to the presenting symptoms

6. Adequately document normal endoscopy anatomy (landmarks).
7. Freeze the frame to focus before storing the picture of interest.
8. Select images for proper labeling, annotating for final endoscopy report.

It is important to include a sufficient number of images to document complete endoscopic examination (Table 49.2). On the other hand, video recording (if available) of the entire procedure or specific important segments of the procedure can also be done. Newer technologies may also provide more accurate images. The addition of narrowband imaging technology built into modern endoscopes enhances the visibility of some mucosal lesions. All negative examinations should also contain standard photographic documentation of specific structures.

Practical Considerations

- Identification and recording of endoscopic landmarks are important.
- Recommended landmarks for photography in EGD and colonoscopy were described in Table 49.2.

Upper Gastrointestinal Endoscopy

Routinely, upper gastrointestinal endoscopies are done using forward-viewing endoscopes. The newer equipments have a wider angle lens and greater degree of tip movement (or deflection), allowing for more efficient examination and survey of the stomach and the duodenum. Some areas are routinely difficult to examine, treat, or even obtain tissue samples. These areas, called "review areas," are (1) just distal to the upper esophageal sphincter, (2) the proximal

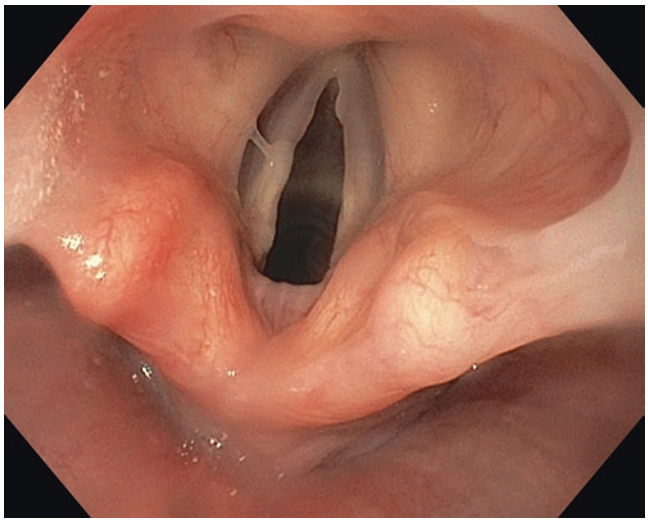

Fig. 49.1 Upper endoscopic view of the hypopharynx (esophageal introitus)

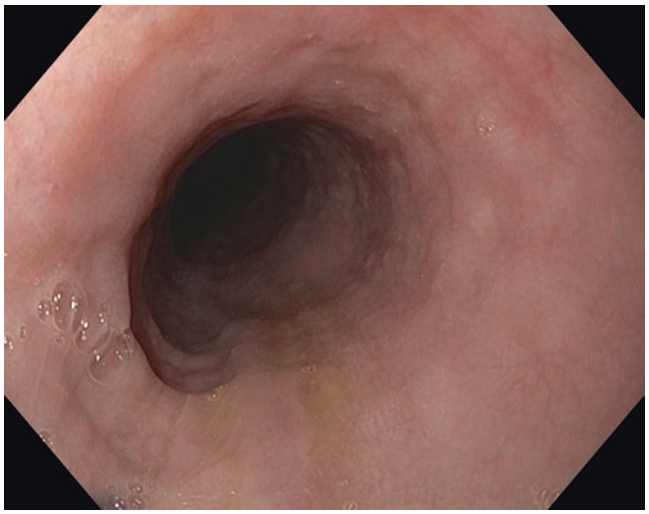

Fig. 49.2 The upper esophagus

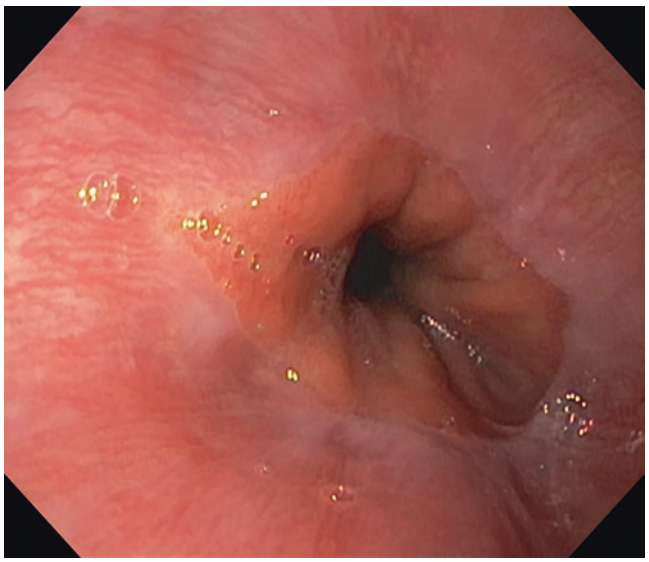

Fig. 49.3 The gastroesophageal junction

lesser curve, (3) proximal duodenal bulb, (4) medial aspect of the second part of the duodenum, and (5) areas immediately distal to surgical anastomoses. The European Society of Gastrointestinal Endoscopy (ESGE) has proposed and recommended that at least eight images of the upper gastrointestinal tract be performed to constitute a complete examination, and additional images should be taken as necessary. These are the minimal recommendations for a normal examination, and any abnormalities should also be well documented with photos and/or videos. For upper endoscopy, the areas of documentation include the following:

- Esophageal introitus including hypopharynx, the esophageal opening posterior to the cricoid prominent, and the cervical esophagus (we propose this *in addition* to ESGE recommendation) (Fig. 49.1).
- The upper esophagus just below the upper sphincter, which also usually demonstrates a forward view of the proximal half of the esophagus (Fig. 49.2).
- Just above the lower esophageal sphincter, allowing proper examination for intestinal metaplasia or esophagitis (Fig. 49.3a).
- The Z-line should be visualized noting the approximate distance from incisors, preferably with a narrowband image (we propose this *in addition* to ESGE recommendation to better define the demarcation of the squamocolumnar junction and facilitate identification of Barrett's esophagus) (Fig. 49.3b).
- A retroflexed view of the cardia and a part of the fundus (we propose two photographs of this area by torqueing the endoscope by 180° in the retroflexed view, an area also amenable to video recording. This would help define lesions close to GE junction and high on the lesser curve with a closer view of cardia by retroflexion) (Figs. 49.4 and 49.5).
- The upper part of the lesser curve (Fig. 49.6); the angulus of the stomach from a partially retroflexed view (Fig. 49.7).
- The antrum (Fig. 49.8); the duodenal bulb photographed from the pylorus (an additional photo of the retroflexed view of the duodenal bulb may also be taken with extreme degree of caution to avoid trauma) (Fig. 49.9).
- The second part of the duodenum with specific attention to the medial wall of this area to confirm a complete examination.
- The ampulla of Vater is often visualized in this photo (Fig. 49.10).

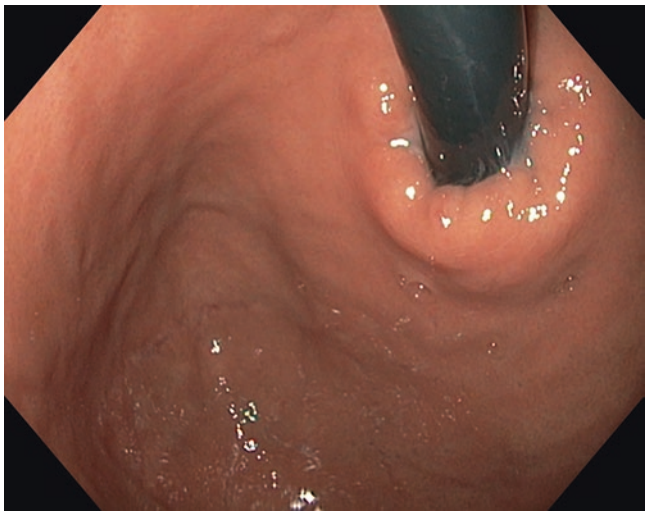

Fig. 49.4 The cardia viewed by retroflexion of the upper endoscope

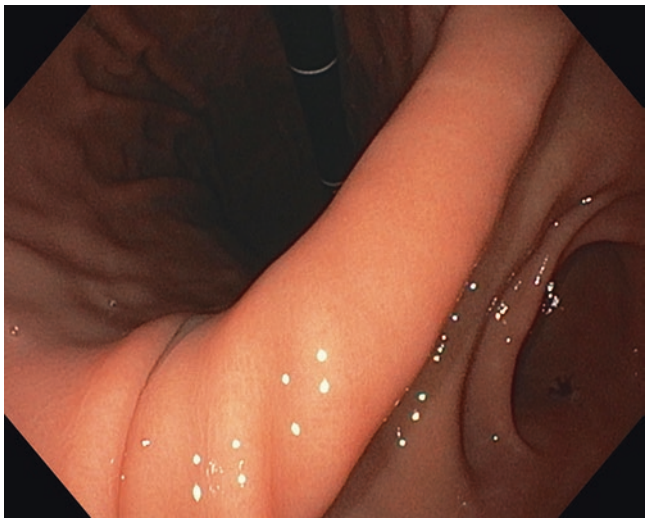

Fig. 49.7 The angulus of the stomach viewed by retroflexion of the upper endoscope

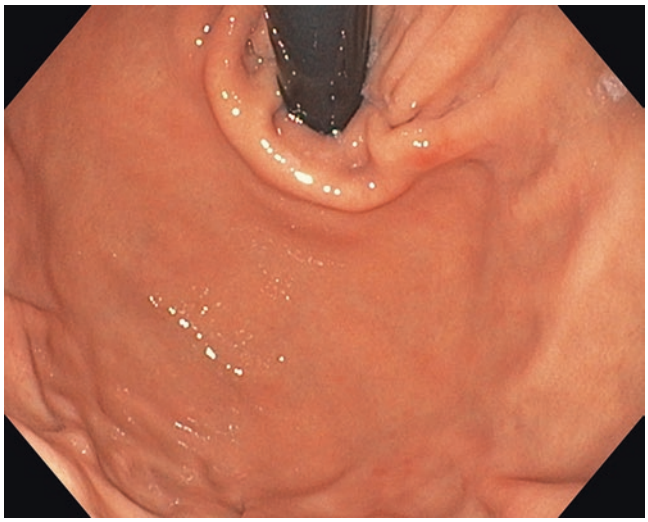

Fig. 49.5 The fundus viewed by retroflexion of the upper endoscope

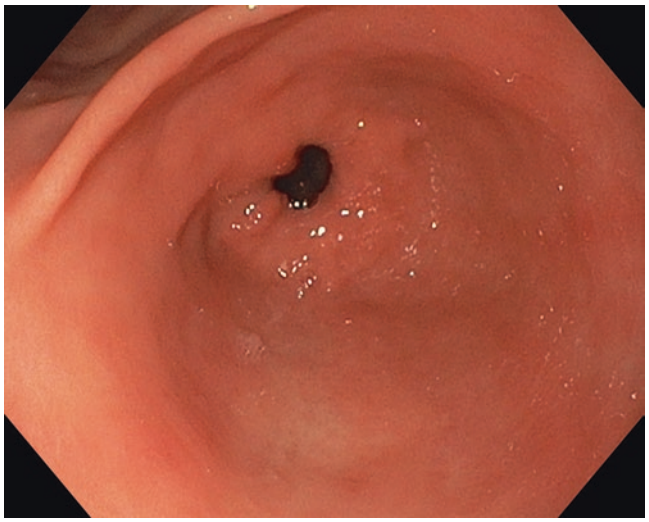

Fig. 49.8 The antrum of the stomach

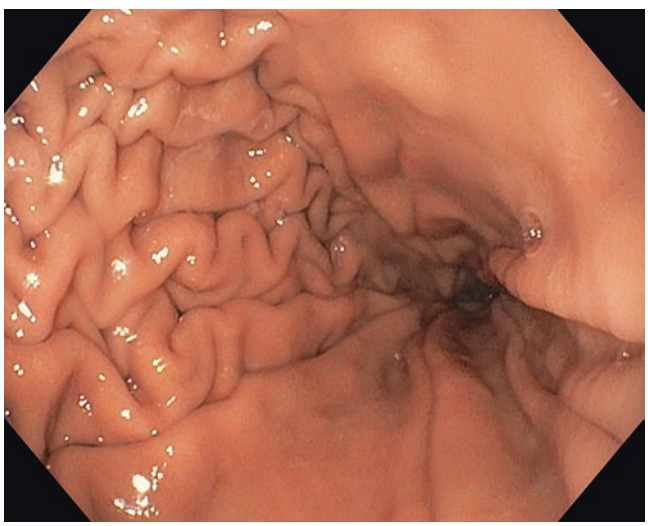

Fig. 49.6 The lesser curvature of the stomach

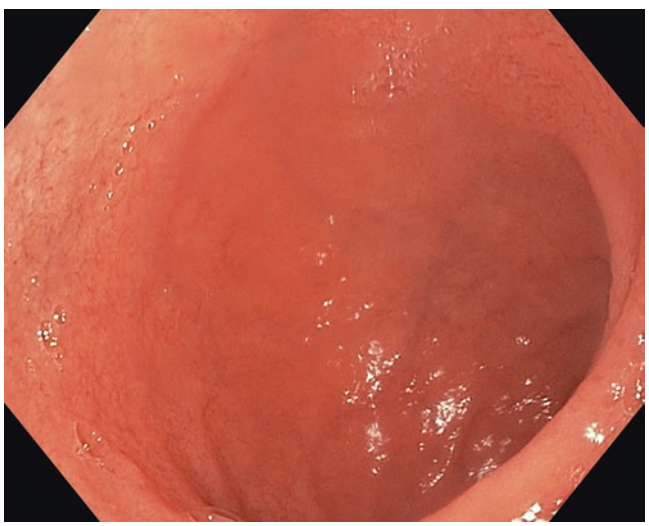

Fig. 49.9 The duodenal bulb

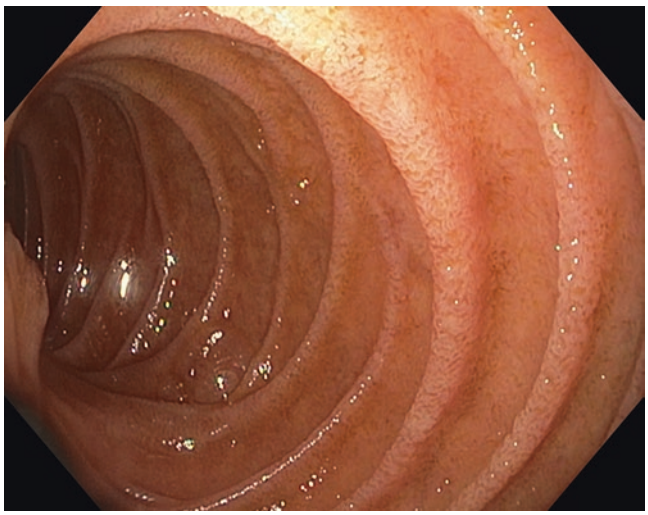

Fig. 49.10 Second part of duodenum (ampulla of Vater is partially visualized along the medial wall)

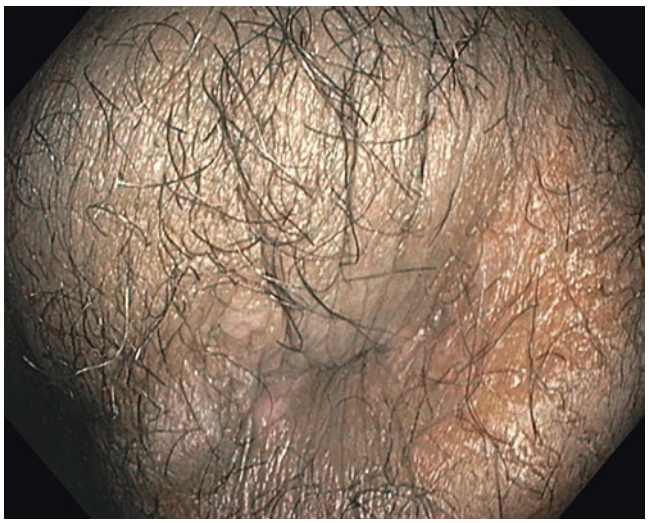

Fig. 49.11 External view of the anus viewed with a colonoscope

Practical Considerations

- ESGE recommended that at least eight images of the EGD be performed to constitute a complete examination, and additional images should be taken as necessary.
- "Review areas" need to be thoroughly examined since the lesion can be missed easily.
- Specific pathologic findings should be reported with generalized acceptable classification.
- For example:
  - LA classification (Los Angeles classification) for erosive esophagitis
  - Prague C & M classification for Barrett's esophagus extension
  - Size classification for esophageal varices
  - Forrest classification for ulcer bleeding

Colonoscopy

Similar to upper gastrointestinal endoscopies, colonoscopies are performed using forward-viewing equipment. Similar to upper gastrointestinal endoscopies, some areas are relatively difficult to examine and treat or even for tissue sampling. These "review areas" are (1) sigmoid colon, (2) inferior aspect of the splenic flexure, (3) medial aspect of the colon just proximal to the hepatic flexure, and (4) areas immediately distal to surgical anastomoses. Physicians should make every attempt to take appropriate numbers of photographs for a complete examination. The ESGE has recommended at least eight images of the lower gastrointestinal tract to constitute a complete examination and additional images may be taken as necessary to document pathology [4]. When colonoscopy is being performed for screening purposes, careful examination of the mucosal details for difficult-to-diagnose flat polyps becomes extremely important in high-risk groups. Documentation of the effort involved in such careful examination is possible only when a report is accompanied by appropriate pictorial records. For colonoscopy, the areas of documentation include the following:

- The anal opening prior to insertion (we propose this *in addition* to ESGE recommendation; this would help in documenting perianal pathology). (Fig. 49.11).
- The terminal ileum when appropriate (we propose this *in addition* to ESGE recommendation and suggest attempting terminal ileal intubation routinely as an added measure of quality to confirm the completeness of colonoscopy) (Fig. 49.12).
- The cecum with appendiceal opening to confirm a complete examination (Fig. 49.13).
- The ileocecal valve (Fig. 49.14).
- The ascending colon just proximal to the hepatic flexure (Fig. 49.15).
- The hepatic flexure (Fig. 49.16).
- The mid-transverse colon (we propose this additional image to document the diligence in examining mucosal detail) (Fig. 49.17).
- Just proximal to the splenic flexure (Fig. 49.17).
- The splenic flexure (Fig. 49.18).
- The descending colon (we propose this additional image) (Fig. 49.19).
- The mid-sigmoid colon (Fig. 49.20).
- The rectal vault, forward view (Fig. 49.21).

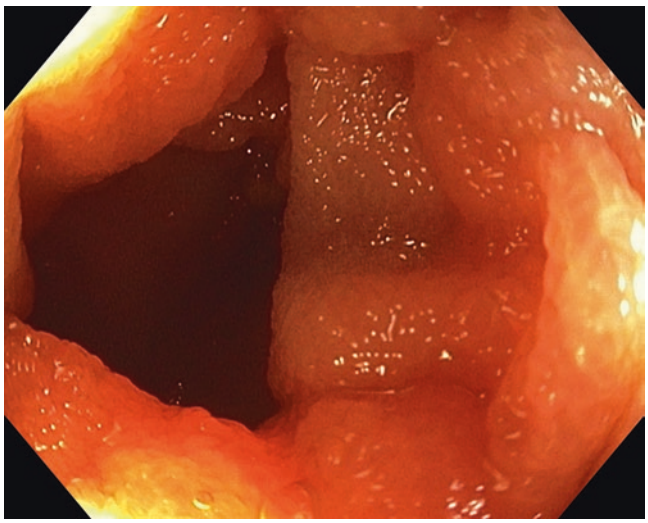

Fig. 49.12 The terminal ileum viewed with a colonoscope

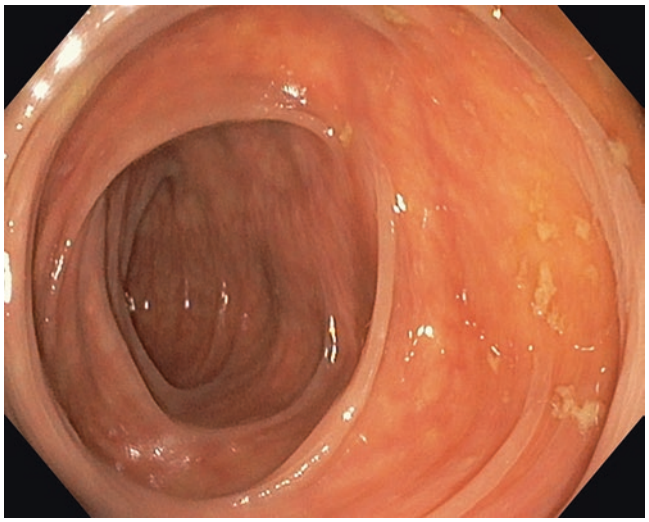

Fig. 49.15 The ascending colon

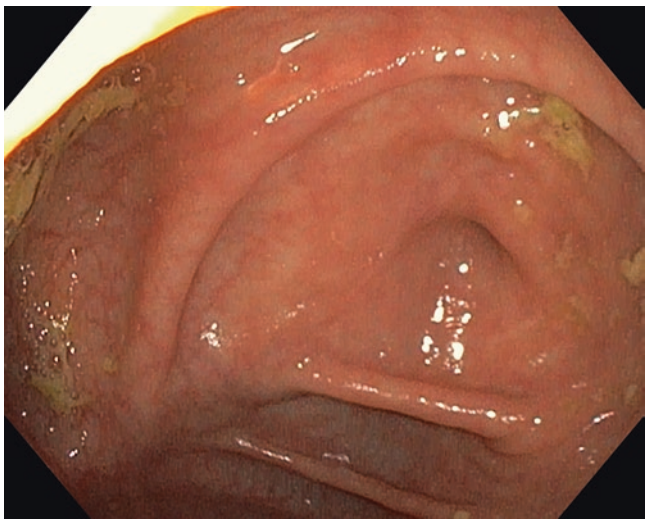

Fig. 49.13 The cecum

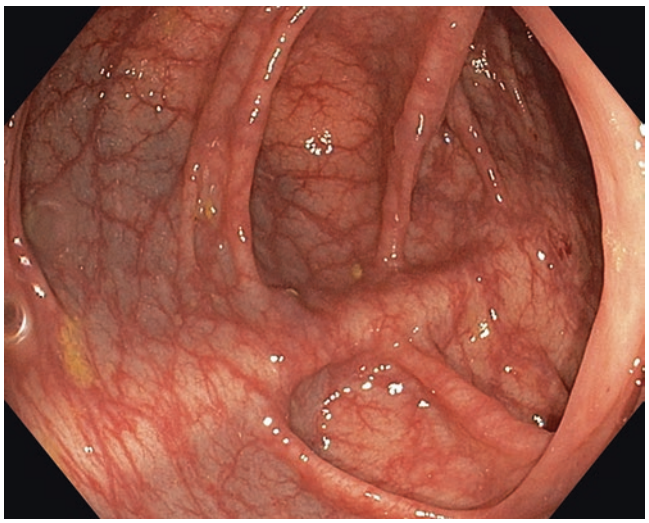

Fig. 49.16 The hepatic flexure

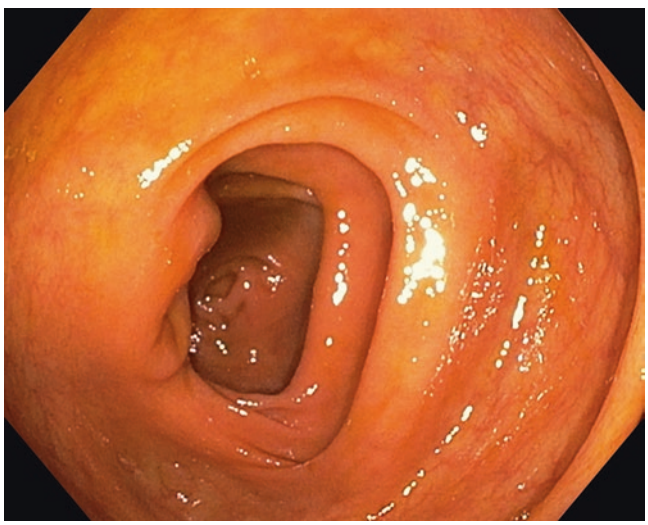

Fig. 49.14 The ileocecal valve

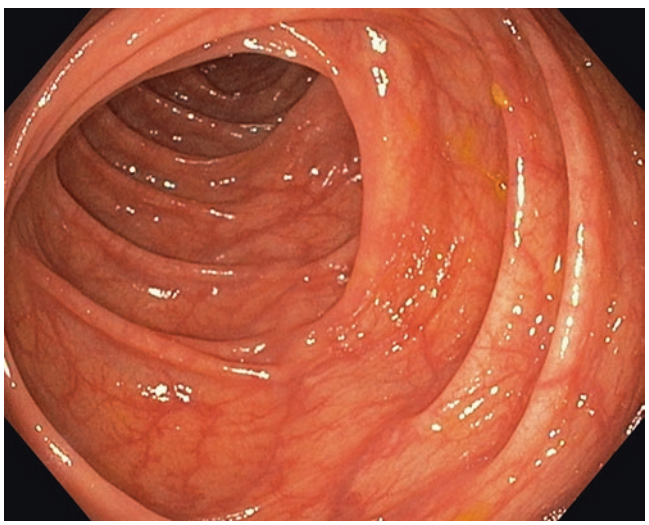

Fig. 49.17 Proximal to the splenic flexure

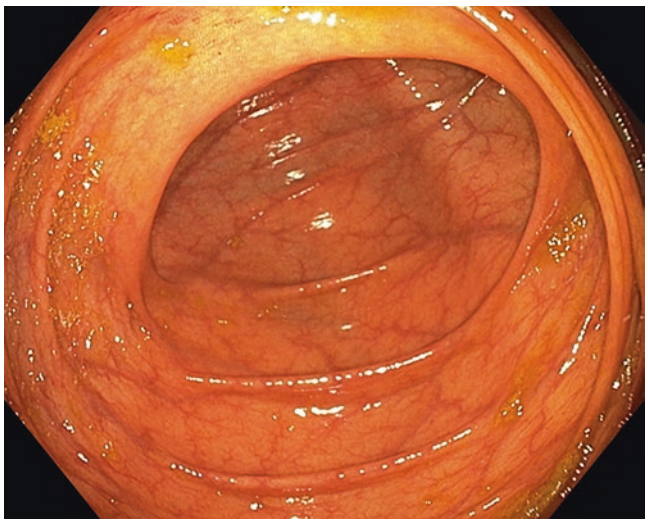

Fig. 49.18 The splenic flexure

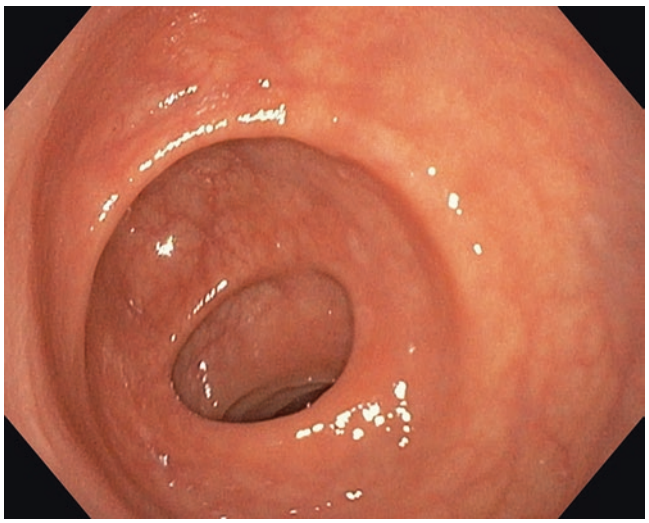

Fig. 49.21 The rectal vault

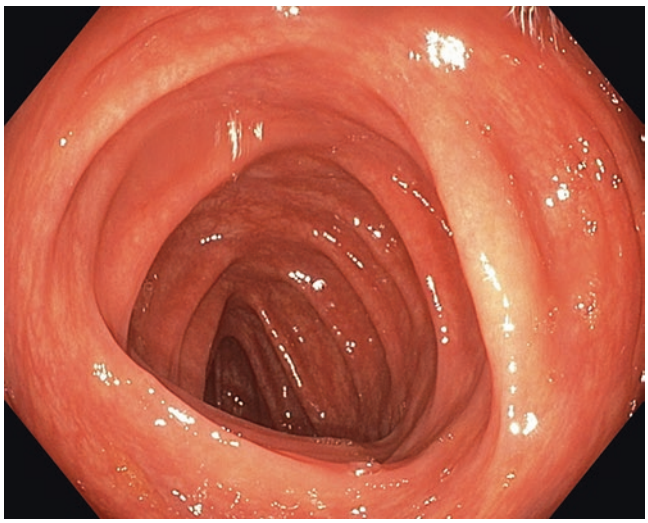

Fig. 49.19 The descending colon

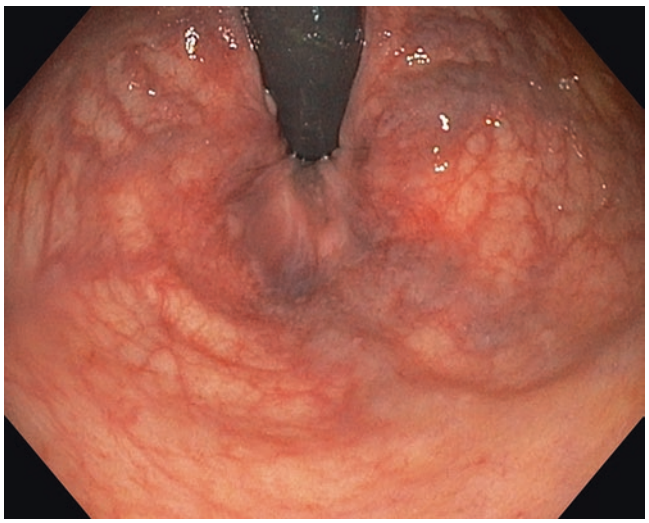

Fig. 49.22 The rectum viewed by retroflexion of a colonoscope

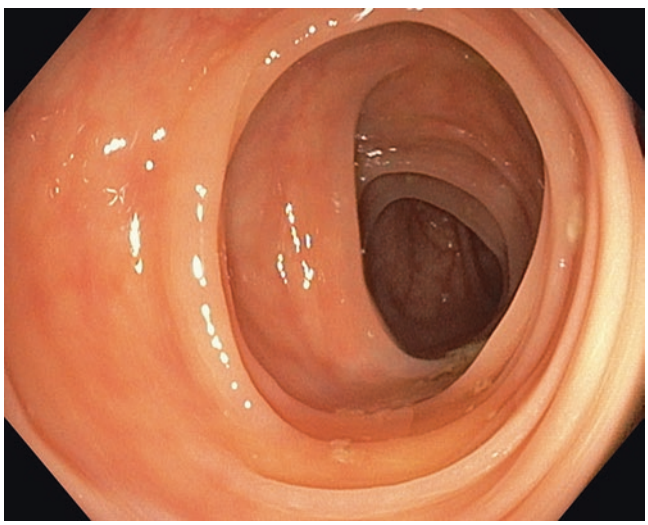

Fig. 49.20 The sigmoid colon

- The rectum, retroflexed view (we propose these additional images to document the completeness of examining the mucosal detail in distal rectum). The second image in the retroflexed view should be taken after torqueing the shaft of the colonoscope to 180° (Fig. 49.22).

Practical Considerations

- ESGE recommended that at least eight images of the colonoscopy be performed to constitute a complete examination, and additional images should be taken as necessary.

(continued)

Table 49.3 Terminology

Impression	Meaning
Normal	Examination is complete and everything is normal
Lumen	Contains all terms regarding an abnormality of the size of the organs, any deformity, compression, and any evidence of previous surgery
Contents	Presence of various materials within the organ
Mucosa	Patterns of the mucosa that are mainly diffuse and may involve all the mucosa of one limited area
Flat lesions	Lesions that remain in the plane of the mucosa
Protruding lesions	Lesions growing above the plane of the mucosa
Excavated lesions	Lesions whose surface is beneath the plane of the mucosa

Modified from Crespi et al. [1]

- Careful examination of the mucosal details for difficult-to-diagnose flat polyps is extremely important in high-risk groups.
- Specific pathologic findings should be reported with generalized acceptable classification.
- For example:
  - Goligher grading of hemorrhoids

Accurate Description of Endoscopic Findings

It is extremely important to describe what exactly one sees rather than making interpretations while reporting a procedure. The endoscopic procedure findings should be concise, using words and phrases to describe the abnormality as accurately as possible.

Terminology

The description of the examinations should be detailed enough using acceptable jargon to make a report easy to read and understand. The terminology used in the report should closely follow the structure of minimal standard terminology for gastrointestinal endoscopy (MST 3.0) laid by the World Organization for Digestive Endoscopy (OMED) (Table 49.3) [3].

Location of the Lesion

Description of the location of the lesion of interest is extremely important for the referring physicians, for the surgeons, and also for the pathologists. Describing a lesion with reference to incisor teeth or the anal verge is rather imprecise, but can be helpful if documented in conjunction with anatomical location (Table 49.4).

Table 49.4 Description of lesion location

Impression	Meaning
Cardia of the stomach	Used to replace hiatus. It is important to indicate the location of Z-line (distance from the incisors) vis-à-vis the proximal extent or the origin of the gastric folds
Gastric fundus	Anatomical part of the stomach that lies under the diaphragm
Gastric body	The area of the stomach above the angulus lined by linear gastric folds

Modified from Crespi et al. [1]

Description of Lesions

At times, the endoscopist may find it difficult to describe the lesion of interest because of ambiguity in terms of description. Certain terms are acceptable in common usage (Table 49.5). Pathologists may prefer certain terminologies to describe a lesion. It is better to describe the lesion with reference to its size and the extent. Certain benign-appearing lesions are better described by stating characteristics (Table 49.6). When biopsies from a particular organ are taken, the endoscopist should document the location from which the biopsies were obtained. This enables the pathologist to interpret the abnormality and the referring physician to understand the implications. Table 49.7 refers to how to report the sites of the biopsies.

Practical Considerations

- To report the accurate endoscopic findings, the terminology of lesion description and location should be concise and closely follow the structure of minimal standard terminology for gastrointestinal endoscopy (MST 3.0) laid by the World Organization for Digestive Endoscopy (OMED).

Conclusion

- The endoscopic reporting standards, image documentation, and appropriate reporting are extremely important permanent part of the patient's record, which can be referenced at a later date.
- Consistency, specificity, and accuracy in descriptions are essential.

Table 49.5 Description of lesions

Impression	Meaning
Red mucosa, erythema, congested mucosa, or hyperemia	Hyperemia is equivalent to erythema. Edema is equivalent to congested mucosa
Mucosal sclerosis	Post-sclerotherapy or post-band ligation-related mucosal changes
Aphtha	Small superficial defect in the mucosa, white or yellow in color, surrounded by red halo. They are single or multiple, frequently seen within erythematous mucosa
Erosion	Small superficial defect in the mucosa, white or yellow in color, with a flat edge. Frequently seen in Crohn's disease
Stenosis	Narrowed segment of the gut by stricture or stenosis or compression
Mass	Preferred to tumor
Angioectasia	Telangiectasia or angiodysplasia
Scar	Preferred to fibrosis. This may be related to healed ulcer or effect of radiotherapy, mucosal ablation, or mucosal resection
Obstruction	Blockage by intraluminal obstacle (foreign body)
Occlusion	Complete closure of the lumen by an intrinsic lesion

Modified from Crespi et al. [1]

Table 49.6 Description of lesion characteristics [6]

Terminology	Should be replaced by
-Itis	Absent vascular pattern, erythema, friability, subepithelial hemorrhages, exudates, erosions
Edema	Swelling, cobblestone appearance, prominent folds
Scar	Depressed or nondepressed, white, stellate, or linear streak
Atrophy	Thin folds, pallor, prominent vessels
Ectasia or angiodysplasia	Better to describe the actual lesion (smooth, non-raised or raised red lesion)

- The European Society of Gastrointestinal Endoscopy (ESGE) has proposed and recommended that at least eight images of the upper gastrointestinal tract and at least eight images of the lower gastrointestinal tract to constitute complete examinations, and additional images may be taken as necessary to document pathology.
- Standardized endoscopic reports can help to provide better care for our patients, which is the most important priority.

Table 49.7 Localization of lesions [6]

Organ/site	Location
Esophagus	State the number of centimeters from the incisor teeth
Stomach	Mention whether the biopsies were obtained from the fundus or the body (proximal or mid or distal and whether anterior or posterior) or the antrum
Duodenum	Bulb (anterior or posterior), second part or third or the fourth part
Colon	Cecum, ascending colon, hepatic flexure, transverse colon (proximal, mid, or distal), descending colon (proximal and then as number of centimeters from the anal verge). Sigmoid colon (in centimeters from the anal verge). Rectum (centimeters from the anal verge)

References

1. Crespi M, Delvaux M, Schaprio M, Venables C, Zwiebel F. Working Party Report by the Committee for Minimal Standards of Terminology and Documentation in Digestive Endoscopy of the European Society of Gastrointestinal Endoscopy. Minimal standard terminology for a computerized endoscopic database. Ad hoc Task Force of the Committee. Am J Gastroenterol. 1996;91(2):191.
2. Lieberman D, Nadel M, Smith RA, Atkin W, Duggirala SB, Fletcher R, Glick SN, Johnson CD, Levin TR, Pope JB, Potter MB. Standardized colonoscopy reporting and data system: report of the Quality Assurance Task Group of the National Colorectal Cancer Roundtable. Gastrointest Endosc. 2007;65(6):757–66.
3. Rey JF, Lambert R. ESGE recommendations for quality control in gastrointestinal endoscopy: guidelines for image documentation in upper and lower GI endoscopy. Endoscopy. 2001;33(10):901–3.
4. Aabakken L, Rembacken B, LeMoine O, Kuznetsov K, Rey JF, Rösch T, Eisen G, Cotton P, Fujino M. Minimal standard terminology for gastrointestinal endoscopy-MST 3.0. Endoscopy. 2009;41(8):727–8.
5. Tang SJ, Raju G. Endoscopic photography and image documentation. Gastrointest Endosc. 2015;82(5):925–31.
6. Weinstein WM, Hill TA. Gastrointestinal mucosal biopsy. In: Berk J, editor. Bockus textbook of gastroenterology. 4th ed. Philadelphia: WB Saunders Co; 1958. p. 626–44.

Gastrointestinal Endoscope Reprocessing

50

Kavel Visrodia and Bret T. Petersen

Introduction

Flexible endoscopes play an integral role in evaluating and treating various gastrointestinal (GI) conditions. An estimated 20 million endoscopic GI procedures are performed annually [1]. With routine exposure to secretions, sputum, feces, and blood, it is not surprising that endoscopes are subject to an extraordinary amount of microbial contamination. Reprocessing therefore is essential for recycling endoscopes while preventing patient-to-patient transmission of microorganisms that may be harmful. However, reprocessing of endoscopes is not easy and involves a multistep sequence, that is, time, labor, and resource intensive, with several potential pitfalls if performed inattentively. Indeed, lapses in endoscope reprocessing have been associated with several infectious outbreaks [2]. In this chapter, we outline the current approach to GI endoscope reprocessing and review emerging challenges in ensuring reprocessing efficacy and safety.

Definitions

Three terms that commonly appear in endoscope reprocessing literature and are important to distinguish include [3]:

- *Sterilization* refers to the elimination of all forms of microbial life, including bacterial spores, typically via physical (pressurized steam, dry heat) or chemical (ethylene oxide, hydrogen peroxide, liquid chemicals) methods.
- *Disinfection* refers to the elimination of potentially all microbial life (including vegetative microorganisms, mycobacteria, small and medium viruses, and fungal spores). Unlike sterilization, disinfection does not eradicate all bacterial spores when present in high levels. Disinfection is typically achieved using liquid chemical germicides, also termed high-level disinfectants. It is important to be aware that high-level disinfection is sometimes erroneously referred to as "sterilization."
- *Cleaning* refers to the removal of visible residue (organic and inorganic debris) from the surfaces of endoscopes and is usually accomplished manually using detergents and enzymatic solutions. Thorough completion of this step cannot be overemphasized, as failure to adequately clean endoscopes may interfere with and compromise subsequent disinfection or sterilization steps.

Practical considerations

- Cleaning refers to the removal of visible residue from the surface of endoscopes.
- Unlike sterilization, disinfection does not eradicate all bacterial spores when present in high levels on endoscopes.

Spaulding Classification of Medical Instruments

In 1968, Dr. E. H. Spaulding described a classification system for patient care items that still forms the basis of our approach to sterilization and disinfection today [4]. Patient care items are categorized as critical, semi-critical, and noncritical, based on their potential for transmitting infection. Critical items are used to enter sterile spaces and thus carry a high risk of transmitting disease if contaminated by any microorganism. This

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category is generally comprised of surgical and intravascular instruments, including laparoscopic endoscopes and endoscope accessories that break mucosal surfaces or enter sterile spaces such as the biliary tree (e.g., biopsy forceps, endoscopic retrograde cholangiopancreatography guidewires). These items must be purchased sterile or undergo sterilization. In contrast, noncritical items confer a low risk of disease transmission because contact is limited to intact skin, which serves as a physiologic barrier to microbes. Examples of such items include stethoscopes and blood pressure cuffs, which can be cleaned by low-level disinfectants. Semi-critical items are believed to carry an intermediate risk of disease transmission by virtue of contact with mucous membrane (or non-intact skin) without intended invasion of sterile spaces. This category includes GI endoscopes. It is thought that intact mucous membranes lining the gastrointestinal and respiratory tracts are resistant to most bacterial spores but may be more susceptible to other organisms such as bacteria and viruses. Therefore, semi-critical items should, at a minimum, receive high-level disinfection (HLD) to eliminate all microorganisms, with few remaining spores [3].

Practical considerations

- Critical patient items enter sterile spaces and require sterilization between uses.
- Semi-critical items, including flexible endoscopes, come in contact with mucous membrane and require high level disinfection.
- Noncritical items are limited to contact with intact skin and require cleaning.

Pathogen Transmission

In the absence of a central repository for reporting procedure-associated infections, the true risk of infection following GI endoscopy remains unknown. However, existing data and broad experience suggest overwhelming safety of current reprocessing practices when performed diligently and reliably.

Until recently, all cases of endoscope-related infections were associated with breaches in disinfection protocols, wherein manufacturer's instructions or established reprocessing guidelines were not correctly followed [2]. In a large review of the medical literature published from 1966 to 2002, 40 reports totaling 317 patients affected by transmission of pathogens linked to endoscopic procedures were identified [5]. Common bacterial pathogens included *Pseudomonas aeruginosa*, *Helicobacter pylori*, and *Clostridium difficile*, while viruses were limited to hepatitis B and C. Each outbreak was traced to demonstrated lapses in reprocessing, including lack of performance or procedural errors in cleaning and/or disinfection of endoscopes or accessories, use of an inappropriate disinfectant, insufficient endoscope exposure time, contaminated irrigation solutions, incorrect use of the automated endoscope reprocessor (AER), or improper drying of endoscope channels [5].

Additional reports describe similar lapses in endoscope reprocessing protocols that have not been directly linked to cases of pathogen transmission [2]. For example, the use of improperly reprocessed endoscopes at Veterans Affairs (VA) facilities in Tennessee, Florida, and Georgia between 2003 and 2009 resulted in notification of over 10,000 potentially exposed patients [6, 7]. Viral testing resulted in the detection of 24 cases of previously unknown hepatitis C, but whether transmission occurred as a result of the breach is uncertain, as this did not exceed the expected rate of undetected subclinical infection in this population of patients. As a result of the breach, 36 additional VA facilities (38 endoscopy units) were subject to unannounced inspections, of which 18.4% were not compliant with standard operating procedure [6]. These and other lapses underscore the risk for potential pathogen transmission and the importance of adherence to established reprocessing guidelines.

More recently, reports have emerged implicating duodenoscopes in patient-to-patient transmission of multidrug-resistant organisms (MDROs). Unlike previous outbreaks, during audits of reprocessing practices, no lapses in protocol were found. The first widely publicized outbreak involved seven patients admitted to a northeastern Illinois hospital in 2013 for infection by a relatively uncommon microbe in the United States named New Delhi metallo-B-lactamase (NDM)-producing carbapenem-resistant *Enterobacteriaceae* (CRE) [8]. The Centers for Disease Control and Prevention (CDC) investigation eventually recovered growth of this CRE from a single duodenoscope and 39 patients (35 with duodenoscope exposure). No lapse in duodenoscope reprocessing protocol was identified. Since then, both published series and press announcements have linked outbreaks of MDROs to duodenoscopes reprocessed in accordance with guidelines, totaling over 60 patients infected at 10–12 centers across the United States and many more worldwide [9]. Transmission is thought to occur due to persistent contamination of the elevator and its actuating wire channel, which are unique to side-viewing endoscopes (i.e., duodenoscopes and curvilinear array echoendoscopes) [8]. An elevator is a small lever recessed in the tip of the endoscope for manipulation of guidewires and endoscope accessories. The elevator position (i.e., up or down) is toggled by a wire which passes through a separate endoscope channel. However, the complex elevator-cable design, with tight tolerances and inaccessible crevices, appears to resist standard cleaning methods, resulting in persistent contamination. Models from all three major duodenoscope manufacturers have been implicated.

Elevator-containing echoendoscopes may carry the same risk, though only one isolated case of echo-endoscope-related infection has been reported [10].

Several stakeholders should be notified when a potential endoscope-related infection or outbreak is suspected. They include, but are not limited to, the institution's authority on infection prevention and control, the patient and treating physician as deemed appropriate, the appropriate state or regional health department, the Food and Drug Administration (FDA) via Medwatch [11], and manufacturers of the endoscope, disinfectant, and AER if applicable.

Practical considerations

- The true rate of infection following gastrointestinal procedures is unknown, but existing data and experience suggest safety of current reprocessing practices when performed diligently and reliably.
- Nearly all reported cases of infection appear to stem from lapses in endoscope reprocessing protocol.
- Recent reports have implicated duodenoscopes in the transmission of MDROs, despite being reprocessed according to protocol. The risk appears to stem from the complex design of the duodenoscope elevator region impeding effective cleaning.

Gastrointestinal Endoscope Reprocessing

Endoscope reprocessing guidelines have evolved considerably since their introduction in 1978 [12], with the most recent update of the US multi-society guideline in 2016 addressing recent reports of duodenoscope-related infections [13]. Endoscopes should at minimum be reprocessed with HLD, and the FDA has strongly encouraged supplemental measures to enhance the safety of duodenoscope reprocessing until definitive solutions are found (see later) [14].

In an effort to improve the efficacy of current endoscope reprocessing guidelines, several aspects must be considered. Adherence to published standards remains less than ideal and cannot be overstressed. In a multisite study, less than half (48%) of 183 endoscopes were observed being properly reprocessed [15]. Similarly, studies by the Society of Gastrointestinal Nursing Association and CDC have revealed compliance with recommendations to be highly variable [16, 17]. Employees involved with the cleaning and reprocessing of endoscopes should receive thorough initial training in all requisite steps and manufacturers' instructions for use (IFU) on all types and models of endoscopes employed in their practice. Moreover, ongoing training should be provided regularly and when devices evolve, and competency should be assessed at least annually thereafter, with appropriate documentation. Finally, a quality control program that enhances and documents the accountability for cleaning and testing of equipment (e.g., AER) must also be maintained.

Practical considerations

- Updated US multi-society guidelines addressing recent reports of duodenoscope-related infections were released in 2016.
- Strict adherence to guidelines, competency training, and a quality control program are necessary to optimize the efficacy of endoscope reprocessing.

Overview of Reprocessing Stages

Endoscope reprocessing can be divided in four major stages: precleaning, manual cleaning, HLD, and drying followed by storage (Fig. 50.1). When performed properly, one cycle of reprocessing requires up to 1 h before an endoscope is ready for storage. In the following sections, each stage is briefly reviewed (Fig. 50.2). To determine the optimal method of reprocessing individual endoscopes, referencing their IFUs and FDA labeling, as well as multi-society guidelines [13] is necessary.

Precleaning

Precleaning refers to the initial step in removing bioburden from endoscopes immediately after use, before they have a chance to dry. To minimize delay, precleaning should occur at the bedside while still in the patient care area. Following use, GI endoscopes harbor 10^6 to 10^{10} CFU/mL of bioburden, with the highest levels in the suction/biopsy channel [18–21]. Precleaning is estimated to reduce this by ~10 [3]. The exterior is wiped clear of all visible bioburden with a clean cloth/napkin soaked in detergent solution, and the detergent solution should be flushed or aspirated through the air/water and suction/biopsy channels until visibly clear. Following precleaning, endoscopes are expeditiously transported to reprocessing areas in a carrying case to limit exposure to other patients, staff, and visitors.

Manual Cleaning

On arrival to the reprocessing area, detachable components (e.g., suction valves, biopsy cap) should be removed, and the endoscope should undergo pressure/leak testing as outlined by manufacturer's instructions to screen for endoscope

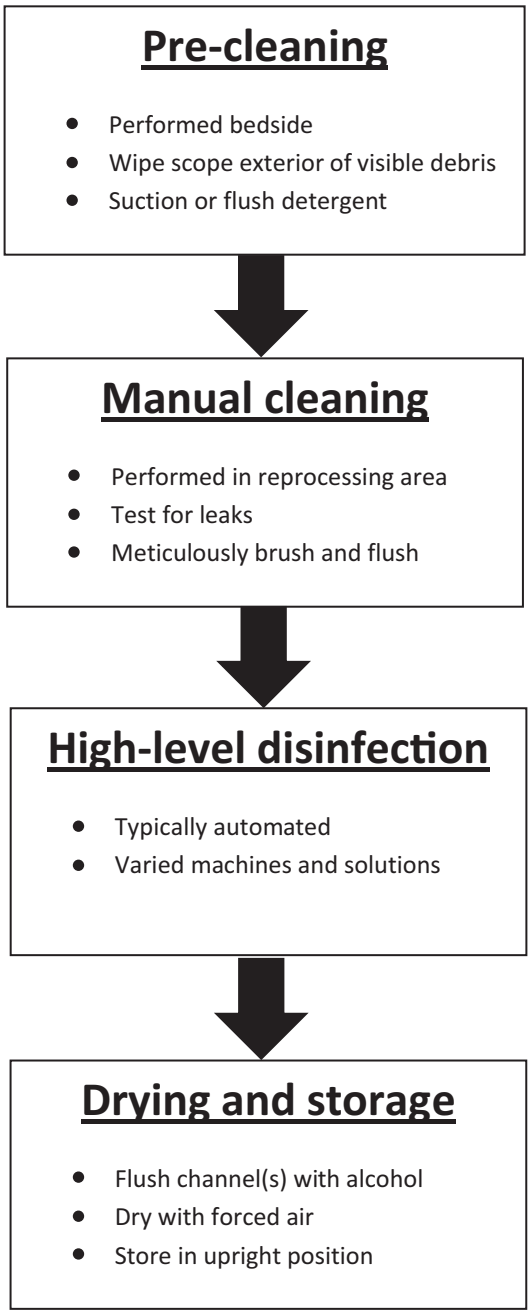

Fig. 50.1 Flowchart of main reprocessing stages

defects that may risk liquid contamination and damage to contained interior portions of the endoscope. After passing pressure/leak testing, the endoscope undergoes meticulous manual cleaning using a detergent solution approved by the manufacturer in combination with mechanical friction (e.g., brushing and scrubbing) and flushing by hand or attached pump. During cleaning the endoscope should be completely immersed in detergent solution, as any areas not in contact with detergent will not be cleaned. Endoscope channels and elevator mechanisms, if present, should be brushed and flushed using only manufacturer-approved cleaning accessories. Upon completion, the endoscope should be thoroughly rinsed with clean water, and detergent solutions should be discarded and replaced for each subsequent endoscope. Any reusable accessories that break the mucosal barrier and are not designed for single use should be similarly cleaned, but must then be sterilized, given their qualification as critical devices.

Cleaning results in a significant (4–6 log) reduction in microbial contamination when performed thoroughly and is necessary to prevent bioburden interference with subsequent HLD [3]. Investigators have found that HLD and even ethylene oxide (EtO) sterilization are impaired without adequate prior cleaning [22]. Unfortunately, manual cleaning remains the most prone to human error, likely due to the number of steps involved, challenging design of endoscopes, increasing pressures of endoscopy practices, and the repetitive nature of the task [15].

High-Level Disinfection

HLD destroys all remaining microorganisms with the exception of some bacterial spores, yielding an additional 10^6 reduction in bioburden. Like manual cleaning, HLD necessitates immersion of the endoscope in the liquid chemical germicide and perfusion of all endoscope channels. Disinfectant type, temperature, and exposure periods should follow manufacturer and FDA specifications. After HLD, the endoscope is rinsed and its channels flushed with sterile or filtered water to remove all disinfectant. Failure to properly rinse colonoscopes of disinfectant has been reported to result in a chemical colitis [23]. The introduction of AERs enhances HLD by automating and standardizing key steps, reducing the impact of human error and exposure of personnel to disinfectants. Nonetheless, it should be recognized that AERs are not immune to failure and may also lead to persistent endoscope contamination [24]. Specifically, AERs require regular maintenance along with routine testing of the disinfectant to ensure minimum effective concentrations (as with manual HLD).

Drying and Storage

Following HLD, endoscope channels should be flushed with isopropyl alcohol (70%–90%), which facilitates subsequent drying with forced air. This can be performed manually but is most often a terminal function during the AER sequence. The alcohol flush followed by purging with forced air has been shown to reduce contamination from waterborne microorganisms, which can proliferate during storage, putting subsequent day procedures at risk [3]. Endoscopes should then be

Fig. 50.2 Pictorial of endoscope reprocessing stages. After patient use, the endoscope should be precleaned at the bedside by wiping the endoscope exterior of visible debris (**a**) and flushing or aspirating detergent solution through the air/water and suction/biopsy channels until visibly clear (**b**). This is followed by manual washing in the reprocessing area, which includes pressure/leak testing and comprehensive cleaning with brushing of internal (**c**) and external (**d**) components. This is followed by high-level disinfection performed either manually or, more commonly, by an automated endoscope reprocessor (**e**). After HLD and alcohol flush of the suction/biopsy channel, the endoscope is dried with filtered forced air (**f**) before hanging vertically in an aerated storage cabinet

inspected once more for any remaining visible residue before being hung vertically (scope handle up and tip down) in an aerated storage cabinet to reduce the risk of contamination [25]. The maximum interval during which the endoscope can be safely reused without reprocessing is unknown. Endoscope reuse appears to be safe up to 21 days or even longer, but some organizations recommend reuse sooner [26].

Practical considerations

- The main stages of endoscope reprocessing are precleaning, manual cleaning, HLD, drying, and storage.
- Precleaning entails removal of debris from the endoscope immediately after use by wiping the endoscope exterior and suctioning detergent through the channel.
- Manual cleaning involves a more comprehensive cleaning process, beginning with pressure/leak testing and followed by repeated scrubbing of exterior and interior components and rinsing. Assiduous manual cleaning is crucial, as high level of residual bioburden may interfere with subsequent HLD.
- HLD is typically performed using an automated reprocessor that allows for immersion of the endoscope and perfusion of its channels with liquid chemical germicide.
- Endoscopes should be thoroughly dried after reprocessing and before being hung vertically for storage.

Interim Considerations for Duodenoscopes

Given the challenges associated with duodenoscope reprocessing, endoscope redesign and/or updated reprocessing techniques are likely forthcoming. Meanwhile, the FDA has strongly encouraged, but not mandated, adoption of one or more supplemental measures to enhance the safety of duodenoscope reprocessing [14]. The options include 1. sterilization following HLD, using EtO, 2. performance of periodic duodenoscope surveillance cultures, 3. employing dual cycles of manual cleaning and HLD between each use, and 4. use of a liquid chemical sterilant.

Sterilization options for endoscopes are limited by the presence of heat-labile components, necessitating low temperature modalities. EtO sterilization is effective but has several limitations, including requisite prolonged treatment cycles (18–41 h) resulting in significant endoscope downtime and need to bolster endoscope inventory, higher cost, and concerns regarding potential health risks to reprocessing personnel, necessitating strict regulation and monitoring [27]. Some large academic hospitals have successfully converted to EtO sterilization of duodenoscopes [28], and guidance from duodenoscope manufacturers has been made available [29, 30]. However, EtO is not readily feasible for the majority of endoscopy centers. Moreover, the long-term impact of repeated EtO sterilization cycles on duodenoscope functional and optics remains to be seen.

Bacterial surveillance cultures following HLD appear to be a logical approach to identifying duodenoscopes with residual contamination. Periodic surveillance cultures have indeed been recommended for the monitoring of all endoscopes by international organizations [31–34]. However, culturing is time-consuming, challenging to perform well, and difficult to interpret, with frequent recovery of non-enteric organisms in variable quantities [28, 35, 36]. Although the CDC has proposed use of the duodenoscope sampling and culturing protocol that is employed in outbreak investigations, this has not been validated for surveillance purposes [37]. For this and other reasons, cultures may not be accepted by in-hospital microbiology laboratories, requiring use of an external reference laboratory. Standard culture results are not available for at least 24–48 h, long after endoscope use in another patient. Some centers have reported successful incorporation of a culture-quarantine protocol wherein duodenoscopes are only released for subsequent use after confirmation of negative culture results [28]. However, this strategy required nearly tripling the endoscope inventory and may be further cost prohibitive.

Based on the success of the culture-quarantine protocol, wherein persistent contamination was reduced by 90%, subjecting each duodenoscope to an additional cycle of manual cleaning and HLD has been proposed, anticipating that routine further reprocessing will clear potential residual microbial contamination. Two studies revealed this strategy results in an additional log reduction of contaminated endoscopes, but does not eliminate the risk of contamination entirely [28, 36]. Hence, repeated reprocessing does not appear to be a definitive solution, but is perhaps the most immediately feasible option for most endoscopy centers.

The FDA has also suggested automated endoscope reprocessing using a liquid chemical sterilant, such as peracetic acid. However, given the failure of existing liquid chemical germicides to sufficiently contact easily inactivated organisms in all recesses of duodenoscopes, it is hard to anticipate that alternate liquid-based approaches will completely suffice.

Ultimately, alternate designs for the functional region of the duodenoscope elevator and endoscope tip will be required to overcome the cleaning and disinfection challenge they represent. Some already available designs incorporate removable tip covers to enhance exposure and access for cleaning. Other designs that are available and soon to be released employ single-use elevators and/or actuating cables.

Practical considerations

- Duodenoscopes will likely require alternate designs to address current cleaning and disinfection challenges.
- Until a definitive solution is identified, the FDA has encouraged adoption of one or more supplemental strategies to enhance duodenoscope reprocessing.
- Strategies include EtO gas sterilization following HLD, bacterial surveillance cultures, dual cycles of manual cleaning and HLD between each use, and use of a liquid chemical sterilant during automated endoscope reprocessing.

Quality Assurance

Periodic surveillance of endoscope reprocessing may help reduce human error and reinforce adherence with guidelines. An ideal test would be relatively easy to perform with rapid and reliable results. Various technologies have been investigated for this purpose, but the lack of benchmarks and validated methods has prevented their recommendation for application to endoscopes reprocessing [38].

Performance of microbiologic surveillance cultures, as alluded previously, has been supported by various international organizations [31–34]. The European Society of Gastrointestinal Endoscopy and European Society of Gastroenterology and Endoscopy Nurses and Associates committee recommend culturing at least every 3 months [31]. Twenty mL of sterile saline are flushed through the suction/biopsy channel, followed by standard plating techniques. Implementation of surveillance cultures remains limited by the challenges presented earlier for duodenoscopes.

Various kits have been designed to enable real-time and relatively easy assessment of endoscope channels for the presence of residual bioburden, suggesting inadequate cleaning. Generally, tests involve sampling the endoscope suction/biopsy channel (via water flush) or exterior (via swab) for protein, blood, carbohydrates, or adenosine triphosphate (ATP) [38]. ATP, which is found in all living tissue, including microorganisms, was initially used as an indirect marker of bioburden in food preparation industries and hospitals before its application to endoscope reprocessing [39]. The correlation between these markers and microbial cultures obtained after HLD, however, is poor [40, 41]. Hence their utility may lie in assessing efficacy of intermediary cleaning steps and not in predicting the overall outcome of HLD. Even if they are not incorporated uniformly on every cycle, they may still prove useful for auditing unit processes and staff performance, rather than assessment of the individual endoscope.

Practical considerations

- Endoscope reprocessing provides a narrow margin of safety that is highly prone to human error.
- Quality assurance of endoscope reprocessing practices is encouraged and may include incorporation of bacterial cultures or periodic assessment of residual bioburden using commercially available kits.

Conclusion

Endoscopes are contaminated by significant levels of bioburden during each procedure. Fortunately, when performed properly, endoscope reprocessing appears to render the risk of pathogen transmission very low. However, recent reports of duodenoscope-related infections have identified opportunities for improvements in endoscope design and reprocessing technology, meanwhile serving as reminders of the need for strict adherence to multi-society, FDA, CDC, and manufacturer recommendations as well as routine competency testing.

Final words

- Endoscope reprocessing allows a narrow margin of safety, necessitating careful understanding, and execution of endoscope manufacturer instructions and multi-society guidelines.
- Existing data and broad experience suggest overwhelming safety of endoscope reprocessing when protocol is followed.
- Recent reports of duodenoscope-related infections likely necessitate duodenoscope redesign, meanwhile underscoring the importance of adherence to currently available protocols and adoption of strategies to enhance reprocessing.

References

1. Petersen BT, Chennat J, Cohen J, et al. Multisociety guideline on reprocessing flexible gastrointestinal endoscopes: 2011. Gastrointest Endosc. 2011;73:1075–84.
2. Dirlam Langlay AM, Ofstead CL, Mueller NJ, et al. Reported gastrointestinal endoscope reprocessing lapses: the tip of the iceberg. Am J Infect Control. 2013;41:1188–94.
3. Rutala WA, Weber DJ. Guideline for disinfection and sterilization in healthcare facilities, 2008. Washington, DC: Department of Health and Human Services, Centers for Disease Control (U.S.); 2008.
4. Spaulding EH. Chemical disinfection of medical and surgical materials. Disinfection, sterilization, and preservation. Philadelphia: Lea & Febiger; 1968. p. 517–31.

5. Nelson DB. Infectious disease complications of GI endoscopy: part II, exogenous infections. Gastrointest Endosc. 2003;57:695–711.
6. Endo reprocessing lapses at the VA. OR Manager 2009;25:19–21.
7. Holodniy M, Oda G, Schirmer PL, et al. Results from a large-scale epidemiologic look-back investigation of improperly reprocessed endoscopy equipment. Infect Control Hosp Epidemiol. 2012;33:649–56.
8. Epstein L, Hunter JC, Arwady MA, et al. New Delhi metallo-beta-lactamase-producing carbapenem-resistant Escherichia coli associated with exposure to duodenoscopes. JAMA. 2014;312:1447–55.
9. United States Senate Health, Education, Labor, and Pensions Committee Minority Staff Report. Preventable tragedies: superbugs and how ineffective monitoring of medical device safety fails patients. http://www.help.senate.gov/imo/media/doc/Duodenoscope%20Investigation%20FINAL%20Report.pdf. Accessed 10 Oct 2016.
10. Petersen BT. Duodenoscope reprocessing: risk and options coming into view. Gastrointest Endosc. 2015;82:484–7.
11. Food and Drug Administration. Medical device reporting (MDR). http://www.fda.gov/medicaldevices/safety/reportaproblem/default.htm. Accessed 10 Oct 2016.
12. Guidelines for cleaning and disinfection of flexible fiberoptic endoscopes (FFE) used in GI endoscopy. AORN J 1978;28:907–10.
13. Petersen BT, Cohen J. Multi-society guideline on reprocessing flexible gastrointestinal endoscopes–2016. Gastrointest Endosc. 2017;85(2):282–294.
14. US Food and Drug Administration (FDA). Supplemental measures to enhance duodenoscope reprocessing: FDA safety communication. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm454766.htm. Accessed 10 Oct 2016.
15. Ofstead CL, Wetzler HP, Snyder AK, et al. Endoscope reprocessing methods: a prospective study on the impact of human factors and automation. Gastroenterol Nurs. 2010;33:304–11.
16. Moses FM, Lee JS. Current GI endoscope disinfection and QA practices. Dig Dis Sci. 2004;49:1791–7.
17. Schaefer MK, Jhung M, Dahl M, et al. Infection control assessment of ambulatory surgical centers. JAMA. 2010;303:2273–9.
18. Chu NS, Favero M. The microbial flora of the gastrointestinal tract and the cleaning of flexible endoscopes. Gastrointest Endosc Clin N Am. 2000;10:233–44.
19. Chu NS, McAlister D, Antonoplos PA. Natural bioburden levels detected on flexible gastrointestinal endoscopes after clinical use and manual cleaning. Gastrointest Endosc. 1998;48:137–42.
20. Alfa MJ, Sitter DL. In-hospital evaluation of orthophthalaldehyde as a high level disinfectant for flexible endoscopes. J Hosp Infect. 1994;26:15–26.
21. Vesley D, Melson J, Stanley P. Microbial bioburden in endoscope reprocessing and an in-use evaluation of the high-level disinfection capabilities of Cidex PA. Gastroenterol Nurs. 1999;22:63–8.
22. Chaufour X, Deva AK, Vickery K, et al. Evaluation of disinfection and sterilization of reusable angioscopes with the duck hepatitis B model. J Vasc Surg. 1999;30:277–82.
23. Rozen P, Somjen GJ, Baratz M, et al. Endoscope-induced colitis: description, probable cause by glutaraldehyde, and prevention. Gastrointest Endosc. 1994;40:547–53.
24. Alvarado CJ, Stolz SM, Maki DG. Nosocomial infections from contaminated endoscopes: a flawed automated endoscope washer. An investigation using molecular epidemiology. Am J Med. 1991;91:272S–80S.
25. Saliou P, Cholet F, Jezequel J, et al. The use of channel-purge storage for gastrointestinal endoscopes reduces microbial contamination. Infect Control Hosp Epidemiol. 2015;36:1100–2.
26. Brock AS, Steed LL, Freeman J, et al. Endoscope storage time: assessment of microbial colonization up to 21 days after reprocessing. Gastrointest Endosc. 2015;81:1150–4.
27. Petersen BT, Koch J, Ginsberg GG. Infection using ERCP endoscopes. Gastroenterology. 2016;151:46–50.
28. Ross AS, Baliga C, Verma P, et al. A quarantine process for the resolution of duodenoscope-associated transmission of multidrug-resistant Escherichia coli. Gastrointest Endosc. 2015;82:477–83.
29. Olympus. 100% ethylene oxide gas for sterilization of olympus flexible endoscopes in North America. http://medical.olympusamerica.com/sites/us/files/pdf/ETO_Letter.pdf. Accessed 10 Oct 2016.
30. Fujifilm. Operation manual: ED-530XT. https://www.fujifilmusa.com/products/medical/endoscopy/pdf/ED530XT_CDS_202B1259902B_140417_3_0_DT_US2.pdf. Accessed 10 Oct 2016.
31. Beilenhoff U, Neumann CS, Biering H, et al. ESGE/ESGENA guideline for process validation and routine testing for reprocessing endoscopes in washer-disinfectors, according to the European standard prEN ISO 15883 parts 1, 4 and 5. Endoscopy. 2007;39:85–94.
32. Gastroenterological Society of Australia. Infection control in endoscopy. http://membes.gesa.org.au/membes/files/Infection_Control_in_Endoscopy_Guidelines_2014.pdf. Accessed 10 Oct 2016.
33. Leung JW. Reprocessing of flexible endoscopes. J Gastroenterol Hepatol. 2000;15(Suppl):G73–7.
34. Systchenko R, Marchetti B, Canard JN, et al. Guidelines of the French Society of Digestive Endoscopy: recommendations for setting up cleaning and disinfection procedures in gastrointestinal endoscopy. Endoscopy. 2000;32:807–18.
35. Brandabur JJ, Leggett JE, Wang L, et al. Surveillance of guideline practices for duodenoscope and linear echoendoscope reprocessing in a large healthcare system. Gastrointest Endosc. 2016;84(3):392–9.
36. Chapman CG, Siddiqui UD, Manzano M, et al. Risk of infection transmission in curvilinear array echoendoscopes: results of a prospective reprocessing and culture registry. Gastrointest Endosc. 2017;85(2):390–7.e1.
37. Centers for Disease Control and Prevention (CDC). Interim protocol for healthcare facilities regarding surveillance for bacterial contamination of duodenoscopes after reprocessing. https://www.cdc.gov/hai/organisms/cre/cre-duodenoscope-surveillance-protocol.html. Accessed 10 Oct 2016.
38. Komanduri S, Abu Dayyeh BK, Bhat YM, et al. Technologies for monitoring the quality of endoscope reprocessing. Gastrointest Endosc. 2014;80:369–73.
39. Turner DE, Daugherity EK, Altier C, et al. Efficacy and limitations of an ATP-based monitoring system. J Am Assoc Lab Anim Sci (JAALAS). 2010;49:190–5.
40. Hansen D, Benner D, Hilgenhoner M, et al. ATP measurement as method to monitor the quality of reprocessing flexible endoscopes. Ger Med Sci. 2004;2:Doc04.
41. Ofstead CL, Wetzler HP, Doyle EM, et al. Persistent contamination on colonoscopes and gastroscopes detected by biologic cultures and rapid indicators despite reprocessing performed in accordance with guidelines. Am J Infect Control. 2015;43:794–801.

Part III

Training and Evaluation

Teaching and Training in Upper and Lower GI Endoscopy

51

Mohammad Yaghoobi

Introduction

Endoscopy is a valuable diagnostic and therapeutic procedure. Accuracy and safety are important components of performing efficient endoscopy. Endoscopists could be from different backgrounds such as gastroenterology, surgery, medicine, family medicine, or nurse practitioners. Trainees are expected to acquire both cognitive and technical skills in endoscopy. These are accomplished through attending endoscopy courses as well as in-service training. Although performing an endoscopy is probably one of the most crucial parts of practicing gastroenterology, optimal methods to teach endoscopy are not well described. In this chapter, evidence-based data on teaching upper and lower GI endoscopy will be reviewed, and the author's view on methods to improve training skills in endoscopy mentorship will be discussed.

Learning Curve for Endoscopic Training

Both teacher and trainee should understand that learning endoscopy is a smooth process, and there is an expected natural progression from easy techniques such as intubation of the esophagus or performing retroflection in the stomach to advanced techniques such as large polyp removal or hemostasis of actively bleeding esophageal varices. Both trainees and teachers should be familiar with the four stages of competence acquisition including unconscious incompetence, conscious incompetence, conscious competence, and unconscious competence [1]. The last stage is what is known as expert level. A trainee might initially perform only part of a procedure before gaining more experience. The teacher should make sure that the trainee is competent in handling the scope in less advanced procedures before moving forward to more advanced techniques. The variation in skill acquisition between trainees (inter-trainee variation) and for the same trainee for different techniques (intra-trainee variation) is well known. Although a trainee may need less supervision approaching the end of the training, most academic centers in North America still require supervision during the whole procedure at any stage of training [2].

American Society of Gastrointestinal Endoscopy (ASGE) classifies endoscopic procedures to standard and advanced. Standard procedures include esophagogastroduodenoscopy (EGD), flexible sigmoidoscopy, colonoscopy, mucosal biopsy, polypectomy, dilation of peptic stricture of the esophagus, percutaneous liver biopsy, and percutaneous endoscopic gastrostomy (PEG) [2]. According to ASGE, advanced endoscopic procedures include endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasound (EUS), pneumatic dilation for achalasia, dilation of complex esophageal strictures, laparoscopy, esophageal stent placement, photodynamic therapy, laser therapy, as well as endoscopic tumor ablation and require additional training.

Practical Points

- The learning curve of training in endoscopy is varied among trainees.
- Teaching endoscopy should start with simpler tasks and continue with more advanced ones.

Who Should Teach Endoscopy?

An endoscopy teacher should be preferably an expert in this area and have experience in teaching with expertise in giving instruction during the procedure, be competent in evaluating

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trainees, giving feedback and know the current literature related to the field of endoscopy and endoscopic procedures. He or she should be able to recognize unsafe techniques and advocate for patient safety. The teacher should be able to recognize technical deficiencies and take over the procedure if needed. For example, if a trainee in early stages of training encounters a polyp requiring an advanced polypectomy technique during a screening colonoscopy, the teacher should properly intervene and remove the polyp. However, this might be a good opportunity to teach principles of advanced polypectomy while the trainee observes the procedure.

Setting of Teaching Endoscopy

Training gastrointestinal endoscopy should be part of an accredited adult or pediatric gastroenterology or general surgery fellowship program and be supported by other programs including internal medicine, pediatrics, diagnostic imaging, and pathology. The training program should integrate teaching lectures and conferences as well as hands-on training. The lectures should be focused on but are not limited to cognitive aspects of teaching endoscopy including indications and contraindications of the endoscopic procedures, informed consent including alternatives to an endoscopic procedure, principles of pathological examination of biopsies including staining, and classifications of endoscopically diagnosed pathologies such as erosive esophagitis. Learning principles of sedation including indications and contraindications for each medication as well as diagnosis and management of adverse events are also necessary before using these medications or obtaining informed consent. Teaching this topic should be part of the endoscopy training in an appropriate clinical context. Although EGD or colonoscopy can be done with no sedation, studies have shown that patient tolerance is significantly better if intravenous medications are used for sedation [3]. There should also be special emphasis on teaching terminology and standardized reporting of endoscopic findings such as Prague classification in reporting esophageal Barrett's or Paris classification in reporting colonic polyps.

Optimally, an experienced endoscopist and teacher should oversee endoscopic training in the division. Regular assessment of the teachers and trainees should be part of the responsibilities of this person. The same person is also responsible to integrate new technologies into the training program. At the beginning of each rotation and optimally each training session, realistic, specific, measurable, and relevant objectives should be set. Too many objectives are unrealistic and often confusing. The objectives and ground rules should be individualized based on the level of training as well as previous skill acquisition and the preference of both parties while respecting patient's safety. Using a competency framework is encouraged as discussed elsewhere.

Each trainee should keep a logbook recording the type of the procedure and any therapeutic interventions assisted by the trainee. The logbook needs to be reviewed by the program director on a regular basis, and specific action should be taken if the trainee does not meet the required number. However, trainees should be advised that the minimum required number of procedures is only one of the components of competency acquisition and does not equate competency.

Physical setting of the endoscopy room is also an important factor in providing proper environment to teach and assess trainees. The setting should provide reasonable direct view of the monitor and trainee's hands for the teacher. Attempts should be made to reduce distractions. Instruction can be given during or after the end of the procedure, based on the level of training and the complexity of task [4]; however if the safety is a concern, the teacher should stop the procedure and either instruct the trainee to take appropriate and specific action or take over the procedure if the situation is deemed too difficult for the trainee's level of competency. Use of standardized language to instruct the trainees are encouraged to maintain consistency and avoid confusion. Terms that are commonly used by the teachers include but are not limited to terms such as "pullback," "advance," "tip up," "tip down," and "torque clockwise or counterclockwise."

One-to-One Supervision

Direct one-to-one supervision is essential in training endoscopic techniques since it provides reasonable observation, assessment of trainee's competency acquisition and ensures patient's safety. Endoscopy is a dynamic procedure and therefore the whole procedure should be observed to enable the teacher to appropriately assess trainee's technique and safely intervene if required. Many centers are still relying on one-to-one in-service training to train practicing endoscopist. A large UK audit study showed that only 17% of colonoscopists were closely supervised for their first 100 colonoscopies [5]. Several aspects of endoscopy training were explored in a qualitative study [6]. Structured interviews were performed with ten trainees on several aspects of teaching endoscopy. These included level of supervision, feedback, other aids to training, and use of simulators or related courses. The investigators identified major gap in one-to-one supervision. Most trainees felt that the amount of one-to-one supervision they received was inadequate and this produced anxiety. Other aspects that were perceived to need improvement were the use of clear explanations, segmentation of skill training, the provision of feedback and a dedicated training environment with patient and committed teachers.

Another survey in the UK was done in 2004 by sending a semi-structured questionnaire on the quality of endoscopic training to all gastroenterology trainees in three levels in England and Wales [7]. Among 172 responses, 11% felt that they were not adequately trained in colonoscopy and 18% in therapeutic EGD at the end of their 6 years of training. Sixty percent of trainees reported that their supervisors were not in the room during the procedure. Twenty to fifty percent of first and second year trainees were performing procedures with no direct supervision. The supervisor was in the room in only 20% of EGDs and 30% of colonoscopies. The study did not differentiate between direct supervision as compared to simple presence of the mentor in the room. Although similar studies are scarce in North America, most academic centers mandates that the teacher supervises the whole duration of the procedure, when a trainee is performing it.

Practical Points

- Endoscopy should be taught by experts in both endoscopy and teaching.
- Both technical and cognitive aspects of endoscopy should be taught in a training program.
- One-to-one supervision is a key component of teaching endoscopy to ensure reliable assessment and patient safety.

Giving Feedback

A recent guideline defined feedback as "a supportive conversation that clarifies the trainee's awareness of their developing competencies, enhances their self-efficacy for making progress, challenges them to set objectives for improvement, and facilitates their development of strategies to enable that improvement to occur" [4]. Trainees should be encouraged to actively seek feedback during their endoscopy training. Both positive and negative feedbacks are important since trainees need to be made aware of their area of competency as well as areas which need improvement. Teachers should also keep in mind specific objectives set at the beginning of each rotation or session and provide relevant feedback. The feedback session should always be interactive and the trainee should be given a chance to reflect own self-assessment and also provide the teacher with feedback and express what they like to change in future training sessions. It is recommended that the feedback be given as part of a conversation rather than unilateral transfer of information [4]. The teacher should reinforce key points done well, identify key points which could have been done better or were overlooked and always recommend strategies for improvement and increasing self-awareness. The trainee should consider the feedback credible and well informed in order for it to be influential. The teacher must indicate the importance of each specific feedback and inform the trainee if an essential requirement for trainee's specific level of training is missing.

It is important to understand that the approach to give feedback is not one size fits all and should be individualized based on each trainee's personality and level of training, and teachers should not assume that one approach is ideal for every trainee. Each negative feedback should be accompanied by suggesting methods for improvement. Emotional impact and distress caused by feedback should not be underestimated [4]. Figure 51.1 depicts the feedback processes and outcomes according to the abovementioned guideline [4].

Practical Points

- Feedbacks should be specific, individualized, credible, and interactive.
- Both strengths and areas for improvement should be discussed.

Use of Nonhuman Subjects in Teaching Endoscopy

There are several reasons why nonhuman subjects are essential in learning endoscopy. Involving trainees in an academic endoscopy setting requires time, energy, patience, and financial sacrifice. A US study showed that involving trainees added 10–37% to the endoscopy time and ended in loosing half a procedure per hour [8]. The estimated financial loss was 500,000–1,000,000 US dollars per year based on a model of 1000 procedures per year. In addition patients' satisfaction and ethical issues are potentially important components of involving trainee endoscopists in procedures. Therefore, using alternative learning devices are important in achieving certain level of competency before hands-on training. On the other hand, most upper and lower GI endoscopies are performed under moderate sedation, and it would be ethically incorrect to compromise patient's comfort and safety by giving higher dose of sedatives for the purpose of training. Another safety issue is the lack of any direct control from the teacher on the scope since the instrument is solely controlled by the trainee, although the verbal guidance could be provided.

The use of nonhuman subjects includes using animal or mechanical models to teach endoscopy before a trainee introduces the scope to a patient. These models have been

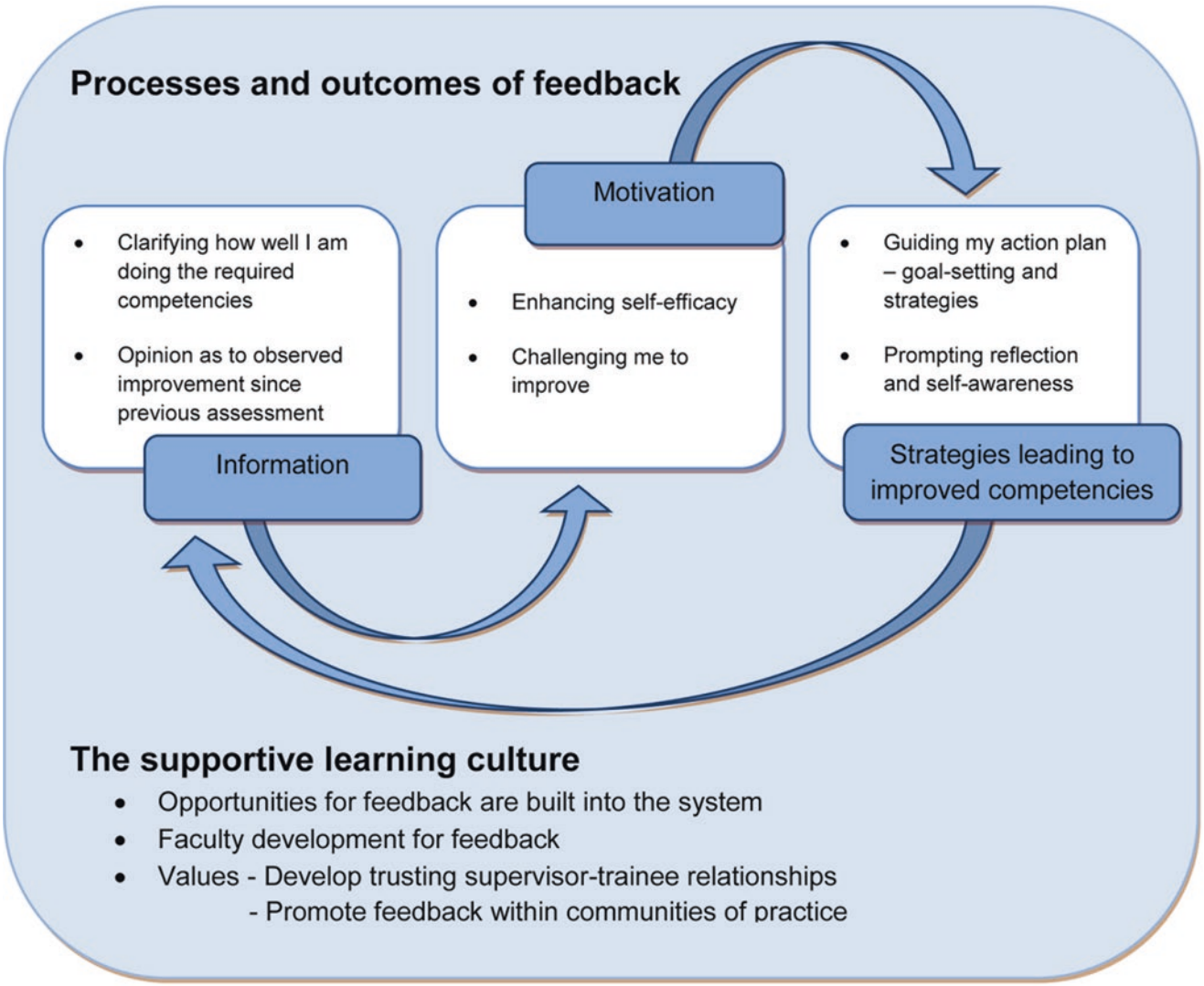

Fig. 51.1 Feedback processes and outcomes – what the trainee wants from the feedback relationship (4- OPEN SOURCE)

used for decades to teach endoscopy. Some historical examples include the use of animal stomach to teach EGD and plastic tubes such as vacuum cleaner tubes to simulate colonoscopy [9].

Simulators are better means of training in endoscopy since several variables could be set. However, like any other tool, reliability and validity of a simulator should be assessed before using it for the teaching purposes. Reliability is defined as the reproducibility of the test or testing device, and validity is the degree that the simulator actually teaches what it is intended to teach [10]. Criterion validity measures the results of a new simulator as compared with those of the existing ones. There are two types of criterion validity: the extent to which the simulator correlates with the "gold standard" and the extent to which the simulator predicts future performance. Construct validity measures the ability of the simulator to distinguish the experienced from the inexperienced surgeon. For competency assessment, performance on a simulator should predict an individual's performance in real life.

Erlangen Active Simulator for Interventional Endoscopy (EASIE) is a pig-based simulator which was introduced in 1997 [11]. In two different studies, EASIE was evaluated in teaching endoscopists and endoscopy teachers. In one study, four tutors who had experience with EASIE trained seven endoscopists with no previous experience with EASIE on endoscopic hemostasis in a 2-day workshop, and the skills were compared before and after intervention [12]. The study showed significant improvement in acquired skill after the workshop.

A 6-h workshop for senior endoscopists with no prior EASIE teaching on how to set up equipment and teach trainees provided the same competence as of the more experienced teachers [12]. Although this study was small and used historical control, it may indicate that a short workshop

could provide reasonable competency in teaching endoscopic techniques using simulators.

In another study with compactEASIE, a lightweight modified version of the original EASIE, 27 GI fellows were randomized into two groups comparable with regard to baseline skills. One group only received clinical training in endoscopic hemostatic techniques at their hospitals. The second group were additionally trained by experienced tutors in 3 full-day hemostasis workshops over 7 months. Both groups underwent a blind final evaluation on the EASIE simulator. All techniques were significantly more improved in the second group as compared to the first group. Combination of compactEASIE simulator training and clinical endoscopic training resulted in objective improvement in the performance [13].

Although there is no direct evidence that playing 3-D games improve endoscopic skills, there is some evidence that playing Wii or PlayStation might improve laparoscopic techniques. A randomized noncontrolled study comparing similar groups of 42 surgeons, residents, and medical students showed that 30 min practicing with Wii™ or PlayStation2® improved some aspects of the laparoscopic bead transfer techniques [14]. This study did not include a control group with no intervention, and therefore it is hard to exclude natural learning curve in learning laparoscopic techniques as the reason for the improvement.

A Cochrane review synthesized 13 studies to investigate the role of virtual reality simulation training in supplementing or even replacing early conventional upper and lower endoscopy training for trainees with limited or no prior endoscopic experience [15]. This study showed some advantage by simulation-based training over other methods in aspects such as composite score of competency, independent procedure completion rate, performance time, independent insertion depth, overall rating of performance, competency error rate, and mucosal visualization. However, most of the included trials suffered from poor methodology, and the overall quality of the evidence was poor. The authors concluded that the simulation-based training could be used to effectively supplement early conventional endoscopy training for trainees with limited or no prior endoscopic experience. However, there remains insufficient evidence to advise for or against the use of simulation-based training as a replacement for early conventional endoscopy in these trainees.

Using Other Technologies

Using magnetic endoscopic imaging provides real-time three-dimensional view of the scope and is a useful tool in training and is proved to increase cecal intubation rate, decreasing number of attempts to straighten the scope and reducing the duration of looping especially when trainees are involved in the procedure [16–18]. A systematic review and meta-analysis of eight RCTs showed the technique to be safe and beneficial in training inexperienced endoscopists, as well as improving the cecal intubation rate (OR = 1.92,95%CI: 1.13–3.27) for both experienced and inexperienced endoscopists [19]. The author believes that this technology should be used whenever available to improve teaching and potentially improve safety profile of the procedure.

Computer technology is relatively underutilized in teaching endoscopy as compared to other areas of science. A German study randomized 200 medical students and residents rotating through gastroenterology service to receive a tablet with full multimedia support and internet service in and off the campus or regular access to in-campus library and databases. Those with access to tablet showed a significantly better performance in the gastrointestinal endoscopy self-assessment program (GESAP®) exam, while the baseline performance was similar between two groups [20].

Assessment of the competence is another area where computer-based technology could be useful. A recent Danish study assessed the role of a 3-D motion sensor in evaluating endoscopic skills [21]. Thirty seven endoscopists in three levels of expertise were included in the study and were asked to perform EGD using a simulator. By using the Microsoft® Kinect motion sensor, which was originally designed for the Xbox gaming platform, the movements of the operators were tracked. The machine was able to accurately predict the level of training by calculating the distance between two hands, the height of the scope hand and the distance moved by the scope hand. The results of this study are interesting but most of the differences were observed between medical students with no experience and experts (advanced endoscopists) while most of the GI trainees fit in the intermediate category (less experienced gastroenterologists) and therefore generalizing the results should be done with caution.

Practical Points

- Using nonhuman subjects to teach endoscopy is important before hands-on training from ethical and efficiency perspectives.
- There is moderate evidence supporting the role of simulation-based training to supplement conventional training.
- Computer-based technology in teaching endoscopy is underdeveloped but might eventually have a role in improving it.

Table 51.1 Checklist items reaching consensus for inclusion in the GiECAT (Adopted with permission from Walsh et al. [37])

Checklist item		Competency domains	Round 5, mean (SD) (max score = 5)	Round 5, consensus level (% rating item ≥ 4)
Before procedure				
1	Reviews relevant patient information (health records, relevant investigations) and obtains history as appropriate (indications, contraindications, medical history, medications, allergies)	Cognitive and integrative	4.56 (0.60)	94.60%
2	Takes action in response to patient history and investigations where appropriate (e.g., prophylactic antibiotics, anesthetic risk factors)	Integrative	4.56 (0.65)	91.90%
3	Demonstrates a sound knowledge of the indications and contraindications to colonoscopy, its benefits and risks, potential alternative investigations and/or therapies, and an awareness of the sequelae of endoscopic or non-endoscopic management	Cognitive	4.67 (0.53)	97.30%
4	Explains to the patient and/or caregivers the perioperative process and procedure (likely outcome, time to recovery, benefits, potential risks/adverse events, and rates), checks for understanding and addresses concerns and questions	Integrative	4.59 (0.55)	97.30%
Procedure, technical				
5	Recognizes loop formation and avoids or reduces appropriately during the procedure (by using pullback, torque, external pressure, patient position change)	Technical	4.70 (0.46)	100.00%
6	Uses rotation and/or torque appropriately	Technical	4.38 (0.72)	91.90%
7	Uses withdrawal (as an advancement strategy) appropriately	Technical	4.39 (0.68)	94.60%
8	Uses abdominal pressure and changes in patient position appropriately to aid endoscope advancement	Technical	4.35 (0.63)	91.90%
9	Advances to cecum (in an appropriate time)	Technical	4.49 (0.61)	94.60%
10	Withdraws from cecum/terminal ileum to rectum in an appropriate time (>6 min)	Technical	4.32 (0.85)	89.20%
11	Withdraws endoscope in a controlled manner	Technical	4.59 (0.64)	91.90%
12	Performs therapeutic maneuvers (biopsy and/or polypectomy) independently, appropriately, and safely	Technical	4.68 (0.67)	94.60%
Procedure, cognitive				
13	Demonstrates recognition of anatomical landmarks (rectum, flexures, ileocecal valve, appendiceal orifice, etc.) and/or incomplete examination	Cognitive	4.73 (0.67)	97.30%
14	Demonstrates recognition of pathologic and anatomic abnormalities	Cognitive	4.86 (0.35)	100.00%
15	Describes findings accurately, interprets abnormalities in the context of the patient, and selects the appropriate strategy/technique to deal with them	Integrative	4.73 (0.45)	100.00%

(continued)

Table 51.1 (continued)

Checklist item		Competency domains	Round 5, mean (SD) (max score = 5)	Round 5, consensus level (% rating item ≥ 4)
Procedure, nontechnical aspects				
16	Administers sedation appropriately (type, dose), monitors the patient's vital signs and comfort level throughout the procedure, and responds appropriately and/or demonstrates appropriate interaction with the anesthetist to ensure appropriate sedation and monitoring throughout the procedure	Cognitive and integrative	4.54 (0.65)	91.90%
17	Demonstrates appropriate interaction and communication with the procedure nurses and/or assistants throughout the procedure	Integrative	4.35 (0.63)	91.90%
After procedure				
18	Educates the patient and/or caregiver about the colonoscopic findings (explanation, significance) and follow-up plan and provides advice regarding potential postprocedure adverse events, recommended course of action, etc.	Integrative	4.46 (0.69)	94.60%
19	Appropriate and timely documentation of procedure (written/dictated/electronic medical records)	Integrative	4.57 (0.55)	97.30%

GiECAT, gastrointestinal endoscopy competency assessment tool

Competence in Performing Endoscopy

American College of Gastroenterology (ACG) and American Society of Gastrointestinal Endoscopy (ASGE) requires the following requirements (direct quote) in order to acquire competency in gastrointestinal endoscopy [22]:

- Ability to integrate GI endoscopy into the overall clinical evaluation of the patient
- Sound general medical or surgical training
- A thorough understanding of the indications, contraindications, individual risk factors, and benefit-risk considerations for the individual patient
- Ability to clearly describe an endoscopic procedure and obtain informed consent
- Knowledge of endoscopic anatomy; technical features of endoscopic equipment; accessory endoscopic techniques, including biopsy, cytology, and photography; and thermal and nonthermal endoscopic therapy
- Ability to accurately identify and interpret endoscopic findings
- A thorough understanding of the principles, pharmacology, and risks of conscious sedation
- Ability to document endoscopic findings and therapy, and communicate with referring physicians and integrate endoscopic findings in patient care

Assessment of Competency

Assessment of competency is necessary before an endoscopist could be certified to perform procedures independently. Ongoing assessment of trainee's competence is also an essential part of the training process which necessitates specific expertise and should be formally integrated into the training program.

Several tools have been developed in order to assess the performance of an endoscopy trainee. These include the Direct Observation of Procedural Skills (DOPS) tool, the Global Assessment of Gastrointestinal Endoscopy Skills (GAGES) by surgical endoscopists, and finally the Mayo Colonoscopy Skills Assessment Tool (MCSAT), along with its derivative, the Assessment of Competency in Endoscopy (ACE) tool reported by the ASGE [23–26]. DOPS and CAGS mainly focus on motor skills and do not assess cognitive competence, while MCSAT and ACE measures both motor and cognitive skills in performing quality endoscopy. Both have been validated in studies [27, 28].

Gastrointestinal Endoscopy Assessment Tool (GiECAT) is a new assessment tool, developed by a panel of 55 expert endoscopists using a Delphi methodology, which measures both technical and cognitive skills in endoscopy. GiECAT consists of 7 global ratings and 19 checklist items measuring technical (psychomotor), cognitive (application of knowledge

Table 51.2 Table 51.3. Global rating items reaching consensus for inclusion in the *GiECAT* (Adopted with permission from Walsh et al. [37]).

Global rating item		Definition	Competency domain(s)	Round 5, mean (SD) (max score = 5)	Round 5, consensus level (% rating item ≥ 4)
1	Technical skill	Demonstrates an ability to manipulate the endoscope by using angulation control knobs, advancement/withdrawal, and torque steering for smooth navigation	Technical	4.67 (0.47)	100.0%
2	Strategies for endoscope advancement	Demonstrates an ability to use insufflation, pullback, suction, loop reduction, external pressure, and patient position change to advance the endoscope independently, expediently, and safely	Technical	4.76 (0.43)	100.0%
3	Visualization of mucosa	Demonstrates an ability to maintain a clear luminal view required for safe endoscope navigation and complete mucosal evaluation	Technical	4.70 (0.46)	100.0%
4	Independent procedure completion (need for assistance)	Demonstrates an ability to complete the procedure expediently and safely without verbal and/or manual guidance	Technical	4.54 (0.55)	97.3%
5	Knowledge of procedure	Demonstrates general procedural knowledge including procedural sequence, endoscopy techniques, equipment maintenance and troubleshooting, indications and contraindications, and potential adverse events	Cognitive	4.65 (0.58)	94.6%
6	Interpretation and management of findings	Demonstrates an ability to accurately identify, interpret, and appropriately manage pathology and/or adverse events	Integrative	4.78 (0.48)	97.3%
7	Patient safety	Demonstrates an ability to perform the procedure in a manner that minimizes patient risk (atraumatic technique, minimal force, minimal redout, recognition of personal and procedural limitations, safe sedation practices)	Technical and integrative	4.84 (0.37)	100.0%

GiECAT, gastrointestinal endoscopy competency assessment tool

and interpretation of findings), and integrative (higher level of competency including safety and communication) components of competency in performing endoscopic procedures. Tables 51.1 and 51.2 present these items. The validity and reliability of this tool was consequently shown in another study by the same group [28].

The number of procedures required to acquire competency in each procedure depends on the type of the procedure and the learning capability of the trainee. Studies have suggested that at least 130 EGDs, 25–30 flexible sigmoidoscopies and 140 colonoscopies should be done before competency is achieved [29, 30]. Table 51.3 presents ASGE suggestions for objective criteria in evaluating technical skills in endoscopy. One should consider that this is the minimum requirement for general competency and specific procedures such as hemostasis in the setting of active bleeding require further training. In addition, the learning curve is varied among trainees, and educators should not solely rely on absolute numbers of the procedures done by a trainee in order to measure clinical and technical competency. Therefore, other methods of assessing competency and criteria for measuring quality of practice should be integrated in training programs. A recent systematic review of 18 studies on learning curves for colonoscopy in GI or surgical trainees included 37,700 colonoscopies performed by 247 trainees [31]. Although the study suffered from major heterogeneity among included studies due to variation in subjects and assessment tools, it showed that the number of colonoscopies required to achieve competency might be more than what was previously thought. Interestingly, in only four included studies defined, competence of more than 90% cecal intubation rate was achieved after performing more than 140 colonoscopies. In most other studies, this was achieved after more than 200 or even 300 colonoscopies. In one study, which used both the motor and cognitive compo-

Table 51.3 Suggested objective performance criteria by ASGE (modified) for the evaluation of technical skills in upper and lower gastrointestinal endoscopy [2]

EGD
Esophageal intubation
Pyloric intubation
Colonoscopy
Intubation of splenic flexure
Intubation of cecum
Intubation of terminal ileum
Flexible sigmoidoscopy
Visualization splenic flexure
Retroflexion
All procedures
Accurate recognition of normal and abnormal findings
Development of appropriate endoscopic/medical treatment in response to endoscopic findings
Others
Polypectomy
Esophageal dilation
Hemostasis successful performance
PEG
Pneumatic dilation

nents of MCSAT to establish competency and competency thresholds, trainees scoring average were subsequently able to surpass the minimal competency criteria for the MCSAT by 275 colonoscopies [26]. Furthermore, it was not until approximately 400 colonoscopies that competency was achieved across all trainees.

Therefore, it is not surprising to see such disparity between different specialties on recommended number of procedures before assessing competency, with ASGE recommending 200 colonoscopies in contrast to the American Board of Surgery and the American Academy of Family Physicians recommending only 50 colonoscopies [32, 33].

Training programs should be able to provide the number of procedures required to achieve competency. ASGE suggests 95–100% technical success rate for an expert endoscopist and 80–90% for new endoscopist to achieve competency [34].

Practical Points

- Programs should use one of the validated tools to assess competency of the trainees.
- The minimum number of performed procedures should be one of the criteria and not the only one to assess competency.

Programs should ensure implementing an appropriate and documented assessment mechanism by teachers. Specific attention should be paid to make sure that the assessment is only provided for the procedures performed by the trainee. Most evaluation forms include several items, and a teacher might not remember if he or she has supervised the trainee performing a specific technique such as injection or hemoclip application for hemostasis. This may provide inaccurate assessment of the trainee's competency and cause inconsistency. An Australian study on similar subject compared the evaluation forms filled by consultants and registrars with logbook prepared by the trainees on performing surgical procedures. In this study, only 39 out of 197 teachers assessed only those surgical procedures directly observed [35]. Although no similar study was found for endoscopic procedures, the results might perhaps be more dramatic since direct supervision is perceived more necessary in surgical procedures, which are deemed riskier, than in endoscopic procedures.

The need for retraining should also be emphasized since new procedures or techniques are often introduced and an endoscopist cannot extend previously acquired competency to a new technique.

Quality Assessment

Adenoma detection rate (ADR) is an important quality indicator in colonoscopy. A recent German study retrospectively looked at the colonoscopies performed by gastroenterology trainees and showed a polyp detection rate of 43%, and an adenoma detection rate was 23% which did not significantly change from the beginning to the end of training [36]. Each trainee had to be competent in EGD by performing a mean of 401 ± 193 EGDs and to observe average of 8.5 ± 5.1 didactic sessions on colonoscopy prior to hands-on training in colonoscopy. The first 50 colonoscopies were directly supervised, and an experienced endoscopist was available to take over in difficult cases or advanced procedures such as polypectomy. However, the retrospective nature of the study as well as the lack of reference standard for adenoma detection in this study makes it impossible to find the real number of adenoma in this population. Also, it is hard to explain similar ADR in this study at the beginning of the training as compared to the end of it. Objectives are set up by ASGE for other endoscopic procedures as well. Table 51.1 presents these objective performance criteria. Assessment of these criteria should be part of the competency assessment in each program and relevance feedback should be given based on trainee's performance.

Conclusions

Teaching upper and lower gastrointestinal endoscopy requires proper qualifications and competency in both technical and educational aspects as well as a proper physical setting in an accredited program. Teaching should cover both cognitive and technical aspects of endoscopy. Appropriate

use of nonhuman models and other technologies is recommended before transition to hands-on training. Moreover, direct one-to-one supervision is the key to train qualified endoscopist. Regular objective assessment of trainee's performance using one of the validated assessment tools and providing specific feedbacks ensures competency and patient's safety before independent practice.

References

1. Flower J. In the mush. Physician Exec. 1999 Jan–Feb;25(1):64–6.
2. Principles of training in gastrointestinal endoscopy. From the ASGE. American Society for Gastrointestinal Endoscopy. Gastrointest Endosc. 1999 Jun;49(6):845–53.
3. Froehlich F, Schwizer W, Thorens J, et al. Conscious sedation for gastroscopy: patient tolerance and cardiorespiratory parameters. Gastroenterology. 1995;108:697–704.
4. Lefroy J, Watling C, Teunissen PW, Brand P. Guidelines: the do's, don'ts and don't knows of feedback for clinical education. Perspect Med Educ. 2015 Dec;4(6):284–99.
5. Bowles CJ, Leicester R, Romaya C, Swarbrick E, Williams CB, Epstein O. A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? Gut. 2004 Feb;53(2):277–83.
6. Thuraisingam AI, MacDonald J, Shaw IS. Insights into endoscopy training: a qualitative study of learning experience. Med Teach. 2006 Aug;28(5):453–9.
7. Wells CW, Inglis S, Barton R. Trainees in gastroenterology views on teaching in clinical gastroenterology and endoscopy. Med Teach. 2009 Feb;31(2):138–44.
8. McCashland T, Brand R, Lyden E, de Garmo P. The time and financial impact of training fellows in endoscopy. CORI research project. Clinical outcomes research initiative. Am J Gastroenterol. 2000 Nov;95(11):3129–32.
9. Griffiths DA. Use of 3-d models in medical education. Med Teach. 1979;1(2):76–81.
10. McDougall EM. Validation of surgical simulators. J Endourol. 2007 Mar;21(3):244–7.
11. Hochberger J, Neumann M, Hohenberger W, et al. Neuer Endoskopie- Teacher fu¨ r die therapeutische flexible Endoskopie [German]. Z Gastro- enterol. 1997;35:722–3.
12. Matthes K, Cohen J, Kochman ML, Cerulli MA, Vora KC, Hochberger J. Efficacy and costs of a one-day hands-on EASIE endoscopy simulator train-the-trainer workshop. Gastrointest Endosc. 2005 Dec;62(6):921–7.
13. Hochberger J, Matthes K, Maiss J, et al. Training with the compact EASIE biologic endoscopy simulator significantly improves hemostatic technical skill of gastroenterology fellows: a randomized controlled comparison with clinical endoscopy training alone. Gastrointest Endosc. 2005;61:204–15.
14. Ju R, Chang PL, Buckley AP, Wang KC. Comparison of Nintendo Wii and PlayStation2 for enhancing laparoscopic skills. JSLS. 2012 Oct–Dec;16(4):612–8.
15. Walsh CM, Sherlock ME, Ling SC, Carnahan H. Virtual reality simulation training for health professions trainees in gastrointestinal endoscopy. Cochrane Database Syst Rev. 2012 Jun 13;6:CD008237.
16. Hoff G, Bretthauer M, Dahler S, Huppertz-Hauss G, Sauar J, Paulsen J, Seip B, Moritz V. Improvement in caecal intubation rate and pain reduction by using 3-dimensional magnetic imaging for unsedated colonoscopy: a randomized trial of patients referred for colonoscopy. Scand J Gastroenterol. 2007;42:885–9.
17. Sathyanarayana S, Schär M, Kraitchman DL, Bottomley PA. Towards real-time intravascular endoscopic magnetic resonance imaging. JACC Cardiovasc Imaging. 2010;3:1158–65.
18. Shah SG, Brooker JC, Williams CB, Thapar C, Saunders BP. Effect of magnetic endoscope imaging on colonoscopy performance: a randomised controlled trial. Lancet. 2000;356:1718–1.
19. Chen Y, Duan YT, Xie Q, Qin XP, Chen B, Xia L, Zhou Y, Li NN, Wu XT. Magnetic endoscopic imaging vs standard colonoscopy: meta-analysis of randomized controlled trials. World J Gastroenterol. 2013;19(41):7197–204.
20. Baumgart DC, Wende I, Grittner U. Tablet computer-based multimedia enhanced medical training improves performance in gastroenterology and endoscopy board style exam compared with traditional medical education. Gut. 2016;65(3):535–6.
21. Arnold SH, Svendsen MB, Konge L, Svendsen LB, Preisler L. Three-dimensional motion tracking correlates with skill level in upper gastrointestinal endoscopy. Endoscopy. 2015 Sep;47(9):825–8.
22. Credentialing for gastrointestinal endoscopy. A reference document for credentialing committees and physicians seeking hospital privileges to perform gastrointestinal endoscopy produced in collaboration by: the American College of Gastroenterology (ACG) and the American Society for Gastrointestinal Endoscopy (ASGE). http://s3.gi.org/nataffairs/Asgeacg.pdf. Last Accessed on 17 Jan 2016.
23. Barton JR, Corbett S, van der Vleuten CP, et al. The validity and reliability of a direct observation of procedural skills assessment tool: assessing colonoscopic skills of senior endoscopists. Gastrointest Endosc. 2012;75:591–7.
24. Vassiliou MC, Kaneva PA, Poulose BK, et al. Global assessment of gastrointestinal endoscopic skills (GAGES): a valid measurement tool for technical skills in flexible endoscopy. Surg Endosc. 2010;24:1834–41.
25. Training Committee ASGE, Sedlack RE, Coyle WJ, Obstein KL, et al. ASGE's assessment of competency in endoscopy evaluation tools for colonoscopy and EGD. Gastrointest Endosc. 2014;79:1–7.
26. Sedlack RE. Training to competency in colonoscopy: assessing and defining competency standards. Gastrointest Endosc. 2011;74:355–66.
27. Walsh CM, Ling SC, Khanna N, et al. Gastrointestinal endoscopy competency assessment tool: development of a procedure-specific assessment tool for colonoscopy. Gastrointest Endosc. 2013;79:798–807.
28. Walsh CM, Ling SC, Khanna N, et al. Gastrointestinal endoscopy competency assessment tool: reliability and validity evidence. Gastrointest Endosc. 2015;81:1417–24.
29. Hawes R, Lehman GA, Hast J, O'Connor KW, Crabb DW, Lui A, et al. Training resident physicians in fiberoptic flexible sigmoidoscopy: how many supervised examinations are required to achieve competence? Am J Med. 1986;80:465–70.
30. Cass OW, Freeman ML, Cohen J, Zuckerman G, Watkins J, Nord J, et al. Acquisition of competency in endoscopic skills (ACES) during training: a multicenter study. Gastrointest Endosc. 1996;43:308A.
31. Shahidi N, Ou G, Telford J, Enns R. Establishing the learning curve for achieving competency in performing colonoscopy: a systematic review. Gastrointest Endosc. 2014 Sep;80(3):410–6.
32. American Academy of Family Physicians. Colonoscopy (position paper). June 13, 2013. Available at: http://www.aafp.org/about/policies/all/colonoscopy.html . Accessed January 17, 2016.
33. American Board of Surgery. ABS statement on GI endoscopy. Available at: http://www.absurgery.org/default.jsp?newsgiresponse. Accessed 17 Jan 2016.
34. Alternative pathways to training in gastrointestinal endoscopy. Manchester: The American Society for Gastrointestinal Endoscopy;1995 Jul. Available at: https://www.asge.org/docs/default-source/education/training/f3cf936-c650-47a-9634-442ed-63ec1d9.pdf?sfvrsn=4 Accessed 18 Oct 2017.

35. Paisley AM, Baldwin PJ, Paterson-Brown S. Accuracy of medical staff assessment of trainees' operative performance. Med Teach. 2005 Nov;27(7):634–8.
36. Klare P, Ascher S, Wagenpfeil S, Rapp D, Bajbouj M, Neu B, Schmid RM, von Delius S. Trainee colonoscopists fulfil quality standards for the detection of adenomatous polyps. BMC Med Educ. 2015 Feb 27;15:26.
37. Walsh CM, Ling SC, Khanna N, Cooper MA, Grover SC, May G, Walters TD, Rabeneck L, Reznick R, Carnahan H. Gastrointestinal endoscopy competency assessment tool: development of a procedure-specific assessment tool for colonoscopy. Gastrointest Endosc. 2014 May;79(5):798–807.

Training in Advanced Endoscopy

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Birtukan Cinnor, Chetan Mittal, and Sachin Wani

Introduction

Advanced endoscopy is vastly expanding in its practical implications and complexity. Over the years, the role of advanced endoscopic procedures has expanded from a primarily diagnostic to complex diagnostic and therapeutic procedures with many conditions that were managed surgically in the past being managed effectively with endoscopic approaches. With the increasing complexity of these procedures, training in advanced endoscopy has gained paramount importance. Training in advanced endoscopy requires acquisition of many skills – technical, cognitive, and integrative, those beyond standard endoscopic skills acquired during a 3-year training program. Expertise in basic endoscopy is a prerequisite for learning advanced endoscopy. Given the overall complexity of these procedures, adequate and appropriate training in advanced endoscopy is critical. These procedures are highly operator dependent and associated with higher rates of adverse events including life-threatening bleeding, perforation, and pancreatitis [1]. Given the changing healthcare landscape, reimbursements will soon be linked to performance and quality of care provided. Hence, in this era of value-based care, adequate training in advanced endoscopy is critical to ensure that quality metrics in endoscopy are being met.

For trainees to gain competency in any of the advanced endoscopy procedures that include endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasound (EUS), small bowel enteroscopy, enteral stenting, endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD), they need to be a part of a training program and training facility that has the necessary number of faculty members (trainers) willing to train effectively along with the ancillary staff, equipment, and most importantly case volume to provide for an optimal training environment.

This chapter will discuss the current status of training in advanced endoscopy and assessment of competency.

Current Status of Advanced Endoscopy Training

Training in endoscopy has classically been based on an apprenticeship model, where a novice endoscopist learns hands-on in a clinical setting under supervision of an expert endoscopist. The current process of endoscopy training in the United States is based on completion of a certain number of procedures within a defined timeframe, i.e., 3 years of a gastroenterology fellowship for basic endoscopy (EGDs and colonoscopy) and 1 year of advanced endoscopy training for ERCP, EUS, small bowel enteroscopy, and other advanced procedures including EMR and enteral stenting among others. Previously, ERCP and EUS training was performed within 3 years of general gastroenterology fellowship, which is still the case for a minority of training programs. However, with the increasing complexity and expansion of ERCP and EUS, a fourth year of training is considered mandatory by almost all training programs. A gastroenterology fellows' survey in 2003 showed that two thirds of fellows did not achieve procedural competence, and yet, more than 90% of them were expected to perform unsupervised ERCPs in practice [2].

Small bowel enteroscopy (SBE) is currently considered an advanced endoscopy procedure, and it is unclear whether "on-the-job" training is adequate or not. American Society of Gastrointestinal Endoscopy (ASGE) provides some guidance regarding SBE training and suggests that trainees should have completed formal training in upper and lower

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endoscopy prior to training in SBE. Also, certain SBE procedures require expertise in advanced endoscopy, e.g., SBE-assisted ERCP in surgically altered anatomy. Hence, ASGE suggests that SBE training should be performed in conjunction with or after advanced endoscopy training. Training in other advanced endoscopy procedures such as esophageal and colonic EMR, enteral stents, radiofrequency ablation (RFA), and ESD is highly variable between different training programs and currently dependent on the case volume and local expertise. ASGE suggests that ex vivo training or training in workshops should not replace training in actual patient care setting. However, training in newer procedures like endoscopic suturing, lumen-apposing metal stents (LAMS), ESDs, and natural orifice transluminal endoscopic surgery (NOTES) among others is extremely limited as these procedures are predominantly performed at specialized centers.

Finally, it should be noted that advanced endoscopy fellowship is currently not an Accreditation Council for Graduate Medical Education (ACGME)-accredited training program. The ASGE provides guidelines on the structure of advanced endoscopy training in the United States [3]. There are currently 57 programs in the United States that provide advanced endoscopy training (www.asgematch.com). Most of these programs provide training in both ERCP and EUS. However, programs highly vary in their procedural volumes and training in other advanced procedures like EMR, ESD, enteral stents, and advanced imaging among others.

Learning Curves and Competence

The ACGME outlined the Next Accreditation System (NAS) with the purpose of advancing competency-based medical education (CBME). The NAS defines "competence" based on objective milestones rather than subjective observations and focuses on the following: (1) ensuring that milestones are reached at various points in training, (2) ensuring that competence is achieved by all trainees, and (3) making certain that these assessments are documented by their programs [4].

A recent survey-based study by Patel and colleagues reported that majority of program directors and gastroenterology trainees believed in milestone-based competency assessment, but most programs still relied on procedure volumes and subjective evaluations to determine readiness for unsupervised practice [5]. Also, the study showed that a substantial proportion of programs lacked an endoscopy curriculum, and less than a third of programs used skills assessment tools or specific metrics to assess competence. In addition, trainees go through the stages of endoscopic learning in a highly variable manner. Thus, the current standards of assessing competency based on procedure volume are not adequate to determine readiness for independent practice. There is a need to move in the direction of CBME and use objective-validated metrics to assess competency. The definition of competence is changing from completion of certain number of procedures to achieving specific milestones and demonstrating ability to practice independently. Although limited, there have been studies that have demonstrated that case volume is not an accurate measure of competence and that trainees achieve competence at different points in training in ERCP and EUS. Studies assessing learning curves for other advanced endoscopic procedures are limited.

Endoscopic Retrograde Cholangiopancreatography

ERCP is an endoscopic procedure that uses a combination of luminal endoscopy and fluoroscopy. Over the past three decades, the use of diagnostic ERCP has decreased sevenfold, while therapeutic ERCP use has increased 30-fold, and this shift of ERCP toward a predominantly therapeutic intervention is associated with a resultant increase in complexity [6–8]. It is utilized to assess and treat disorder of the pancreas, liver, gallbladder, and biliary tree including in cases of disruption of flow through the hepatic, biliary, cystic, or pancreatic ducts due to obstruction due to stones, benign or malignant strictures, primary sclerosing cholangitis, papillary stenosis, and anatomic abnormalities associated with pancreatitis such as pancreas divisum. ERCP is now routinely utilized to manage complex pancreaticobiliary diseases such as chronic pancreatitis, malignant jaundice, and liver transplant complications.

The endoscopic portion of the procedure is done using a side-viewing duodenoscope, which is passed through the esophagus and stomach and into the second portion of the duodenum, where the major and minor duodenal papillae are located. The diagnostic and therapeutic goals of ERCP are achieved through the successful cannulation of the biliary ductal system and pancreatic duct, which is done through the major duodenal papilla and sometimes the minor papilla. A scout radiograph should be obtained, while the patient is on the fluoroscopy table and before insertion of the duodenoscope, which can be used as a baseline for comparison with subsequent fluoroscopic images taken after contrast injection. The esophagus, stomach, and duodenum should be examined as best as possible as the side-viewing scope is passed into the second portion of the duodenum. Once the scope is well positioned in the second portion of the duodenum, the papilla should be examined carefully for abnormalities. It is after this point that cannulation of the desired duct, either the common bile duct or the ventral pancreatic duct, should be done. After successful cannulation of the target duct, a radiopaque contrast dye is injected fluoroscopically in order to obtain a cholangiogram in the case of CBD cannulation or a pancreatogram in the case of pancreatic duct cannulation, which allows the endoscopist to visualize the necessity and approach for intervention. In some cases,

cannulation of the minor papilla is necessary when anatomic variance such as pancreas divisum is suspected [9]. Once abnormalities are identified, therapeutic interventions are done by passing a guide wire under fluoroscopy guidance into the duct where the abnormality is identified and various interventions such as dilations, sweeping of sludge and debris, removal of stones, brushings, and stenting of ducts can be done. Fluoroscopic imaging is also typically performed after interventions to assess the adequacy of the treatment.

ERCP is a technically challenging and complex procedure and can be associated with a higher rate of complications such as pancreatitis, bleeding, and perforation [1, 10–12]. Given the complexity of the procedure and its associated high risk for serious complications compared to other endoscopic procedures, it should be done by highly trained and skilled endoscopists in order to accomplish the intended endoscopic or therapeutic goals successfully and minimize the associated complications. As in the case of routine endoscopy procedures, training in ERCP should incorporate cognitive, technical, and integrative skills. Trainees should learn and clearly understand the indications, contraindications, potential risks, and management of complications. They should also learn how to interpret endoscopic findings including cholangiograms and pancreatograms and incorporate them into medical and endoscopic management of the patient. Before starting training in ERCP, trainees should have already achieved proficiency in performing routine upper endoscopy, which includes but not limited to visualization of the upper gastrointestinal tract, proper identification of normal and abnormal findings, minimizing patient discomfort, and proficiency in basic therapeutic techniques [13].

To achieve the competency needed to perform ERCP successfully and safely, the Core Curriculum for training in ERCP by the American Society for Gastrointestinal Endoscopy (ASGE), which has become the standard in the United States, calls for minimum of 12 months of dedicated ERCP training (combined with training in EUS). This typically requires an additional year of training after completion of the standard 3-year general gastroenterology fellowship. At the present time, the Gastroenterology Core Curriculum requires trainees to perform a minimum of 200 ERCPs after which competency can be assessed. The ASGE ERCP Core Curriculum requires the same minimum procedural volumes as the Gastroenterology Core Curriculum except that at least half of the procedures need to be therapeutic in nature [13, 14]. In the current state, training is done by a combination of cognitive education through reading, attending lectures, viewing videos and atlases, and supervised hands-on procedures under the tutelage of an expert endoscopist [3]. However, what constitutes adequate training to achieve proficiency and maintain expertise in ERCP is unclear. For a long time, it was accepted that performing about 180-200 diagnostic ERCPs was sufficient to achieve proficiency in order to perform ERCPs independently, based on a study by Jowell and colleagues who demonstrated an 80% success rate of cannulating the desired duct after doing 180 ERCPs under direct observation and training [15].

However, basing assessment of proficiency on the number of ERCPs performed under supervision alone is problematic as trainees have different learning curves to achieve competency and acquire the necessary skills at different time points, which has been demonstrated previously [16, 17]. Ekkelenkamp and colleagues used Rotterdam Assessment Form for ERCP (RAF-E) to assess learning curves for ERCP competence and found that common bile duct cannulation rates varied between 60% and 84% after 100 ERCPs. Similar variations in learning curves were found for native papilla cannulation and therapeutic interventions including stone extractions, sphincterotomy, and stent placement.

In another study, Wani and colleagues performed a large multicenter prospective study to assess learning curves for technical and cognitive aspects of biliary and pancreatic ERCP, including five advanced endoscopy trainees with different pretraining ERCP experience (from 0 to 250). Using cumulative sum (CUSUM) analysis, their study found a wide variation in procedure numbers required to achieve biliary cannulation. In addition, none of the trainees achieved competence in biliary cannulation of native papilla, suggesting that competence cannot be assessed based on number of procedures alone (Fig. 52.1). Instead, frequent assessment of endoscopic skills and milestones is required to determine the need for tailored training and individualized remediation [18].

Verma and colleagues reported a single endoscopists learning curve during and after training, reporting that biliary cannulation of native papilla improved to >80% after 350 procedures, with aggregate success rate of >96% for 300 procedures post training, suggesting that endoscopic skills continue to improve during and after completion of training [19]. Based on these findings, native papilla cannulation should be used as a benchmark to assess ERCP competence and determine readiness for independent practice. Studies have shown that for individuals seeking credentialing to perform independent ERCP after training, current ASGE guidelines emphasize objective measures over case volume, which is the goal of the NAS where proficiency is measured by objective competence measures rather than case volume.

Endoscopic Ultrasound (EUS)

EUS is an endoscopic procedure that combines the principles of ultrasound technology with endoscopy and has both diagnostic and therapeutic applications. It allows detailed visualization of not only the inner lining (mucosa) of the

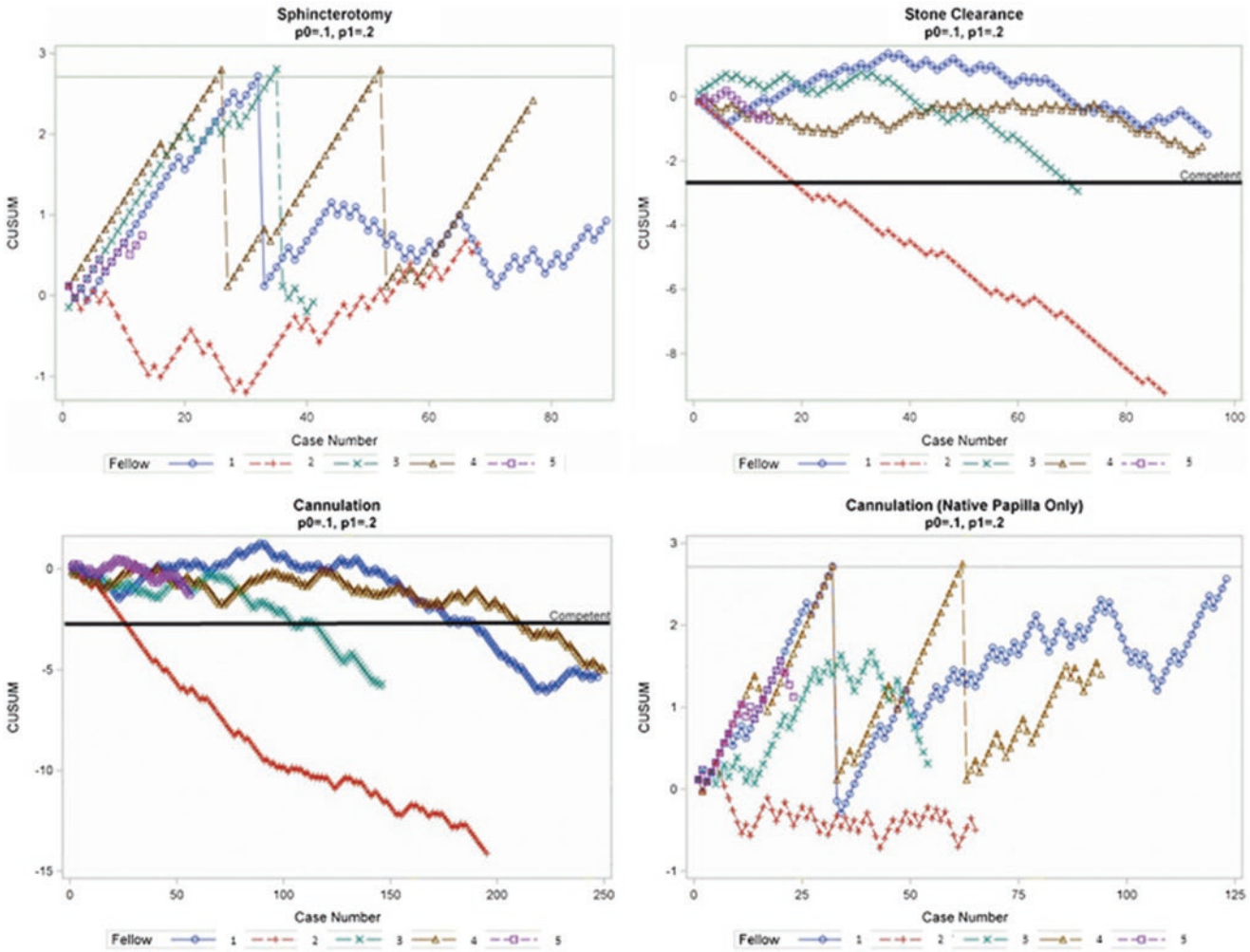

Fig. 52.1 Overall graphic representation of the learning curves in ERCP (cannulation, sphincterotomy, and stone clearance) among advanced endoscopy trainees by using cumulative sum analysis (Reprinted with permission [18])

digestive tract but also the deep mucosa, submucosa, muscularis propria, serosa, adventitia, as well as surrounding structures. EUS has a wide array of utility including diagnosis and staging of gastrointestinal cancers, detection of common bile duct stones, evaluation of masses in the submucosal lining of the gastrointestinal tract, barrett's esophagus with neoplasia, neuroendocrine tumors, common bile duct stones, pancreatitis, enlarged lymph nodes, fineneedle aspiration and biopsy to obtain fluid/tissue, pseudocyst drainage, and pain management with celiac plexus blockade and neurolysis. Currently, EUS is considered to be the most accurate and safe procedure to obtain tissue samples from gut wall and structures in its vicinity [20].

EUS is a highly operator-dependent procedure, and training in EUS also requires the development of technical, cognitive, and integrative skills beyond that required for standard endoscopic procedures as discussed for ERCP [21]. Trainees should understand proper indications, applications, contraindications, complications, and appropriate alternatives for EUS and EUS-FNA [22]. The American Society for Gastrointestinal Endoscopy recommends a minimum of 150 total supervised procedures, 75 of which have a pancreatobiliary indication and 50 cases of fine-needle aspiration (FNA) of which 25 should be pancreatic FNA before competency can be determined [23, 24]. This recommendation is based on expert opinion and limited scientific evidence. The ASGE EUS Core Curriculum states that before initiating training in EUS, fellows are expected to have completed at least 18 months of a standard GI training program and should have already achieved expertise in basic endoscopy, including diagnostic and therapeutic EGD and colonoscopy.

As is the case in ERCP, what constitutes adequate training to achieve proficiency in EUS is also unclear. In a prospective multicenter trial conducted at tertiary referral centers in the United States, Wani and colleagues concluded that the current guidelines of performing 150 EUS examinations are inadequate to achieve competence in EUS. In their study of

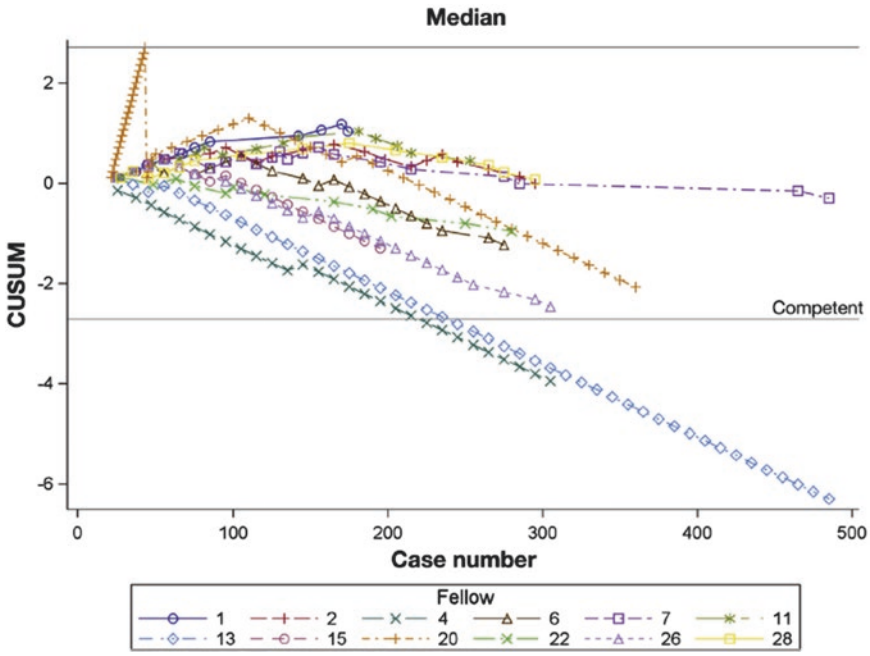

Fig. 52.2 Overall graphic representation of the learning curves in EUS among advanced endoscopy trainees by using cumulative sum analysis (Reprinted with permission [21])

17 advanced endoscopy trainees (AETs), none of them achieved competency at fewer than 225 cases [21].

They suggested 225 cases be considered the minimum case load in training programs. This study showed that trainees acquire EUS skills at different rates where eight trainees required additional training and supervision at the end of fellowship (Fig. 52.2). This again forms the basis for their recommendation for emphasis to be shifted away from the number of procedures performed to performance metrics with defined and validated competency thresholds of performance.

Small Bowel Enteroscopy

Small bowel enteroscopy (SBE) refers to endoscopic evaluation of small bowel, extending from ligament of Treitz to ileocecal valve using special enteroscopy equipment. SBE has evolved since inception and its use in small bowel disorders is expanding. The most common indication for SBE is in evaluation of mid-gastrointestinal bleeding, i.e., bleeding source not identified by conventional upper endoscopy and colonoscopy [25]. Current guidelines recommend starting with video capsule endoscopy to locate the site of bleeding which can help determine the route of deep enteroscopy (anterograde versus retrograde) [26]. In selected cases, a therapeutic intervention in highly probable, deep enteroscopy can be performed directly without a capsule study and may be more cost-effective [27]. SBE can be used for endoscopic diagnosis, surveillance, and treatment of Crohn's disease and related complications including strictures [28]. SBE has been used in endoscopic diagnosis, biopsies, preoperative tattooing, endoscopic mucosal resection, palliative stenting, and dilation of tumors and mass lesions [29]. Removal of foreign bodies including retained video capsules in the small intestine can also be accomplished through SBE [30].

In addition, SBE equipment has been used in special situations including pancreatobiliary interventions in patients with postoperative anatomy including after liver transplantation [31], Roux-en-Y surgery [32], and bariatric surgeries [33], difficult colonoscopy cases after failed attempt with pediatric colonoscope [34, 35], and diagnosis and management of genetic syndromes including familial adenomatous polyposis, Peutz-Jeghers, and Gardner's syndrome [36].

The three main types of equipment used to perform deep enteroscopy are single-balloon, double-balloon, and spiral enteroscopy. For trainees, the main technical advantage of single-balloon enteroscopy is ease of setup and ability to use in patients with latex allergy [37, 38]. The main limitation is decreased depth of insertion into small bowel [39]. The main advantage of spiral endoscopy is decreased procedure time but potentially limited by difficult retrograde insertion [40–42]. The main differences between depth of insertion, procedure time, diagnostic/therapeutic yield, and total enteroscopy success rate have been compared in a few retrospective studies and randomized trials, summarized in Table 52.1.

Trainees should be proficient in upper and lower endoscopy including hemostasis, polypectomy, balloon dilation, tattooing, and EMR. A few training programs have included deep enteroscopy training within 3 years of gastroenterology fellowship, but most programs offer an additional year of training along with ERCP and EUS. The endoscope is first inserted through the mouth or anus into the stomach or colon just like routine endoscopy, followed by advancing the

Table 52.1 Differences between depth of insertion, procedure time, diagnostic/therapeutic yield, and total enteroscopy success rate

Technique	Double balloon	Single balloon	Spiral
Depth of insertion	200 cm [42]	Anterograde – 133–256 cm Retrograde – 73–163 cm [22]	176–250 cm [22] Maximum reported – 301 cm [43]
Procedure time	60 min [42]	53 min [43]	47–55 min [42, 43]
Diagnostic/therapeutic yield	72% [38]	47–60% [38, 43]	43% [43]
Total enteroscopy	66–92% [22, 38]	15–25% [22]	8% [45]

overtube till it reaches the tip of endoscope. Endoscope balloon is then inflated to stabilize it followed by advancing the overtube as much as possible. Overtube balloon is then inflated, followed by withdrawing the endoscope along with overtube to reduce loop formation. Endoscope is then advanced after deflating its balloon while keeping the overtube balloon inflated to keep it in position. This push-pull technique is repeated to examine deeper lengths of small bowel.

Inserting the endoscope past ileocecal valve and maintaining position may be difficult, especially for learners [43]. Certain maneuvers can be used to improve this technique. With the overtube balloon inflated in ascending colon, the acute ileocecal angle can be improved by pulling back the overtube while advancing the endoscope through the ileocecal valve. Also, supine or right lateral decubitus positioning with manual pressure on right lower quadrant can improve ileocecal valve insertion. Difficult insertion may also be encountered in case of intra-abdominal adhesions related to previous surgery and fixed angulations in Crohn's disease. In these cases, avoiding loop formation, using fluoroscopy and abdominal pressure, changing patient position, and linear endoscope shortening or a combination of the above may be required to achieve maximal insertion [44]. Contrary to colonoscopic examination during withdrawal, mucosal exam during small bowel enteroscopy should be performed during insertion, as examination during withdrawal could be misleading due to mucosal trauma from insertion which may look like bleeding sites.

A few studies have addressed the learning curve and number of procedures required to attain competence in small bowel enteroscopy. Gross and colleagues reported no significant improvement with experience in depth of insertion and procedure time for 115 anterograde double-balloon enteroscopies. However, procedure duration and depth of insertion improved for retrograde small bowel enteroscopy with experience during 85 reported procedures [45]. Tee and colleagues also concluded that extensive training might not be required for an experienced endoscopist to perform anterograde double-balloon enteroscopy. However, at least 30–35 retrograde exams were required before achieving meaningful technical success [46]. In a multicenter US study by Mehdizadeh and colleagues involving 237 procedures in 188 patients, mean procedure time reduced from an average of 109.1 min to 92.4 min after first ten procedures. Fluoroscopy usage also decreased from average of 4.8 min to 2 min after first seven procedures, likely due to increased comfort level, but the depth of insertion did not change with experience [50]. Another study retrospectively evaluated 59 retrograde double-balloon enteroscopies and reported shorter procedure time, reduced fluoroscopy use, and increased depth of insertion after 20 procedures [47]. Above data and numbers can probably be extrapolated to single-balloon and spiral enteroscopy learning curves, but no studies currently exist to appropriately define learning curves for these techniques.

Enteral Stenting

Enteral stents are cylindrical devices placed endoscopically to restore and/or maintain luminal patency in various benign and malignant conditions of the gastrointestinal tract. Self-expandable metallic stents (SEMSs) are the most commonly used stents and are typically made of alloys like Nitinol (nickel and titanium), Elgiloy (cobalt, nickel, and chromium), or silicon to improve flexibility and increase radial force. Enteral stents can be further classified as uncovered, partially covered, and fully covered or on the basis of delivery system as through the scope (TTS) or over the wire (OTW).

With improvement of the composition and delivery systems, the indications for enteral stents have expanded from palliation of malignant strictures (esophageal [48], gastric, duodenal [49], and colonic [50]) to treatment of benign disorders such as refractory or recurrent benign esophageal strictures [51, 52], esophageal perforations, leaks and fistulas [6], and colonic disorders such as postsurgical stenosis and Crohn's-related and post radiation therapy strictures [53]. Recent data suggests that the use of anchoring systems including endoscopic and over-the-scope clips and endoscopic suturing and stapling may reduce the risk of migration rates [54].

Appropriate imaging of the involved area to assess length of stricture and severity of narrowing is key to successful placement of a stent. Endoscopic assessment of stricture can be limited by degree of stenosis and often requires fluoroscopy to determine the distal end of stricture. Ultrathin scope, dye injection, or gentle balloon dilation can be carefully

attempted in narrow strictures to evaluate the distal end. Radiographic markers placed over the skin, endoscopic metal clips, or subcutaneous injection can be used to delineate proximal and distal end of stricture, for accurate stent deployment. As a general rule, stent should be 4 cm longer than stricture to have at least 2 cm margin at each end, to allow for stent migration. Foreshortening or reduction in length of stent after deployment varies by stent type and manufacturer, which should be accounted for in selecting an appropriate stent. For proximal esophageal and distal rectal stenting, a 2 cm margin should be left from upper esophageal sphincter and anal verge, respectively, to avoid globus sensation and incontinence. Successful stent deployment generally leads to immediate symptom improvement. Enteral stents are generally placed by endoscopists with special training in therapeutic procedures. Trainees should have a comprehensive knowledge of available SEMS, indications, contraindications, adverse events, as well as basic knowledge in the interpretation of fluoroscopy, and, finally, proficiency in upper and lower endoscopy is essential. There are no studies at this time addressing learning curve or number of procedures required to attain competence in enteral stent placement. Williams and colleagues performed a study of 40 enteral stent procedures and showed that technical success improved from 82% for first 11 procedures to 94% for last 16 procedures. Procedure time and number of stents used also improved with case volume [55]. Thus, although there is no currently standardized minimum number of procedures required prior to assessing competency in enteral stent placement, it is expected that higher procedure volumes during training can produce improved clinical outcomes.

Radiofrequency Ablation

RFA uses radiofrequency energy, which is delivered by an endoscopic balloon catheter or a focal ablation device, to ablate Barrett's esophagus [56]. Radiofrequency energy is delivered through the electrodes to produce heat that destroys the Barrett's epithelium and coupled with acid suppression results in conversion of the metaplastic epithelium to neosquamous epithelium [57–63]. There are limited data on learning curves or published minimum procedure thresholds for assessment of competency with regard to any ablative therapy in the management of Barrett's-related neoplasia. Trainees learning ablative techniques should not only focus on appropriate techniques for ablation but also be trained in mucosal inspection of Barrett's esophagus and the use of advanced imaging techniques such as narrow band imaging and EMR. An initial study that involved seven endoscopists suggested that increased procedure volume was associated with increased complete eradication rates of intestinal metaplasia (the goal of endoscopic eradication therapy in the management of Barrett's-related neoplasia patients) [64]. Pasricha and colleagues showed that the number of procedures required to achieve complete eradication of intestinal metaplasia in Barrett's esophagus using RFA improves with case volume, suggesting a learning curve. This effect was negligible after 30 procedures, and there was no association between case volumes and adverse events [65].

Endoscopic Mucosal Resection

EMR is now a well-established and widely utilized endoscopic technique for the resection of dysplastic and early cancer lesions mainly confined to the mucosa throughout the GI tract [66–69]. The commonly used EMR techniques can be categorized as injection and cap-assisted and ligation-assisted EMR [70, 71]. Injection-assisted EMR is also called saline solution lift-assisted polypectomy where a lifting solution is injected into the submucosal space under the lesion creating a safety cushion. The cushion lifts the lesion, facilitating capture and removal by using a snare while minimizing mechanical or electrocautery damage to the deeper layers of the GI wall. The lesion may then be removed in a single resection or a piecemeal fashion [63, 73]. In ligation-assisted EMR, a band ligation device is attached to the endoscope, and the banding cap is positioned over the target lesion with or without previous submucosal injection. Suction is applied to retract the lesion into the banding cap, and a band is deployed to capture the lesion, thereby creating a pseudopolyp. An electrocautery snare is then used to resect the pseudopolyp above or below the band [72, 73]. Cap-assisted EMR also uses submucosal injection to lift the target mucosal lesion, and dedicated single-use mucosectomy devices have been developed that use a cap affixed to the tip of the endoscope. The device comes equipped with a specially designed crescent-shaped electrocautery snare that must be opened and positioned on the internal circumferential ridge at the tip of the cap. The endoscope is then immediately positioned over the target lesion, and suction is used to retract the mucosa into the cap after which the snare is closed to capture the lesion. The lesion is then resected with standard snare excision technique by using electrocautery [63, 73–75].A randomized controlled trial that compared cap-assisted EMR after saline lift and band ligation with snare resection showed a shorter procedure time with the latter (34 vs. 50 min, $p = 0.02$) [76]. Although the band ligation technique resulted in smaller resection specimens, there was no difference in the maximum thickness of specimens. The technique used is a matter of endoscopist preference, and both techniques are considered to be equally effective.

There are limited data on learning curves and the minimum number of procedures required to attain competence and minimum number of procedures per year required to

maintain competence in EMR. A study showed that performance of 20 EMRs is not sufficient to reach the peak of the learning curve in EMR [64, 77]. The British Society of Gastroenterology guidelines recommend a minimum of 30 supervised cases of EMR to attain competence and a minimum of 15 EMRs/year to maintain competence [78]. Choi et al. performed a retrospective study to assess learning curves for gastric EMR and found significant improvement in complete resection rates of 55% for the first 40 cases to 85% for the next 40 cases. Procedure time and perforation rates also improved after the first 20 cases [79]. Similar data for colonic EMR in the management of large colon polyps are lacking. It is intuitive that competency with colonoscopy and snare polypectomy for smaller lesions is essential prior to training in advanced polypectomy of large colon polyps.

Endoscopic Submucosal Dissection (ESD)

Endoscopic submucosal dissection (ESD) is a well-established technique of endoscopic resection that allows for en bloc removal of GI epithelial lesions [80]. ESD has been used primarily in Japan predominantly for the treatment of gastric neoplasia. It starts with injection of fluid into the submucosa, followed by incision around the mucosal segment to be removed using a cutting device (e.g., ceramic tip knife, triangle tip knife, flex knife, hook knife, standard needle knife), and, finally, submucosal dissection of the lesion [81]. This technique requires meticulous endoscopic control and the use of a cap to help with the submucosal dissection. The major proposed advantage of ESD over EMR is the ability to remove a neoplastic lesion en bloc, which provides more precise determination of its vertical and lateral margins allowing for greater potential for the complete removal of the entire neoplastic lesion. ESD is a technically challenging procedure due to the complexity, procedure length, steep learning curves, and its association with high adverse events compared to EMR [82, 83]. Although ESD is routinely practiced in Japan and other parts of Asia, its availability is limited in the West as very few providers have been trained in this technique [84]. Trainees interested in learning ESD must be skilled in the assessment of mucosal surface patterns and tumor depth, EMR, and thorough knowledge of the equipment used for incision and dissection and management of adverse events such as bleeding and perforation. It is suggested that trainees should perform ESD in animal models prior to embarking on clinical cases [85]. A single study showed that performance of 30 ex vivo ESD procedures by trainees on simulated gastric lesions led to a 100% en bloc resection rate without perforation during subsequent in vivo exams [86]. Competency to perform ESD in the lower stomach may be achieved after 30 cases [87], whereas colorectal ESD is more challenging with data suggesting that 40–50 cases are required to avoid adverse events and 80 to ensure en bloc resections of colorectal lesions [88–90].

Use of Simulators

Major disadvantages of the current hands-on apprenticeship model of training include increased risk to patient, higher stress environment, and added time to procedures. Therefore, simulator-based training, especially early on in training, has recently gained importance. Starting with simulator training reduces stress and improves manual dexterity in a learning environment. The four main types of simulators include mechanical simulators, live animal models, ex vivo simulators, and virtual reality (VR) computer simulators, each with its own advantages and disadvantages. The latest VR simulators are promising and appealing to the younger generation of trainees. The role of simulators in basic endoscopic training including EGD and colonoscopy is well established. A recent systematic review reported accelerated acquisition of practical skills with the use of simulators in novice learners but no change in basic endoscopic skills for experts [16]. Many studies using "GI Mentor" VR simulator have shown reduced procedure time and improved technical accuracy in novice learners [91–93].

Training on VR colonoscopy simulators is focused mainly on insertion technique and not on mucosal examination or therapeutic procedures like polypectomy. Nevertheless, evidence suggests improved performance after training on simulator versus no training but no difference in performance between simulator training versus patient-based training [94]. Given the complexity, therapeutic intent, and high complication rates of ERCP, simulator-based training intuitively appears to be an ideal training platform. Simulator-based ERCP training focuses mainly on biliary cannulation, although sphincterotomy and stenting have been incorporated in live porcine models. A few studies have evaluated utility of simulator training in basic ERCP skills, and evidence suggests increase in biliary cannulation rates and improved confidence scores [95, 96]. Sedlack and colleagues compared live anesthetized pig model, harvested porcine model, and computer-simulated model for ERCP training and concluded that harvested porcine model scored highest on realism, usefulness, and performance, although computer-generated model was felt to be easiest to include in a training program [97]. As stated above, most ERCP simulators focus on biliary cannulation, which is a prerequisite for ERCP but not a good predictor of successful ERCP completion, which requires many advanced skills. Barthet and colleagues evaluated EUS training in a live pig model and showed significantly increased competence in anatomic visualization, fine-needle aspiration, and celiac neurolysis [98]. The use of

simulator training in advanced endoscopic procedures like hemostasis, EMR, ESD, and stenting is best performed in in vivo or ex vivo animal models. Computer-generated simulator training for advanced endoscopy is limited by lack of tactile feedback and tissue elasticity. Even though simulators have been used in endoscopy training, it appears that current simulators are unable to assess performance and competence in patient-based endoscopy. Hence, the utility of simulators in procedural certification or determining readiness for unsupervised practice is extremely limited. The main role for simulators currently is training of novice endoscopist in basic skills using VR simulators and training advanced endoscopist in complex uncommon procedures using ex vivo and live animal models.

Future Directions

With the currently changing healthcare landscape in the United States, the importance of measuring and monitoring quality in endoscopy needs to be instilled early during training. Available data suggests that trainees have limited knowledge of quality measures, and training programs should promote a culture of continuous quality improvement among trainees and adopt formal approaches to educate training on defining and measuring quality of care. Trainees need to recognize that quality measurement is the new normal in gastroenterology, and several gastroenterology quality measures have been endorsed by the National Quality Forum. Quality indicators in EUS and ERCP were recently outlined by the ASGE/American College of Gastroenterology Task Force on Quality in Endoscopy [22, 99]. Future studies are needed to assess the performance of trainees at the onset of independent practice to better characterize the adequacy of training which in turn will help modify the current training structure to help ensure that trainees achieve competency at the time of completion of their formal training. Strategies to increase trainee exposure to advanced EUS and ERCP techniques are warranted. Finally, standardized methods of assessing learning curves and competency, including evaluation tools, need to be defined.

Conclusions

Training in advanced endoscopy is closest to the apprenticeship model. Available data clearly demonstrate that substantial variability in learning curves among trainees exists and a specific volume threshold during training does not ensure competence. With the increasing focus on competency-based medical education, emphasis clearly needs to be shifted away from the number of procedures performed to well-defined and validated competency thresholds. Ensuring that trainees achieve these thresholds, attaining the necessary skills for safe and effective independent practice, and monitoring key quality measures in clinical practice will ultimately improve the quality of patient care.

References

1. Andriulli A, Loperfido S, Napolitano G, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Am J Gastroenterol. 2007;102(8):1781–8.
2. Kowalski T, Kanchana T, Pungpapong S. Perceptions of gastroenterology fellows regarding ERCP competency and training. Gastrointest Endosc. 2003;58(3):345–9.
3. ASGE Training Committee, Adler DG, Bakis G, Coyle WJ, et al. Principles of training in GI endoscopy. Gastrointest Endosc. 2012;75(2):231–5.
4. Nasca TJ, Philibert I, Brigham T, et al. The next GME accreditation system--rationale and benefits. N Engl J Med. 2012;366(11):1051–6.
5. Patel SG, Keswani R, Elta G, et al. Status of competency-based medical education in endoscopy training: a nationwide survey of US ACGME-accredited gastroenterology training programs. Am J Gastroenterol. 2015;110(7):956–62.
6. Moffatt DC, Yu BN, Yie W, et al. Trends in utilization of diagnostic and therapeutic ERCP and cholecystectomy over the past 25 years: a population-based study. Gastrointest Endosc. 2014;79(4):615–22.
7. McCune WS, Shorb PE, Moscovitz H. Endoscopic cannulation of the ampulla of vater: a preliminary report. Ann Surg. 1968;167(5):752–6.
8. Kawai K, Akasaka Y, Murakami K, et al. Endoscopic sphincterotomy of the ampulla of Vater. Gastrointest Endosc. 1974;20:148–51.
9. Feurer ME, Draganov PV. Training for advanced endoscopic procedures. Best Pract Res Clin Gastroenterol. 2016;30(3):197–408.
10. Christensen M, Matzen P, Schulze S, et al. Complications of ERCP: a prospective study. Gastrointest Endosc. 2004;60(5):721–31.
11. Cotton PB, Garrow DA, Gallagher J, et al. Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. Gastrointest Endosc. 2009;70(1):80–8.
12. Colton JB, Curran CC. Quality indicators, including complications, of ERCP in a community setting: a prospective study. Gastrointest Endosc. 2009;70(3):457–67.
13. ASGE Training Committee, Jorgensen J, Kubiliun N, et al. Endoscopic retrograde cholangiopancreatography (ERCP): core curriculum. Gastrointest Endosc. 2016;83(2):279–89.
14. Chutkan RK, Ahmad AS, Cohen J, et al. ERCP core curriculum. Gasterointest Endosc. 2006;63:361–76.
15. Jowell PS, Baillie J, Branch MS, et al. Quantitative assessment of procedural competence. A prospective study of training in endoscopic retrograde cholangiopancreatography. Ann Intern Med. 1996;125(12):983e9.
16. Ekkelenkamp VE, Koch AD, Rauws EA, et al. Competence development in ERCP: the learning curve of novice trainees. Endoscopy. 2014;46(11):949–55; 35.
17. Shahidi N, Ou G, Telford J, et al. When trainees reach competency in performing ERCP: a systematic review. Gastrointest Endosc. 2015;81:1337–42.
18. Wani S, Hall M, Wang AY, et al. Variation in learning curves and competence for ERCP among advanced endoscopy trainees by using cumulative sum analysis. Gastrointest Endosc. 2016;83:711–9.
19. Verma D, Gostout CJ, Petersen BT, et al. Establishing a true assessment of endoscopic competence in ERCP during training and beyond: a single-operator learning curve for deep biliary cannula-

tion in patients with native papillary anatomy. Gastrointest Endosc. 2007;65(3):394–400.
20. Wang KX, Ben QW, Jin ZD, et al. Assessment of morbidity and mortality associated with EUS-guided FNA: a systematic review. Gastrointest Endosc. 2011;73(2):283–90.
21. Wani S, Hall M, Keswani R, et al. Variation in aptitude of trainees in endoscopic ultrasonography, based on cumulative sum analysis. Clin Gastroenterol Hepatol. 2015;13:1318–25.
22. Wani S, Wallace MB, Cohen J, et al. Quality indicators for EUS. Am J Gastroenterol. 2015;110(1):102–13.
23. ASGE EUS Core Curriculum. Gastrointest Endosc. 2012;76:3.
24. Eisen GM, Dominitz JA, Faigel DO, et al. Guidelines for credentialing and granting privileges for endoscopic ultrasound. Gastrointest Endosc. 2001;54:811–4.
25. Gralnek IM. Obscure-overt gastrointestinal bleeding. Gastroenterology. 2005;128:1424–30.
26. ASGE Standards of Practice Committee, Khashab MA, Pasha SF, Muthusamy VR, et al. The role of deep enteroscopy in the management of small-bowel disorders. Gastrointest Endosc. 2015;82(4):600–7.
27. Gerson L, Kamal A. Cost-effectiveness analysis of management strategies for obscure GI bleeding. Gastrointest Endosc. 2008;68:920–36.
28. ASGE Standards of Practice Committee, Shergill A, Lightdale J, Bruining DH, et al. The role of endoscopy in inflammatory bowel disease. Gastrointest Endosc. 2015;81:1101–21.
29. Islam RS, Leighton JA, Pasha SF. Evaluation and management of small- bowel tumors in the era of deep enteroscopy. Gastrointest Endosc. 2014;79:732–40.
30. Flynn AD, Chiorean MV. Retrieval of a large foreign body from the ileum with double-balloon enteroscopy (with videos). Gastrointest Endosc. 2014;79:519–20.
31. Haruta H, Yamamoto H, Mizuta K, et al. A case of successful enteroscopic balloon dilation for late anastomotic stricture of choledochojejunostomy after living donor liver transplantation. Liver Transpl. 2005;11:1608–10.
32. Kuno A, Yamamoto H, Kita H, et al. Double−balloon enteroscopy through a Roux−en−Y anastomosis for EMR of an early carcinoma in the afferent duodenal limb. Gastrointest Endosc. 2004;60:1032–4.
33. Sakai P, Kuga R, Safatle Ribeiro AV, et al. Is it feasible to reach the by− passed stomach after Roux−en−Y−gastric bypass for morbid obesity? The use of the double−balloon enteroscope. Endoscopy. 2005;37:566–9.
34. May A, Nachbar L, Ell C. Push−and−pull Enteroscopy using a single−balloon technique for difficult colonoscopy. Endoscopy. 2006;38:395–8.
35. Kaltenbach T, Soetikno R, Friedland S. Use of a double balloon enteroscope facilitates caecal intubation after incomplete colonoscopy with a standard colonoscope. Dig Liver Dis. 2006;38:921–5.
36. Pohl J, Blancas JM, Cave D, et al. Consensus report of the 2nd international conference on double balloon endoscopy. Endoscopy. 2008;40(2):156–60.
37. Tierney WM, Adler DG, Conway JD, et al. Overtube use in gastrointestinal endoscopy. Gastrointest Endosc. 2009;70:828–34.
38. May A, Farber M, Aschmoneit I, et al. Prospective multicenter trial comparing push and pull enteroscopy with single and double balloon techniques in patients with small bowel disorders. Am J Gastroenterol. 2010;105:575–81.
39. Domagk D, Mensink P, Aktas H, et al. Single- vs. double-balloon enteroscopy in small-bowel diagnostics: a randomized multicenter trial. Endoscopy. 2011;43:472–6.
40. Schembre DB, Ross AS. Spiral enteroscopy: a new twist on overtube- assisted endoscopy. Gastrointest Endosc. 2009;69:333–6.
41. Nagula S, Gaidos J, Draganov PV, et al. Retrograde spiral enteroscopy: feasibility, success, and safety in a series of 22 patients. Gastrointest Endosc. 2011;74:699–702.
42. Rahmi G, Samaha E, Vahedi K, et al. Multicenter comparison of double- balloon enteroscopy and spiral enteroscopy. J Gastroenterol Hepatol. 2013;28:992–8.
43. Mehdizadeh S, Ross A, Gerson L, et al. What is the learning curve associated with double-balloon enteroscopy? Technical details and early experience in 6 U.S. tertiary care centers. Gastrointest Endosc. 2006;64:740–50.
44. Sunada K, Yamamoto H. Double-balloon endoscopy: past, present, and future. Department of Internal Medicine, Division of Gastroenterology, Jichi Medical University, 3311–1 Yakushiji, Shimotsuke, Tochigi 329–0498, Japan.
45. Gross SA, Stark ME. Initial experience with double-balloon enteroscopy at a U.S. center. Gastrointest Endosc. 2008 May;67(6):890–7.
46. Tee HP, How SH, Kaffes AJ. Learning curve for double-balloon enteroscopy: findings from an analysis of 282 procedures. World J Gastrointest Endosc. 2012;4(8):368–72.
47. Mehdizadeh S, Han NJ, Cheng DW, et al. Success rate of retrograde double-balloon enteroscopy. Gastrointest Endosc. 2007;65(4):633–9.
48. Homs MYV, Steyerber EW, Eijkenboom WMH, et al. Single-dose brachytherapy versus metal stent placement for the palliation of dysphagia from esophageal cancer: multicenter randomized trial. Lancet. 2004;364:1497–504.
49. Nagaraja V, Eslick GD, Cox MR. Endoscopic stenting versus operative gastrojejunostomy for malignant gastric outlet obstruction-a systematic review and metaanalysis of randomized and non-randomized trials. J Gastrointest Oncol. 2014;5(2):92–8.
50. Lee HJ, Hong SP, Cheon JH, et al. Long-term outcome of palliative therapy for malignant colorectal obstruction in patients with unresectable metastatic colorectal cancers: endoscopic stenting versus surgery. Gastrointest Endosc. 2011;73(3):535–42.
51. de Wijkerslooth LR, Vleggar FP, Siersema PD. Endoscopic management of difficult or recurrent esophageal strictures. Am J Gastroenterol. 2011;106:2080–91.
52. Fuccio L, Hassan C, Frazzoni L, et al. Clinical outcomes following stent placement in refractory benign esophageal stricture: a systematic review and meta-analysis. Endoscopy. 2015;48D2:141–8.
53. van Boeckel PG, Sijbring A, Vleggaar FP, et al. Systematic review: temporary stent placement for benign rupture or anastomotic leak of the oesophagus. Aliment Pharmacol Ther. 2011;33:1292–301.
54. Dabizzi E, Arcidiacono PG. Update on enteral stents. Curr Treat Options Gastroenterol. 2016;14(2):178–84.
55. Williams D, Law R, Pullyblank AM. Colorectal stenting in malignant large bowel obstruction: the learning curve. Int J Surg Oncol. 2011;2011:917848.
56. Spechler SJ, Fitzgerald RC, Ganapathy AP, et al. History, molecular mechanisms, and endoscopic treatment of Barrett's esophagus. Gastroenterology. 2010;138(3):854–69.
57. Shaheen NJ, Sharma P, Overholt BF, et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. N Engl J Med. 2009;360:2277–88.
58. Phoa KN, van Vilsteren FG, Weusten BL, et al. Radiofrequency ablation vs endoscopic surveillance for patients with Barrett esophagus and low-grade dysplasia: a randomized clinical trial. JAMA. 2014;311:1209–17.
59. Shaheen NJ, Overholt BF, Sampliner RE, et al. Durability of radiofrequency ablation in Barrett's esophagus with dysplasia. Gastroenterology. 2011;141:460–8.
60. Orman ES, Li N, Shaheen NJ. Efficacy and durability of radiofrequency ablation for Barrett's esophagus: systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11:1245–55.

61. Pasricha S, Bulsiewicz WJ, Hathorn KE, et al. Durability and predictors of successful radiofrequency ablation for Barrett's esophagus. Clin Gastroenterol Hepatol. 2014;12:1840–7.
62. Phoa KN, Pouw RE, van Vilsteren FG, et al. Remission of Barrett's esophagus with early neoplasia 5 years after radiofrequency ablation with endoscopic resection: a Netherlands cohort study. Gastroenterology. 2013;145:96–104.
63. Wani S, Early D, Edmundowicz S, et al. Management of high-grade dysplasia and intramucosal adenocarcinoma in Barrett's esophagus. Clin Gastroenterol Hepatol. 2012;10:704–11.
64. Fudman DI, Lightdale CJ, Poneros JM, et al. Positive correlation between endoscopist radiofrequency ablation volume and response rates in Barrett's esophagus. Gastrointest Endosc. 2014;80(1):71–7.
65. Pasricha S, Cotton C, Hathorn KE, et al. Effects of the learning curve on efficacy of radiofrequency ablation for Barrett's esophagus. Gastroenterology. 2015;149(4):890–6.e2.
66. ASGE. Technology evaluation status report. Endoscopic mucosal resection. GIE. 2015;82(2); Submucosal dissection. Gastrointest Endosc. 2015;82(2):215–26.
67. Rembacken BJ, Gotoda T, Fujii T, Axon R. Endoscopic mucosal resection. Endoscopy. 2001;33(8):709–18.
68. Ponchon T. Endoscopic mucosal resection. J Clin Gastroenterol. 2001;32(1):6–10.
69. Yamamoto H, Yube T, Isoda N, et al. A novel method of endoscopic mucosal resection using sodium hyaluronate. GIE. 1999;50(2):251–6.
70. ASGE Technology Committee, Hwang JH, Konda V, Abu Dayyeh BK, et al. Endoscopic mucosal resection. Gastrointest Endosc. 2015;82(2):215–26.
71. Chandrasekhara V, Ginsberg GG. Endoscopic mucosal resection: not your father's polypectomy anymore. Gastroenterology. 2011;141(1):42–9.
72. de Melo SW, Cleveland P, Raimondo M, et al. Endoscopic mucosal resection with the grasp-and-snare technique through a double-channel endoscope in humans. GIE. 2011;73(2):349–52.
73. Keshani A, Lo S, Laith JH. Cap-assisted endoscopic mucosal resection is highly effective for nonpedunculated colorectal lesions. J Clin Gastroenterol. 2016;50(2):163–8.
74. Conio M, De Ceglie A, Filiberti R, et al. Cap-assisted EMR of large, sporadic, nonampullary duodenal polyps. Gastrointest Endosc. 2012;76(6):1160–9.
75. Yang DH, Park Y, Park SH, et al. Cap-assisted EMR for rectal neuroendocrine tumors: comparisons with conventional EMR and endoscopic submucosal dissection (with videos). Gastrointest Endosc. 2016;83(5):1015–22.
76. Pouw RE, van Vilsteren FG, Peters FP, et al. Randomized trial on endoscopic resection-cap versus multiband mucosectomy for piecemeal endoscopic resection of early Barrett's neoplasia. Gastrointest Endosc. 2011;74:35–43.
77. van Vilsteren FG, Pouw RE, Herrero LA, et al. Learning to perform endoscopic resection of esophageal neoplasia is associated with significant complications even within a structured training program. Endoscopy. 2012;44:4–12.
78. Fitzgerald RC, di Pietro M, Ragunath K, et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. Gut. 2014;63:7–42.
79. Choi IJ, Kim CG, Chang HJ, et al. The learning curve for EMR with circumferential mucosal incision in treating intramucosal gastric neoplasm. Gastrointest Endosc. 2005;62(6):860–5.
80. ASGE. Technology evaluation status report. Endoscopic submucosal dissection. GIE. 2015;81(6):1311–25.
81. Gotoda T, Yamamoto H, Soetikno RM. Endoscopic submucosal dissection of early gastric cancer. Rev J Gastroenterol. 2006; 41(10):929–42.
82. Farhat S, Chaussade S, Ponchon T, et al. Endoscopic submucosal dissection in a European setting. A multi-institutional report of a technique in development. Endoscopy. 2011;43(8):664–70.
83. Othman MO, Wallace MB. Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) in 2011, a western perspective. Clin Res Hepatol Gastroenterol. 2011;35(4):288–94.
84. Draganov PV, Coman RM, Gotoda T. Training for complex endoscopic procedures: how to incorporate endoscopic submucosal dissection skills in the west? Expert Rev Gastroenterol Hepatol. 2014;8(2):119–21.
85. Goda K, Fujishiro M, Hirasawa K, et al. How to teach and learn endoscopic submucosal dissection for upper gastrointestinal neoplasm in Japan. Dig Endosc. 2012;24(Suppl 1):136–42.
86. Kato M, Gromski M, Jung Y, et al. The learning curve for endoscopic submucosal dissection in an established experimental setting. Surg Endosc. 2013;27(1):154–61.
87. Oda I, Odagaki T, Suzuki H, et al. Learning curve for endoscopic submucosal dissection of early gastric cancer based on trainee experience. Dig Endosc. 2012;24(Suppl 1):129–32.
88. Hotta K, Oyama T, Shinohara T, et al. Learning curve for endoscopic submucosal dissection of large colorectal tumors. Dig Endosc. 2010;22(4):302–6.
89. Jeon HH, Lee HS, Youn YH, et al. Learning curve analysis of colorectal endoscopic submucosal dissection (ESD) for laterally spreading tumors by endoscopists experienced in gastric ESD. Surg Endosc. 2016;30(6):2422–30.
90. Probst A, Golger D, Anthuber M, et al. Endoscopic submucosal dissection in large sessile lesions of the rectosigmoid: learning curve in a European center. Endoscopy. 2012;44(7):660–7.
91. Di Giulio E, Fregonese D, Casetti T, et al. Training with a computer-based simulator achieves basic manual skills required for upper endoscopy: a randomized controlled trial. Gastrointest Endosc. 2004;60(2):196–200.
92. Ferlitsch A, Schoefl R, Puespoek A, et al. Effect of virtual endoscopy simulator training on performance of upper gastrointestinal endoscopy in patients: a randomized controlled trial. Endoscopy. 2010;42(12):1049–56.
93. Ende A, Zopf Y, Konturek P, et al. Strategies for training in diagnostic upper endoscopy: a prospective, randomized trial. Gastrointest Endosc. 2012;75(2):254–60.
94. Haycock A, Koch AD, Familiari P, et al. Training and transfer of colonoscopy skills: a multinational, randomized, blinded, controlled trial of simulator versus bedside training. Gastrointest Endosc. 2010;71(2):298–307.
95. Hirdes MM, Siersema PD, Houben MH, et al. Stent-in-stent technique for removal of embedded esophageal self-expanding metal stents. Am J Gastroenterol. 2011;106(2):286–93.
96. Liao WC, Leung JW, Wang HP, et al. Coached practice using ERCP mechanical simulator improves trainees' ERCP performance: a randomized controlled trial. Endoscopy. 2013;45(10):799–805.
97. Sedlack R, Petersen B, Binmoeller K, et al. A direct comparison of ERCP teaching models. Gastrointest Endosc. 2003;57(7):886–90.
98. Barthet M, Gasmi M, Boustiere C, et al. EUS training in a live pig model: does it improve echo endoscope hands-on and trainee competence? Endoscopy. 2007;39(6):535–9.
99. Adler DG, Lieb JG, Cohen J, et al. Quality indicators for ERCP. Am J Gastroenterol. 2015;110(1):91–101.

Teaching and Training in Endoscopic Ultrasound

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Key Points

- EUS is a valuable tool for multiple indications, especially cancer evaluation and pancreatobiliary conditions.
- Comprehensive understanding of ultrasound technology, anatomical landmarks, and clinical indications are required to achieve competency.
- Although minimal threshold numbers have been established for attaining competency, learning curves vary greatly between trainees.
- Emphasis on performance skills with validated goals should be sought.
- Training adjuncts provide interesting supplemental information but should not replace formal "hands-on" training.

Teaching and Training in Endoscopic Ultrasound

Endoscopic ultrasound (EUS) is a remarkable tool with multiple applications. Since its introduction approximately 30 years ago, it has become a pivotal modality for numerous indications such as the evaluation of pancreatobiliary pathologies, staging of luminal gastrointestinal cancers, assessment of subepithelial lesions, and for tissue acquisition [1, 2]. During the past few years, EUS has shifted from a purely diagnostic tool to a more interventional procedure. For example, it can now be used to drain fluid collections, to provide biliary access and decompression, to perform celiac plexus neurolysis, and to deposit fiducial markers [3].

Like all endoscopic procedures, EUS requires the acquisition of basic knowledge and skills to achieve competency, with some cases being more challenging than others. However, difficulty does not necessarily correlate with clinical impact. For example, fine needle aspiration (FNA) of a large 4 cm subcarinal lymph node can be performed with limited training yet can prevent a mediastinoscopy, whereas accurate vascular staging of pancreatic cancer requires significant training and experience but is often not the sole determinant of whether a patient remains a surgical candidate.

When learned after acquiring basic endoscopic skills, EUS is often seen as a difficult technique to master, with a steep learning curve. Several endoscopic "reflex" skills become counterproductive: insufflating air instead of collapsing the gut wall, broad pushing, and simultaneous torquing instead of breaking down the movements of the echoendoscope to dedicated meticulous motions or correctly positioning the probe in unusual anatomic landmarks. The following chapter addresses teaching and training issues in endoscopic ultrasound.

Background in EUS Training

Like any new procedure, first-generation endosonographers were self-taught. Training opportunities remained limited given the lack of dedicated EUS training centers. A 2004 international survey showed that only 23% of US endosonographers received more than 6 months of formal EUS training, that 20% learned by simply observing procedures, and that 12% were self-taught [4]. A similar study covering the Asia-Pacific region in 2006 also noted that up to 49% of respondents were self-taught and that only 22% had undergone hands-on fellowships lasting at least 6 months [5]. Limited numbers of academic training centers and adequate access to *quality* EUS may explain why this procedure was initially slow to gain widespread acceptance [6].

In the past decade, supervised EUS training has become more accessible. However, access to sufficient training still remains challenging. In order to provide an adequate experience, a training center requires sufficient patient volume and faculty expertise. There are currently over 50 recognized

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programs in the Unites States offering a fourth year fellowship [7].

In an attempt to standardize training in EUS, the American Society for Gastrointestinal Endoscopy (ASGE) published EUS core curriculum guidelines in 2012. The document details the basic benchmarks trainees should achieve to help them attain proficiency in EUS [8]. They include a general knowledge of ultrasound principles, an understanding of EUS technology and applied indications, recognition of anatomical landmarks, acquisition of tissue sampling skills (and possibly skills for more advanced techniques), and the ability to manage complications (Table 53.1).

EUS can be performed with a radial or curvilinear instrument. Although trainees could become proficient in using both instruments, attaining competency with the curvilinear instrument is paramount, given its ability to perform EUS-guided FNA or therapeutic procedures. Many experts would agree that given the choice, linear should be favored over radial training. While it is commonly thought that learning EUS with a radial instrument is easier than with a curvilinear instrument, a recent study showed that prior radial EUS training did not contribute to improved performance with a curvilinear endoscope [9].

Table 53.1 EUS core curriculum [8]

EUS core curriculum
General comprehension of ultrasound principles
General comprehension of oncology (TNM classification, stage-directed therapy)
Indication, contraindications, alternatives to EUS
EUS equipment: processors, radial and curvilinear scopes
Passage of the echoendoscope
Evaluation of structures
Luminal: esophagus, stomach, duodenum, ampulla, ano-rectum
Pancreas
Biliary tree and gallbladder
Liver
Lymph nodes (mediastinum, abdomen, pelvis)
Vascular structures: (mediastinum, abdomen, pelvis)
Non-GI organs:
Mediastinum: heart, lungs, trachea, bronchi
Abdomen: spleen, kidneys, adrenal glands
Pelvis: urinary bladder, seminal vesicles, prostate, urethra, uterus, vagina
Interpretation of images and pathology
Tissue sampling
Management of complications
Advanced EUS techniques

EUS Training Guidelines

In 2001, the ASGE recommended that the minimum number of EUS procedures before assessing comprehensive competence in all aspects of EUS should include at least 150 supervised cases. Of these, 75 should be pancreatobiliary. A minimal number of 50 FNA is required, with at least 25 pancreatic cases. Minimal requirement for competency in evaluating mucosal tumors is 75 cases, and 40 cases for submucosal tumors (Table 53.2). These numbers, based on expert opinion and limited data, are meant as a guide to assess individual trainees, and should not be taken to indicate that competency has been achieved [10].

Although ASGE guidelines remained the same for the past 15 years, other countries have proposed EUS training guidelines in more recent years. In 2011, a Working Group mandated by the British Society of Gastroenterology recommended that EUS trainees should undergo minimal threshold numbers of 250 hands-on cases before assessing competency, including 150 pancreatobiliary cases (at least half of which are likely pancreatic adenocarcinomas), 80 luminal cancers (including at least ten rectal cases), and 20 subepithelial lesions. A total of 75 FNA should be performed, of which at least 45 are likely pancreatic adenocarcinomas [11].

The Australian Conjoint Committee for Recognition of Training in Gastrointestinal Endoscopy mandates that a minimum of 200 EUS examinations be performed, including a minimum of 100 examinations for gastroesophageal lesions and a minimum of 100 examinations for pancreatobiliary investigations. A minimum of 50 FNA, with at least 25 pancreatobiliary cases, are also required (http://www.conjoint.org.au/).

More recently, the Forum on Canadian Endoscopic Ultrasound (FOCUS), a network of Canadian endosonographers, proposed training guidelines as an objective framework to help Canadian institutions assess training of endosonographers. These included a total of 250 supervised hands-on cases, with at least 100 pancreatobiliary cases, 50 FNA performed independently, 25 rectal cases, and 10 celiac plexus blocks/neurolysis [12]. Table 53.3 shows a comparison chart of all four training guideline proposals (Table 53.3).

Table 53.2 EUS training guidelines in the United States [10]

Minimum number of EUS procedures prior to assessing competency	
Site/lesion	Number of cases required
Comprehensive competence	150
Pancreatobiliary	75
Mucosal tumors	75
Submucosal lesions	40
EUS-FNA Pancreatic Non-pancreatic	50 25 25

Table 53.3 Minimum EUS procedures recommended prior to assessing competency in four different countries [10–12]

Comparison chart of minimum EUS procedures guidelines prior to assessing competency				
	ASGE (2001)	UK (2011)	Australia	Canada (2016)
Comprehensive competence	150	250	200	250
Pancreatobiliary	75	150	100	100
Gastroesophageal lesions			100	
Mucosal tumors	75	80 at least 10 rectal		25 rectal
Submucosal lesions	40	20		
EUS-FNA Pancreatic FNA	50 25	75 45	50 25	50
CPB/N				10

UK United Kingdom, *CPB/N* Celiac plexus block/neurolysis

As noted earlier, these guidelines represent minimal threshold numbers recommended before assessing competency, and may not ensure competency for an individual trainee. Moreover, cognitive aspects of the procedure are important, such as understanding the indications, contraindications, risks, benefits, and alternatives for the procedure. Most experts recommend a 6–24-month "hands-on" training in EUS before achieving competency [13].

Assessment of Training Guidelines and Training Centers

Assessment of Training Guidelines

Recent studies have demonstrated that the learning curve for EUS proficiency may be much more than what was previously anticipated. Some authors suggest that at least 1000 procedures are needed to get comfortable with all aspects of EUS [14].

A 2013 study by Wani evaluated the learning curves for EUS by using cumulative sum analysis. Five advanced endoscopic trainees at three training centers were evaluated at intervals of ten EUS examinations during a 1-year training period. Standardized data collection graded evaluation of various anatomic stations, lesion identification, accurate uTNM staging, proper wall layer origin of subepithelial lesions, and technical success with FNA. Results showed substantial variability in achieving competency in all trainees in regard to the current recommendations of 150 cases: 2 trainees achieved competence after 255 and 295 cases, 2 showed a trend toward acceptable performance at 225 and 196 cases, while the fifth trainee needed ongoing training after 402 cases [15].

A similar study by the same author in 2015 prospectively evaluated 17 EUS trainees over 1 year at 15 centers. Five trainees were excluded from the study based on insufficient cases (<150 cases). The remaining 12 trainees had performed between 230 and 540 procedures. Again, results showed a large amount of variation in their learning curve. Only 2 trainees crossed acceptable performance threshold after 225 and 245 cases. Two trainees had a trend toward acceptable performance after 290 cases, while the remaining 8 trainees required additional training. Although the overall sample size was limited, these results prompted the authors to conclude that the current guidelines of performing 150 EUS examinations are inadequate to achieve competency, and that 225 cases should be considered the minimum case load in training programs [16]. These studies also raised the issue that assessing competency should concentrate more on training milestone achievement more than attaining minimal case load numbers [17].

A more focused study retrospectively evaluated the learning curve for EUS gastric cancer T staging in four trainees, using cumulative sum analysis. It found that all trainees reached acceptable performance after 65 cases or less (as compared to the proposed 75 cases for mucosal cancer staging) [18].

A recently developed assessment tool designed to measure competence in EUS and FNA during mediastinal staging of non-small cell lung cancer demonstrated that it could discriminate between experienced endosonographers and trainees [19]. It consists of direct supervision and digital recordings of cases that were evaluated using a 12-point scoring system. Points were attributed based on insertion of the endoscope, proper identification of pertinent anatomical structures, and adequate performance of the FNA sequence. Results showed that experienced endosonographers scored better than trainees, thus suggesting that this objective assessment tool could be useful in assessing competency.

Assessment of Training Centers

A 2006 study surveyed EUS training programs in the USA. Ninety-one of 142 contacted centers responded. Of those, 72% reported performing more than 200 procedures per year. The median number of EUS performed by 3-year GI fellows was only 50. Programs offering advanced endoscopy fellowships offered a median of 200 procedures to advanced fellows (range 50–1100 procedures), with 20% not receiving "hands-on" training and 52% performing <200 procedures [20]. This study underlined that many centers were unable to provide sufficient EUS training experience.

Proper training is pivotal to ensure that future endosonographers will be able to provide quality EUS examinations. A 2005 survey evaluated EUS training and practice patterns

amongst gastroenterologists since 1993. It found that although the majority of respondents felt well trained regardless of training type, those with advanced training obtained higher training volumes and performed higher volumes of EUS compared to those with EUS training during GI fellowship alone or by other means [21].

Programs that wish to train endosonographers should ideally have at least one experienced, expert physician that can perform EUS and FNA, in numbers sufficient to ensure adequate hands-on exposure. It should provide access to a multidisciplinary team (including surgeons, pathologists, radiologists, oncologists, and radio-oncologists) so trainees can better appreciate the role that EUS can play in cancer management [8].

Training in EUS-FNA

Fine needle aspiration provides some of the most powerful information that EUS can offer [22]. Any person wishing to acquire training in EUS must also become proficient at FNA. While it was initially recommended that training in FNA required competence in standard EUS imaging [10, 23], a recent study has shown that introducing attending-supervised EUS-FNA from the onset of training is safe and can maximize exposure to the technique during training [24]. Similar to diagnostic EUS, training plays a key role in mastering the FNA technique, and observation does not appear to compensate for hands-on training [25].

Current ASGE recommendations require at least 50 FNA procedures (minimum 25 pancreatic) be performed before assessing competency [10]. A 2004 study retrospectively compared the FNA results of the first 57 pancreatic masses performed by a single endosonographer. It showed a significant increase in sensitivity after the first 30 cases, suggesting that the current ASGE guidelines are reasonable [26]. However, adequate results with difficult cases likely require much more experience. A study by Eloubeidi showed that after completing a formal 1-year EUS training, the median number of passes to achieve a diagnosis significantly decreased after 100 additional FNA procedures and that complication rates decreased after 200 additional procedures [27].

Live animal porcine models can be cumbersome to create but seem to offer the best EUS-FNA training experience, next to procedures in humans. Porcine models are similar to human anatomy in regard to sampling lymph nodes. Prior exposition to lymph node FNA in porcine models may improve trainee performance, confidence, and procedural comfort when returning to patient examinations [22, 28]. Ex vivo models using porcine organs or inorganic phantoms with no animal materials have also been developed [29–31].

Training in Interventional EUS

EUS has become more interventional in the past decade. Techniques include celiac plexus block/neurolysis [32], gastric variceal eradication [33], fiducial marker placement for stereotactic radiosurgery [34], peripancreatic fluid collection drainage [35], pelvic abscess drainage [36], and biliary decompression [37]. Some of these techniques are easier to learn and may be indicated more commonly, such as celiac plexus block/neurolysis. Given its role in the management of pancreatic cancer pain, trainees are encouraged to be comfortable with this technique [38]. Other procedures like biliary drainage are more complex and risky, are currently evolving, and may not be taught routinely during EUS training.

Recently, a prototype of a polycarbonate dilated biliary system was created by computer-aided design and 3D printing. Its role was to evaluate EUS-guided bile duct drainage (BD) by using a 4-step procedure consisting of needle puncture, guidewire manipulation, tract dilation, and stent placement. Success rate for stent placement was 80%, and mean overall procedure time was less than 20 minutes [39]. Although further studies are needed to confirm that this model can influence training for EUS-BD, the advent of 3D printing represents an interesting venue for teaching phantoms [40].

A recent ex vivo model mimicking peripancreatic collections was created by Baron [41]. Its cost is relatively low (<300$) and can withstand multiple punctures and drainage without needing replacement. Given the added complexity of performing peripancreatic fluid collection drainage compared to standard FNA, this model may be helpful in acquiring the skills to perform this technique.

Training Adjuncts

Dedicated hands-on fellowship training is considered the best way to achieve competency in EUS [21]. However, several training adjuncts are available to increase trainee knowledge and exposure. Direct observation of cases performed by experienced endosonographers can provide useful information. There are also several video libraries that demonstrate EUS through various websites (e.g., ASGE Endoscopic Learning Library Videos – www.asge.org; Cook Medical Endoscopic Ultrasound Video Library – www.cookmedical.com). Short-term endoscopic training programs have been shown to improve trainee skill and knowledge [42]. As discussed earlier, teaching phantoms are available for EUS-guided FNA and therapeutic procedures.

Access to endoscopic simulators may provide trainees with initial experience with scope manipulation and can help them

familiarize themselves with the technique. Although several simulators have been developed for upper endoscopy, colonoscopy, and ERCP, few exist for EUS [43]. The Simbionix GI Mentor (Simbionix Corp, OH) is a computer-based simulator that can be equipped with an EUS module (www.simbionix.com). This simulator allows the trainee to receive visual and tactile feedback while manipulating a specially designed echoendoscope. EUS images are generated from 3D anatomical models composed of CT and MRI images from real patients [7].

Another model labeled the Erlangen Active Simulator for International Endoscopy (EASIE-R) consists of an ex vivo porcine GI tract including bile duct and pancreatic anatomy embedded in an ultrasound gel (www.endosim.com). Artificial cysts created by using balloons are sutured to the gut wall and can be punctured by FNA. Solid lesions or submucosal depots can also be created. This model has been evaluated in a small study and was thought to be easy to use, realistic, and useful for teaching EUS skills [44].

Although EUS simulators can provide some exposure to the skills required to perform EUS, there are currently no studies evaluating their impact on EUS competency. Given their high cost, access to them remains limited.

Summary

EUS has become a pivotal instrument for the management of several pathologies. Its use for the diagnosis and treatment of GI and non-GI pathology will likely continue to increase, and the need for competent endosonographers will continue to increase with it. However, if there is sufficient local access to experienced endosonographers, it is now no longer acceptable to begin performing EUS without having performed sufficient supervised cases in humans. Training adjuncts such as videos and simulators may help accelerate the hands-on training process, but should not replace it.

Like any endoscopic tool, adequate training is essential to fully master the technique. Trainees wishing to acquire EUS skills should seek sufficient exposure from centers that can provide a sufficient number of expertly supervised cases. Although a minimal threshold number of cases are recommended before assessing competency, emphasis on performance skills with validated goals should be sought given that learning curves may vary greatly between trainees. Recent studies have demonstrated that actual minimal requirements for assessing competency may be insufficient [15, 16]. Therefore, trainees should ideally seek to surpass these requirements during their training and understand that, to truly master EUS, they will have to commit to continue the training process by making EUS as a regular part of their daily practice.

References

1. Luthra AK, Evans JA. Review of current and evolving clinical indications for endoscopic ultrasound. World J Gastrointest Endosc. 2016;8(3):157–64.
2. Eckardt AJ, Jenssen C. Current endoscopic ultrasound-guided approach to incidental subepithelial lesions: optimal or optional? Ann Gastroenterol. 2015;28(2):160–72.
3. Sharma V, Rana SS, Bhasin DK. Endoscopic ultrasound guided interventional procedures. World J Gastrointest Endosc. 2015;7(6):628–42.
4. Das A, Mourad W, Lightdale CJ, et al. An international survey of the clinical practice of EUS. Gastrointest Endosc. 2004;60(5):765–70.
5. Ho KY. Survey of endoscopic ultrasonographic practice and training in the Asia-Pacific region. J Gastroenterol Hepatol. 2006;21(8):1231–5.
6. Sahai AV. Some thoughts on endoscopic ultrasound training. J Gastroenterol Hepatol. 2006;21(8):1229–30.
7. Salah W, Faigel DO. Training and simulators. In: Hawes RH, Fockens P, Varadarajulu S, editors. Endosonography. 3rd ed. Philadelphia: Elsevier; 2016. p. 26–34.
8. ASGE Training Committee, Di Maio CJ, Mishra G, Mc Henry L, et al. EUS core curriculum. Gastrointest Endosc. 2012;76(3):476–81.
9. Xu W, Liu Y, Pan P, et al. Prior radial-scanning endoscopic ultrasonography training did not contribute to subsequent linear-array endoscopic ultrasonography study performance in the stomach of a porcine model. Gut Liver. 2015;9(3):353–7.
10. American Society for Gastrointestinal Endoscopy, Eisen GM, Dominitz JA, Faigel DO, et al. Guidelines for credentialing and granting privileges for endoscopic ultrasound. Gastrointest Endosc. 2001;54(6):811–4.
11. Meenan J, Harris K, Oppong K, et al. Service provision and training for endoscopic ultrasound in the UK. Frontline Gastroenterol. 2011;2:188–94.
12. Arya N, Sahai AV, Paquin SC. Credentialing for endoscopic ultrasound: a proposal for Canadian guidelines. Endosc Ultrasound. 2016;5(1):4–7.
13. European Society of Gastrointestinal Endoscopy (ESGE), Polkowski M, Larghi A, Weynand B, et al. Learning, techniques, and complications of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) technical guideline. Endoscopy. 2012;44(2):190–206.
14. Eloubeidi MA. Developing an academic EUS program: the University of Alabama at Birmingham experience. Gastrointest Endosc. 2007;65(7):1039–41.
15. Wani S, Coté GA, Keswani R, et al. Learning curves for EUS by using cumulative sum analysis: implications for American Society for Gastrointestinal Endoscopy recommendations for training. Gastrointest Endosc. 2013;77(4):558–65.
16. Wani S, Hall M, Keswani RN, et al. Variation in aptitude of trainees in endoscopic ultrasonography, based on cumulative sum analysis. Clin Gastroenterol Hepatol. 2015;13(7):1318–25.
17. Vargo J. Cumulative sum analysis and endoscopic ultrasound training competency: a requiem for expert opinion? Clin Gastroenterol Hepatol. 2015;13(7):1326–7.
18. Park CH, Park JC, Kim EH, et al. Learning curve for EUS in gastric cancer T staging by using cumulative sum analysis. Gastrointest Endosc. 2015;81(4):898–905.
19. Konge L, Vilmann P, Clementsen P, et al. Reliable and valid assessment of competence in endoscopic ultrasonography and fine-needle aspiration for mediastinal staging of non-small cell lung cancer. Endoscopy. 2012;44(10):928–33.
20. Azad JS, Verma D, Kapadia AS, et al. Can U.S. GI fellowship programs meet American Society for Gastrointestinal Endoscopy

recommendations for training in EUS? A survey of U.S. GI fellowship program directors. Gastrointest Endosc. 2006;64(2):235–41.
21. Wasan SM, Kapadia AS, Adler DG. EUS training and practice patterns among gastroenterologists completing training since 1993. Gastrointest Endosc. 2005;62(6):914–20.
22. Paquin SC. Training in endoscopic ultrasound-guided fine needle aspiration. Endosc Ultrasound. 2014;3(1):12–6.
23. Boyce HW. Training in endoscopic ultrasonography. Gastrointest Endosc. 1996;43:S12–5.
24. Coté GA, Hovis CE, Kohlmeier C, et al. Training in EUS-guided fine needle aspiration: safety and diagnostic yield of attending supervised trainee-directed FNA from the onset of training. Diagn Ther Endosc. 2011;2011:378540.
25. Nayar M, Joy D, Wadehra V, et al. Effect of dedicated and supervised training on achieving competence in EUS-FNA of solid pancreatic lesions. Scand J Gastroenterol. 2011;46(7–8):997–1003.
26. Mertz H, Gautam S. The learning curve for EUS-guided FNA of pancreatic cancer. Gastrointest Endosc. 2004;59(1):33–7.
27. Eloubeidi MA, Tamhane A. EUS-guided FNA of solid pancreatic masses: a learning curve with 300 consecutive procedures. Gastrointest Endosc. 2005;61(6):700–8.
28. Fritscher-Ravens A, Cuming T, Dhar S, et al. Endoscopic ultrasound-guided fine needle aspiration training: evaluation of a new porcine lymphadenopathy model for in vivo hands-on teaching and training, and review of the literature. Endoscopy. 2013;45:114–20.
29. Sorbi D, Vazquez-Sequeiros E, Wiersema MJ. A simple phantom for learning EUS-guided FNA. Gastrointest Endosc. 2003;57:580–3.
30. Matsuda K, Tajiri H, Hawes RH. How shall we experience EUS and EUS-FNA before the first procedure? The development of learning tools. Dig Endosc. 2004;16:236–9.
31. Bussen D, Sailer M, Fuchs KH, et al. A teaching model for endorectal ultrasound-guided biopsy and drainage of pararectal tumors. Endoscopy. 2004;36:217–9.
32. Kaufman M, Singh G, Das S, et al. Efficacy of endoscopic ultrasound-guided celiac plexus block and celiac plexus neurolysis for managing abdominal pain associated with chronic pancreatitis and pancreatic cancer. J Clin Gastroenterol. 2010;44(2):127–34.
33. Binmoeller KF, Weilert F, Shah JN, et al. EUS-guided transesophageal treatment of gastric fundal varices with combined coiling and cyanoacrylate glue injection. Gastrointest Endosc. 2011;74:1019–25.
34. Pishvaian AC, Collins B, Gagnon G, et al. EUS-guided fiducial placement for CyberKnife radiotherapy of mediastinal and abdominal malignancies. Gastrointest Endosc. 2006;64(3):412–7.
35. Giovannini M, Bernardini D, Seitz JF. Cystogastrotomy entirely performed under endosonography guidance for pancreatic pseudocyst: results in six patients. Gastrointest Endosc. 1998;48(2):200–3.
36. Giovannini M, Bories E, Moutardier V, et al. Drainage of deep pelvic abscesses using therapeutic echo endoscopy. Endoscopy. 2003;35(6):511–4.
37. Law R, Baron TH. Endoscopic ultrasound-guided biliary interventions: an update on recent developments. Curr Opin Gastroenterol. 2016;7(2):94–102.
38. Wyse JM, Carone M, Paquin SC, et al. Randomized, double-blind, controlled trial of early endoscopic ultrasound-guided celiac plexus neurolysis to prevent pain progression in patients with newly diagnosed, painful, inoperable pancreatic cancer. J Clin Oncol. 2011;29(26):3541–6.
39. Dhir V, Itoi T, Fockens P, et al. Novel ex vivo model for hands-on teaching of and training in EUS-guided biliary drainage: creation of "Mumbai EUS" stereolithography/3D printing bile duct prototype (with videos). Gastrointest Endosc. 2015;81(2):440–6.
40. Chandrasekhara V. Thinking inside the box: 3-dimensional printing for interventional EUS training. Gastrointest Endosc. 2015;81(2):447–9.
41. Baron TH, DeSimio TM. New ex-vivo porcine model for endoscopic ultrasound-guided training in transmural puncture and drainage of pancreatic cysts and fluid collections (with videos). Endosc Ultrasound. 2015;4(1):34–9.
42. Wang MH, Dy F, Vu VK, et al. Structured endoscopic ultrasonography (EUS) training program improved knowledge and skills of trainees: results from the Asian EUS group. Dig Endosc. 2015;27(6):687–91.
43. ASGE Technology Committee, Desilets DJ, Banerjee S, Barth BA, et al. Endoscopic simulators. Gastrointest Endosc. 2011;73(5):861–7.
44. Yusuf TE, Matthes K, Lee Y, et al. Evaluation of the EASIE-R simulator for the training of basic and advanced EUS. Gastrointest Endosc. 2009;69:S264.

Credentialing and Privileging for Gastrointestinal Endoscopic Procedures

54

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Introduction

The field of gastrointestinal endoscopy like many areas of medicine is dynamic and rapidly evolving. Standard endoscopic procedures are being constantly refined, and new techniques and technology are continuously being introduced. Some of these techniques can be easily adopted by practicing endoscopists, while others require more rigorous and formal training under an expert. Endoscopy also covers a diverse number of procedures that can be performed by a variety of providers from gastroenterologists, surgeons, family medicine physicians, internal medicine doctors, to even nurse practitioners. With such a complex, ever-changing field, determining who can perform which procedures safely and effectively is of paramount importance. As such, many of the endoscopic societies have proposed practical guidelines to assist organizations in creating policies for the granting and renewal of endoscopic privileges which will be reviewed in this chapter.

General Principles

Before going into the key areas of endoscopy for which credentialing is required, it is important to define certain terms that are involved, including competence, credentialing, and clinical privileges. Competence, as defined by a combined American College of Gastroenterology and American Society for Gastrointestinal Endoscopy (ACG/ASGE) Taskforce on Quality in Endoscopy, is "the minimal level of skill, knowledge, and/or expertise derived through training and experience that is required to safely and proficiently perform a task or procedure" [1]. Credentialing is the review of evidence that a prospective endoscopist possesses the proper licensure, education, and adequate training to qualify for privileges at an institution and requires competence as a prerequisite. After competence has been achieved and the endoscopist has gone through a credentialing process, clinical privileges or authorization by an institution to perform a particular procedure or service can be granted to those who qualify [2].

How an endoscopist achieves competence to allow for these further steps can vary, but generally requires some formalized training. This is typically accomplished by training under the guide of expert preceptors with a recommended number of procedures performed prior to competence assessment (See Tables 54.1 and 54.2 for the US and international recommendations). Nevertheless, some variations do occur, especially given the rapid development of new techniques and procedures. Most of these techniques are modifications of a basic procedure, such as addition of radiofrequency ablation to upper endoscopy, where most of the clinical skills are already inherent in a capable endoscopist, but do require some additional knowledge that can be obtained outside of formalized training. Other techniques require new skills and knowledge that should only be obtained in a formalized setting like a fellowship or preceptorship, such as endoscopic submucosal dissection, etc.

Maintenance of clinical privileges for endoscopic procedures is the responsibility of the granting institution and is typically mandated to occur every few years. The goals of this requirement are to ensure continued clinical competence, promote continuous quality improvement, and maintain patient safety [2, 13]. While no formal guidelines exist for this purpose nor are there any required number of procedures required to maintain competency, granting institutions should take into account procedurally related quality benchmarks as well as outcomes of a particular endoscopist. In the event a previously credentialed endoscopist demonstrates inadequate competence for a procedure or their competence cannot be adequately assessed, then clinical

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Table 54.1 Minimum numbers of common endoscopic procedures required prior to competence assessment by country

Procedure	USA [2]	Surgery (USA) [3]	Primary care (USA) [4]	Canada [5–8]	Australia [9]	Europe [10]	Poland [11]	India [11]
EGD	130	35	35	100	200	200	500	190
Colonoscopy	275	50	50	150	100	200	500	120
ERCP	200	–	–	200	200	100	200	140

– did not stipulate, *EGD* esophagogastroduodenoscopy, *ERCP* endoscopic retrograde cholangiopancreatography

Table 54.2 Comprehensive list of number of procedures required prior to competence assessment for countries with established guidelines

Procedure	USA [2]	Canada [5–8]	Australia [9]	Europe [10]
EGD Variceal bleeding Nonvariceal bleeding	130 25	100 20 20	200 20 (therapeutic including for bleeding)	200 30 (combined variceal and nonvariceal)
PEG tube placement	20	20	–	15
Flexible sigmoidoscopy	30	30	–	50
Colonoscopy Polypectomy	275 - (30 polypectomies for upper/lower [12])	150 30	100 30	200 50 (interventions including polypectomy or hemostasis)
ERCP Sphincterotomy Stent placement	200 80 60	200 80 60	200 80 60	100 75 30
EUS FNAs Pancreaticobiliary Mucosal cancer Subepithelial lesion	225 50 75 75 40	200 50 100 - -	200 50 100 - -	250 50 - - -
Capsule endoscopy	20	20	50	30
Luminal stent placement	10	–	–	10
Ablative techniques (i.e., RFA)	30	–	–	–
Endoscopic mucosal resection	20	–	–	–
Deep enteroscopy	20-lower 10-upper	–	–	–
Moderate sedation	20	–	–	–

– did not stipulate, *EGD* esophagogastroduodenoscopy, *ERCP* endoscopic retrograde cholangiopancreatography, *EUS* endoscopic ultrasound, *FNA* fine needle aspiration, *RFA* radiofrequency ablation

privileges may be revoked. Recredentialing for such privileges has not been specifically studied, but some form of remediation is necessary with competence subsequently assessed by a qualified endoscopist.

Esophagogastroduodenoscopy

Depending on the society, a minimum of 35–200 procedures are recommended prior to assessment of competence for EGD [2, 3, 5, 9, 10].This wide range likely represents the diverse uses of this procedure from assessing anatomy prior to upper gastrointestinal surgery to therapeutic interventions such as variceal hemostasis. Most of the nonsurgical societies have further divided this procedure into standard interventions which are limited to basic inspection with biopsy sampling, control of hemorrhage, esophageal dilation, snare polypectomy, and PEG tube placement. Therapeutic interventions such as pneumatic dilation, luminal stent placement, radiofrequency ablation, complex polypectomy, endoscopic mucosal resection or submucosal dissection, and peroral endoscopic myotomy are felt to require separate credentialing and monitoring to retain privileges [14].

Flexible Sigmoidoscopy

Flexible sigmoidoscopy is essentially a limited colonoscopy, so proficiency in colonoscopy implies competence in it as well. However, flexible sigmoidoscopy, unlike other endoscopic procedures, has previously been taught to non-endoscopists in order to help decrease the burden of colon cancer screening. Many societies have recommendations regarding competence in sigmoidoscopy. In general, 30 procedures are

recommended prior to assessment of competence with benchmarks including the ability to perform a full examination of the left side of the colon including a retroflexed view of the rectum, obtain targeted biopsy specimens, and achieve a consistent insertion depth to more than 50 cm [2]. Further privileging is necessary for other interventions such as hemorrhoidal banding or luminal stent placement, etc.

Colonoscopy

Colonoscopy is inherently a more technically challenging or difficult procedure to learn, and most endoscopic societies have recommended that more than 150 procedures be performed prior to assessment of competency. Despite this requirement, some data have shown that many endoscopists do not achieve technical competence until 500 procedures have been performed [15]. Expected skills for credentialing include the ability to perform full examination of the colon (including retroflexed view of the rectum), obtain targeted biopsy specimens, perform snare polypectomy, and control bleeding. More advanced skills requiring additional credentials include stricture dilation, luminal stent placement, and endoscopic submucosal dissection [2, 6].

The assessment of competence and maintaining privileges for colonoscopy relies on the ability of an endoscopist to perform a quality examination. Quality indicators in their guidelines have addressed by most societies including the American Gastrointestinal Association which has published its version recently. It encompasses 15 indicators with the notable ones including ≥95% cecal intubation rate for screening examination, ≥25% adenoma detection rate (both men and women), post polypectomy bleeding rate < 1%, and perforation rate less than 1:1000 [16]. While assessment of indicators is important in maintaining privileges, such broad-based measures are imperfect and likely can overestimate the quality of a particular endoscopist. On the other hand, what to do if an endoscopist does not meet these criteria is also unclear! If a benchmark is not met, resolution could involve a change in mentorship or additional training in colonoscopy (Endoscopy Society organized courses) or may require remediation if more related to technique.

Endoscopic Retrograde Cholangio-Pancreatoscopy (ERCP)

ERCP is an advanced endoscopic technique for the evaluation of biliary and pancreatic disease and is one with the most technically challenging procedures and the one with the highest complication rate. As a result, assessment of competence is vital prior to granting privileges for such procedures. Endoscopy societies vary somewhat in the number of procedures needed prior to competence assessment, but most agree that some endoscopists do not achieve target goals until 300–400 procedures have been performed [17]. These targets include achievement of selective cannulation of the duct of interest (recommended 80–90%), accurate interpretation of endoscopic and radiologic images, and successful therapeutic interventions, i.e., sphincterotomy, relief of biliary obstruction, and/or stent placement (at least 85% of the time). Maintaining such competence is also a challenge as evidenced by the increased rate of complications seen with endoscopists who perform less than 40–50 ERCP procedures annually [18].

Practical Considerations

- Therapeutic interventions such as pneumatic dilation, luminal stent placement, radiofrequency ablation, complex polypectomy, endoscopic mucosal resection or submucosal dissection, and peroral endoscopic myotomy require separate credentialing and monitoring.
- With regard to flexible sigmoidoscopy, further privileging is necessary for interventions such as hemorrhoidal banding or luminal stent placement.
- The assessment of competence for colonoscopy relies on the ability of an endoscopist to perform a quality examination and not a quick in and out procedure.

Endoscopic Ultrasound (EUS)

EUS is one of the newer major technologic advancements in endoscopy and allows for diagnostic evaluation of a variety of GI and non-GI-related disorders as well as provides a means for therapeutic interventions such as pancreatic cyst drainage or biliary access. With such a diversity of disease states to be assessed, a minimal number of procedures to assess competence must be subdivided into different areas such as pancreatobiliary disease, subepithelial lesions, and mucosal cancer staging. The major societies all have such recommendations (see Table 54.2) with further stipulation that endoscopists who perform such procedures should understand the indications, applications, contraindications, adverse events, and proper alternatives to an EUS examination [2, 7, 9, 10]. Depending on whether the endoscopist will use ultrasound-based techniques for advanced therapeutics such as pancreatic cyst drainage or image-guided biliary or pancreatic duct access will also have to be taken into account when granting privileges. As the therapeutic possibilities of EUS continue to evolve, this may become an area of

controversy regarding credentialing in the future, and such procedures may be limited to academic centers until proper competency thresholds can be established.

Practical Considerations

- Endoscopy societies vary somewhat in the number of ERCP procedures needed to be performed prior to competence assessment, but most agree that some endoscopists do not achieve target goals until 300–400 procedures.
- As the therapeutic possibilities from EUS continue to evolve, this may become an area of controversy regarding credentialing, and such procedures may be limited to academic centers only.

Other Endoscopic Interventions

Within endoscopy there are several therapeutic interventions as well as imaging techniques that encompass many of the skills inherent to a general endoscopist, but also require some additional skills and knowledge such that many of the sponsoring societies recommend competence evaluation prior to credentialing. Examples of such procedures would be ablative techniques for Barrett's esophagus including radiofrequency ablation, cryotherapy, or argon plasma coagulation. In these examples, the interventions are not difficult to learn, but experience from performing such procedures will ensure that the endoscopist only uses these techniques in appropriate situations, i.e., does not ablate if there is a nodule (could bury a mucosal-based cancer), and is aware of the complications and how they are managed. For such procedures, the number required prior to competence evaluation is not excessive with most societies recommending anywhere from 20 to 30 procedures performed [2, 9, 10]. The procedures that such guidelines address include endoscopic mucosal resection, ablative therapies, capsule endoscopy, and deep enteroscopy. Of these procedures, capsule endoscopy is unique in that it is not a procedure that the endoscopist performs, rather it is one the endoscopist interprets and again highlights that a minimal amount of experience and familiarity is required for such procedures to be performed satisfactorily.

One technique without any evidence regarding the specific number of procedures required prior to competence assessment is enteral stent placement. While not an overly difficult procedure, it does bear some special consideration. First, it does require familiarity with the use of fluoroscopy as a necessary prerequisite, and some endoscopists may not have such familiarity. More importantly, stent placement may be associated with significant complications including bleeding, perforation, stent migration, and stent occlusion with tissue ingrowth. As such, any endoscopist who wishes to perform stent placement needs to be able to manage such complications with the ASGE recommending expertise in removal/repositioning of stents, placement of additional stents, stricture dilation, and bleeding control. Despite such issues, the ASGE recommends only ten procedures prior to assessing competence; however, many credentialing institutions will revoke privileges if an endoscopist does not regularly perform this procedure [2].

Motility Studies

There are no specific guidelines regarding credentialing for gastrointestinal motility tests. However, the current guidelines for gastroenterology fellowship training in motility divide the level of training in motility tests into two levels [19]. Level 1 is basic training that all gastroenterology fellows should be able to perform. Level 2 is for those who seek to be true experts in the performing motility studies and management of gastrointestinal motility and functional disorders. For level 2 training, the number for required procedure varies from 50 for esophageal manometry to 10 for anorectal biofeedback (see Table 54.3). However, this guideline is old (from 2007), and since then more studies have become available in the practice. The number needed to be comfortable with some newer studies has been suggested by motility experts [20] (see Table 54.4). Despite no formal guidelines regarding credentialing for the motility studies, it is reasonable to consider this guideline and recommendations for motility experts as a guide for credentialing in the hospital.

Future Procedures

As endoscopic procedural techniques continue to be developed and refined, credentialing for such procedures will also need to be continuously refined accordingly. Even now there are several procedures that are performed by endoscopists where consensus recommendations for minimum requirements are

Table 54.3 Guidelines for level 2 training in motility

Study	Number required
Esophageal manometry	50
Gastric and small bowel motility studies	25
Gastric emptying scintigraphy	25
Colonic motility studies	20
Anorectal manometry	30
Anorectal biofeedback training	10
Colonic transit time study	20

Table 54.4 Other motility studies to be done by experts

Study	Number required
Wireless motility capsule test	50
Impedance esophageal pressure topography	50
Impedance pH metry	50
Esophageal balloon distention test	25
Breath tests	25 for each breath test.
Gastric electrical stimulation for gastroparesis and sacral nerve stimulation for fecal incontinence	10
Esophageal pH metry	25
Gastroduodenal manometry	25

not defined. Most of these procedures are emerging technologies, such as transoral incisionless fundoplication, an endoscopic serosa-serosa plication of the upper stomach to create a valve, which are not widely performed. But, if such a procedure is widely adopted, then objective criteria of competency should be developed. Unfortunately, there is a gap between implementation of the procedure by endoscopists and recommendations from the major endoscopic societies. In such a case, as it is with all endoscopic credentialing, the decision is ultimately up to the local institution governing an endoscopist, and variations are to be expected based on need, resources, and local expertise. As the landscape of endoscopy continues to change with increasing focus on safety and quality of procedures currently available and an increasing trend for minimally invasive endoscopic approaches to traditionally surgical interventions, credentialing will only become more important to ensure only qualified providers are granted privileges.

Conclusions

Gastroenterology is a rapidly evolving field and is heavily procedure based. The standard endoscopic procedures are being constantly refined, and new techniques and technology are continuously being introduced. Some of these techniques can be easily adopted by practicing endoscopists, but others require more rigorous and formal training under an expert. As the technology improves, newer procedures are added to the list of currently available techniques. We strongly urge the endoscopy societies across the world to keep pace with these developments.

References

1. ASGE/ACG Taskforce on Quality in Endoscopy. [November 27, 2007]. Ensuring Competence in Endoscopy.
2. Faulx AL, Lightdale JR, Acosta RD, et al. Guidelines for privileging, credentialing, and proctoring to perform GI endoscopy. Gastrointest Endosc. 2017;85:273–81.
3. Pearl J, Fellinger E, Dunkin BJ, et al. Guidelines for privileging and credentialing in gastrointestinal endoscopy. Soc Am Gastrointest Endosc Surg. 2016;30(8):3184–90.
4. America Academy of Family Physicians Position Statement: EGD, Training and Credentialing of Family Physicians In. AAFP.org (Accessed 3 2017).
5. Ponich T, Enns R, Romagnuolo J, et al. Canadian credentialing guidelines for esophagogastroduodenoscopy. Can J Gastroenterol. 2008;22:349–54.
6. Romagnuolo J, Enns R, Ponich T, et al. Canadian credentialing guidelines for colonoscopy. Can J Gastroenterol. 2008;22:17–22.
7. Arya N, Sahai AV, Paquin SC. Credentialing for endoscopic ultrasound: a proposal for Canadian guidelines. Endosc Ultrasound. 2016;4:4–7.
8. Springer J, Enns R, Romagnuolo J, et al. Canadian credentialing guidelines for endoscopic retrograde cholangiopancreatography. Can J Gastroenterol. 2008;22:547–51.
9. Conjoint Committee for recognition of training in gastrointestinal endoscopy. Gastroenterological Society of Australia 2015. Web 23 April 2017.
10. Vilstrup H, Jeppesen P, Nyenberg D, et al. The European section and Board of Gastroenterology and Hepatology Training Programme: the blue book. United European Gastroenterol J. 2017;5(3):459–60.
11. Faigel DO, Cotton PB. London OMED guidelines for credentialing and quality assurance in digestive endoscopy. Endoscopy. 2009;41:1069.
12. Eisen GM, Baron TH, Dominitz JA, et al. For the American Society for Gastrointestinal Endoscopy methods of granting hospital privileges to perform gastrointestinal endoscopy. Gastrointest Endosc. 2002;55:780–3.
13. Shahidi N, Ou G, Telford J, et al. When trainees reach competency in performing ERCP: a systemic review. Gastrointest Endosc. 2015;83:1137–42.
14. Park WG, Shaheen NJ, Cohen J, et al. Quality indicators for EGD. Gastrointest Endosc. 2015;81:17–30.
15. Spier BJ, Benson M, Pfau PR, et al. Colonoscopy training in gastroenterology fellowships: determining competence. Gastrointest Endosc. 2010;71:319–24.
16. Rex D, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. Am J Gastroenterol. 2014;0:0–0.
17. Verma D, Gostout CJ, Petersen BT, et al. Establishing a true assessment of endoscopic competence in ERCP during training and beyond: a single-operator learning curve for deep biliary cannulation in patients with native papillary anatomy. Gastrointest Endosc. 2007;65:394–400.
18. Freeman ML, DiSario JA, Nelson DB, et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. Gastrointest Endosc. 2001;54:425–34.
19. A journey toward excellence: training future gastroenterologists. Available at: http://gi.org/wp-content/uploads/2011/07/fellows-GICoreCurriculum.pdf.
20. Rao SS, Parkman HP. Advanced training in neurogastroenterology and gastrointestinal motility. Gastroenterol. 2015;148(5):881–5.

The Future of Endoscopy

55

Megan McKnight and Pankaj Jay Pasricha

Introduction

We live in tumultuous times, and as recent political events can attest to, making predictions about the future can be particularly hazardous. Therefore, although this chapter will attempt to convey our thoughts and impressions about where gastrointestinal endoscopy is headed, it would perhaps be more important to provide an (entirely idiosyncratic) opinion on where it should be headed.

The Present: For Most, the Future Never Comes or Is Worse

Numerous chapters in this book describe how far we have come with endoscopic techniques and approaches, and we all need to take pride in these accomplishments. However, it is sobering to also recount how little progress we have made in the procedures that the vast majority of gastroenterologists spend their time doing, such as screening colonoscopy. Medicine is a public trust and this is perhaps no truer than when patients expect us to reassure them that they do not have life-threatening diseases such as cancer. The unspoken understanding between the gastroenterologist (despite perfunctory caveats in the consent form) and the patient undergoing screening colonoscopy is therefore simple and understand: in exchange for a day or two of unpleasant preparation and time off for the endoscopy itself, a procedure will be performed which will more or less eliminate the risk of cancer for at least 10 years. Yet, as a multitude of studies have shown, the procedure still misses 5–10% of large polyps, possibly cancerous in nature. This is unacceptable for a procedure that the profession proudly declares as the "gold standard" whenever alternative methods of screening are proposed. There are many reasons for such a high miss rate, but all converge on the most proximate cause – the failure to visualize all of the colonic surface area – and all are amenable to a solution that is comfortably within our current technological abilities. Endoscopists and the endoscope industry by and large have been reluctant to embrace even the incremental improvements that recent small-scale innovations have tried to introduce into the market. Indeed, such is our complacency (or perhaps insecurity) that we have not even asked for a simple tool to document exactly what proportion of the colonic mucosa was not seen by us during the course of any given colonoscopy. This is analogous to interpreting a CT abdomen and not knowing whether the entire organ in question was actually imaged, a situation which radiologists would find unacceptable. We must therefore be proactive in demanding such changes to display our respect for the trust patients put in us, or else, others will demand these at our cost.

Our attitude to our "bread and butter" procedures also has a direct effect on the costs of healthcare which is increasingly straining our social systems. The simplicity and safety of most routine endoscopies, coupled with a fee-for-service incentive system, has led to tremendous waste in terms of duplicate and unnecessary procedures for common and benign conditions. Patients with reflux disease (and no Barrett's) undergoing multiple upper endoscopies just as patients with chronic abdominal pain are subject to several colonoscopies, all in the interest of "making sure we are not missing something." Embarrassingly, only one of our professional societies (the AGA) has even bothered to participate

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in the "choosing wisely" initiative of the American Board of Internal Medicine, and even so, these commonly overused practices are not questioned (although the AGA does recommend no further CT imaging for patients with functional abdominal pain, remaining silent on the need for multiple endoscopies). Other professional societies such as the ASGE and ACG are conspicuous by their absence in this effort.

Similarly, we have nearly doubled the cost by the push for requiring monitored anesthesia care (MAC) for simple and short (10–20 min) procedures, a change that has nearly doubled the cost of these procedures. This practice is an example of "if it's not broken, don't fix it." Conscious sedation, performed by the endoscopist, was adequate for the vast majority of routine procedures and is still offered to most patients in the world including much of the developed world. Although proponents often cite "safety" as the motivation for having MAC, other considerations must be at play since recent studies have shown that the overall risk of complications after colonoscopy including perforations but also cardiovascular events is higher when individuals receive anesthesia services as compared with those who receive standard sedation. Thus, as a profession, we have wittingly, or not, undermined the very elements (simplicity and safety) which made flexible gastrointestinal endoscopy so appealing in the first place.

The Near Future: The "Technicalization" of Advanced Endoscopists

Beyond diagnostic procedures, it is clear that "interventional endoscopy" has continued to steadily follow the direction laid out by trailblazers several decades ago when complex surgical procedures were replaced by simpler endoscopic ones. Examples include variceal ligation/ablation instead of portacaval shunts, biliary stents instead of bypass surgery, and percutaneous gastrostomy instead of surgical placement. We are now in an era where endoscopic approaches to myotomy are being embraced as first-line therapy instead of a laparoscopic Heller operation, and mucosal resections are increasingly being substituted for surgical resection. These are highly desirable and laudable advances that should be hailed by professionals and patient alike. Advanced endoscopists are increasingly adopting more aggressive approaches to lesions that were once the target of traditional surgery, commensurate with quantum improvements in available tools and skill sets.

There is perhaps a darker side of this trend that may be worth pondering. We are producing an entire generation of endoscopic technocrats who not only lack surgical training (and the rigor and deep anatomical insight that comes with it) but also a robust physiological grounding. While one could make up in part for the former, it is the latter lacuna that may become more constraining for the growth of this discipline. A question I often ask young endoscopists who seek career advice from me is if they want to be an architect or a mason when thinking about constructing a building. While the latter is necessary, it is not sufficient. To be able to make a truly beautiful monument, however, one has to equip oneself with a much more sophisticated set of skills and ideally have both, such as Filippo Brunelleschi, one of the fathers of modern architecture and discoverer of the linear perspective, who transitioned from goldsmith to the foremost designer of the Renaissance period. Most of the unmet needs in gastroenterology are not amenable to simplistic anatomical remodeling such as cutting sphincters. The experience with so-called sphincter of Oddi dysfunction illustrates the peril of this approach in solving a complex problem such as chronic abdominal pain. Similar caveats apply to the emerging trend of pyloric sphincterotomy to treat patients with gastroparesis. If we are to use the great endoscopic tools that we have wisely and effectively, then we must get grounded in the physiology and pathophysiology of what we are targeting. The importance of this is discussed in the next section.

Transforming Disease Rather than Procedure Paradigms: The Future of Endoscopy for Gastroenterological and Systemic Disorders

There is no question that as a group, functional and motility disorders constitute the largest unmet medical need in our specialty and represent a huge burden of suffering and cost. However, we remain in the "dark ages" as far as these syndromes are concerned with little insight into their pathogenesis and few therapeutic options. Endoscopy can play several important roles here. First, by providing simple and safe access to the deeper layers (muscle and myenteric plexi), we can begin to understand the pathological basis for these disorders in a comprehensive manner. Our prediction is that such an approach will be as transformative for this field as routine liver biopsies were for modern hepatology. Further, such access can also provide us the means to modulate the nerves and muscles in clinically impactful ways.

Beyond the gut, we also have the opportunity now to influence systemic health with the recognition of the gut-brain axis and the gut-metabolic axis. With a broader understanding of the physiology underlying these connections, it is not difficult to imagine how we can use endoscopic approaches to modulate behavior, stress responses, and mood as well as fatty liver and insulin resistance, going beyond current anatomy-based efforts.

Conclusions and Implications for Training

While it is always important to look ahead and plan accordingly, we must not ignore what we are neglecting in our rush for better and more technology. This includes our current set of staple procedures as well as highly prevalent gastrointestinal disorders. Clearly, as advanced endoscopists, we are improving in our ability to provide alternatives to surgery, but by our single-minded obsession with technology, there is no reason why next-generation tools may replace us as well. We are gastroenterologists first and foremost – endoscopes and their accessories are simply the current tools we have and a means rather than an end. We must improve on these tools and build better ones, but more importantly we need to understand the target before getting to work on it.

It is also worth considering that "advanced" is a relative term that changes with time; many of the techniques we routinely perform in the community (such as polypectomy) were considered advanced and high risk when first introduced. Similarly, many techniques that today are relegated to an additional year of training can be translated into the skill sets of most of our graduating class of fellows. Conversely, we must give far more attention for all fellows to have a comprehensive training in the physiology and pathophysiology of these disorders. So rather than continuing the current trends toward "dichotomization" of our specialty – those with advanced endoscopic skills and those without – perhaps it is time to consider how to better integrate both science and technology into the training of all gastroenterologists; this requires more of a true commitment by fellowship programs rather than any drastic changes in the length of the fellowship. As a trained "therapeutic" endoscopist and an enteric neuroscientist, we firmly believe that endoscopy, our specialty and medicine in general, will be greatly enriched by such an approach.

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