Matthew Kroh
Kevin M. Reavis *Editors*

The SAGES Manual Operating Through the Endoscope

Springer

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To my wife, Jean, for her love and support, and to our wonderful children, Sophia, Eva, and Carter, who fill me with joy.

–Matthew Kroh, MD, FACS

This book is dedicated to the SAGES family of surgeons committed to excellence in surgical endoscopy. I am most grateful to my amazing wife Kelly, to our wonderful son Nathan, and to my dedicated partners and professional friends whose collective support allowed this book to become a reality.

–Kevin M. Reavis, MD, FACS

Preface

Advances in care for gastrointestinal disorders continue to evolve. With the advent of laparoscopy and widespread adoption in the 1990s, an era of minimally invasive surgery commenced. Since then refinements in technique and instruments have allowed us to perform more complicated procedures across a broad spectrum of disease processes. Improved outcomes such as diminished postoperative pain, faster return to preoperative activities, and decreased perioperative complications have all promoted adoption of these operations.

In an effort to further improve upon these results for our patients, new technologies including robotics, single-site surgery, and natural orifice translumenal endoscopic surgery (NOTES™) have also been explored. Based on diminishing access site trauma, these procedures have further encouraged the development of new tools and operating paradigms.

Endoscopy allows access to the gastrointestinal tract without transgressing the abdominal or chest walls, by means of a truly less invasive route. Recent significant advances in endoscopic tools and methods are allowing endoscopists to perform an expanding array of procedures. From combining endoscopic ultrasound (EUS) with endoscopic retrograde cholangiopancreatography (ERCP) to diagnose and treat hepato-biliary disease, to removing cancerous lesions *en bloc* without making any incisions, these techniques more closely resemble traditional surgery. Endoscopy has advanced from diagnostic and rudimentary interventions to operations that are now performed through the scope.

This text is unique in that it examines advanced interventional endoscopy across a broad spectrum of GI tract diseases. Written by pioneers and recognized experts in these new, rapidly evolving fields, each chapter focuses on the specific conduct involved and available data supporting these innovative procedures. We are grateful for the participation of these esteemed endoscopists, and

we understand that through the efforts of such luminaries, we can continue to advance this field.

We hope that you enjoy this comprehensive resource on cutting-edge, minimally invasive operations for GI tract disorders.

Cleveland, OH, USA — Matthew Kroh
Portland, OR, USA — Kevin M. Reavis

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Part I
Introduction to Operative Endoscopy

1. Surgical Endoscopy: A Historical Perspective

Jeffrey L. Ponsky and John H. Rodriguez

Background

Modern endoscopy of the gastrointestinal tract is about 100 years old. Rudolph Schindler introduced techniques and descriptions of examination of the esophagus and stomach utilizing semiflexible instruments [1]. Developments in flexible optical technology and in the understanding of gastrointestinal disease have led to the ability to perform sophisticated assessment of the gastrointestinal tract with the evaluation of normal and abnormal anatomy, the effects and progression of disease processes, and the capability to intervene in the diagnosis and treatment of pathological conditions.

To be sure, the majority of gastrointestinal endoscopic procedures performed today are done so by medical gastroenterologists. This is entirely appropriate. However, the role of surgeons in the development of therapeutic endoscopy and the utilization of these techniques in the care of their patients are indisputable. An examination of the influence of surgeons and surgical thinking in evolution of diagnostic and therapeutic gastrointestinal endoscopy will clearly elucidate the importance of endoscopy in surgical practice and of the surgeon in advancing the field.

History

While gastroenterologists such as Schindler clearly added tremendously to the techniques for examination of the esophagus and stomach, it was the surgeon who first dealt with therapeutic interventions in the

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gastrointestinal tract. Chevalier Jackson, a noted otolaryngologist and endoscopist in Philadelphia, described the methods for utilizing rigid endoscopes to remove foreign bodies of the gastrointestinal tract [2]. Many of the principles he described over a century ago remain crucial to the management of foreign bodies with flexible instruments today.

In the late 1950s Basil Hershowitz developed the first workable flexible endoscope utilizing fiber-optic technology [3]. Robert Turell, a colorectal surgeon, was the first to employee this technology in the examination of the colon. Colonoscopy was rapidly adopted and refined by gastroenterologists such as Bergein Overholt of Knoxville Tennessee, and the ability to perform cecal intubation became commonplace. It was two surgeons, Hiromi Shinya and William Wolfe of New York, however who first added a therapeutic dimension to colonoscopy by describing and publishing a large series of colonoscopic polypectomies [4]. This step revolutionized the treatment of colonic neoplasia and led to other major advances in therapeutic endoscopy. The first report of endoscopic injection for marking neoplastic colonic lesions was published by Ponsky, a surgeon, in 1975 [5]. This facilitated finding the site of previously resected malignant polyps.

As diagnostic endoscopy of the esophagus, stomach, and duodenum matured, definition of the source of gastrointestinal hemorrhage became routine. Therapeutic intervention, at first with monopolar coagulation, was described by John Papp, a gastroenterologist, and by Walter Gaisford, a surgeon. Bipolar technology and heater probes which delivered a more predictable and safer result soon followed. Other methods such as injection of alcohol as described by the surgeon Choichi Sugawa of Detroit were also shown to be effective [6]. With time, other surgical technologies such as application of clips and suturing were applied to the treatment of bleeding lesions and resection sites. A simple solution to a surgical problem using endoscopy was introduced by Michael Gauderer and Jeffrey Ponsky of Cleveland, Ohio with the description of percutaneous endoscopic gastrostomy (PEG) [7].

Endoscopic retrograde cholangiopancreatography is a sophisticated intervention with numerous therapeutic applications. Although there are only a few surgeons actively practicing the method, it is of note that the technique was first described by the surgeons Shorb and McCune of Washington DC [8], and that numerous advances in the method have been introduced by surgeons. These have included the description of endoscopic biliary stenting by Nib Soehendra of Hamberg Germany and advances in the management of biliary strictures and leaks by Gary Vitale and Guido Costamagna [9, 10].

As the era of minimally invasive and videoscopic surgery progressed, the integration of flexible gastrointestinal endoscopy into the performance of procedures and management of surgical problems expanded. Surgeons used endoscopes as invaluable and indispensable tools to facilitate their surgery and manage old problems in new ways.

The concept of Natural Orifice Transluminal Surgery (NOTES) was extremely provocative and stimulated much research and development of new techniques and technology. Although most of these methods have not become widely practiced to date, many advances of the period have led to other techniques such as single-site surgery, full-thickness endoscopic resection, endoscopic mucosal resection, and endoscopic submucosal dissection. Perhaps the newest procedure to have evolved from the concept of NOTES is peroral endoscopic myotomy for achalasia (POEM). First performed by the thoracic surgeon Haruhiro Inoue of Yokahama Japan, this intramural endoscopic procedure has gained wide popularity in the management of achalasia [11].

It is clear from the examination of the history and practice of gastrointestinal endoscopy that surgeons have played an ongoing and integral role. Surgeons use endoscopy to provide optimal therapy for their patients and to solve surgical problems. It is imperative that surgeons remain involved in the practice and development of endoscopic technique.

References

1. Schindler R. Ein vollig ungefahrliches flexibles Gastroskop. Munch Med Wochenschr. 1932;79:1268–9.
2. Jackson C. Foreign bodies in the trachea, bronchi and esophagus: the aid of bronchoscopy, esophagoscopy and magnetism in the extraction. Laryngoscope. 1905;15:527.
3. Hirschowitz BI, Curtiss LE, Peters CW, et al. Demonstration of a new gastroscope, the "fiberscope". Gastroenterology. 1958;35:50–3.
4. Wolff IW, Shinya H. Colonofiberoscopy. JAMA. 1974;217:1509–12.
5. Ponsky JL, King JF. Endoscopic marking of colonic lesions. Gastrointest Endosc. 1975;22:42–3.
6. Sugawa C, Lucas CE, Walt AJ. Serial endoscopic observation of the effects of histamine, aspirin, steroids, and alcohol on standardized gastric ulcers in dogs. Gastrointest Endosc. 1971;18(2):56–8.
7. Gauderer MW, Ponsky JL, Izant Jr RJ. Gastrostomy without laparotomy: a percutaneous endoscopic technique. J Pediatr Surg. 1980;15:872–5.
8. McCune WS, Shorb PE, Moscovitz H. Endoscopic cannulation of the ampulla of vater: a preliminary report. Ann Surg. 1968;167(5):752–6.

9. Soehendra N, Rynders-Frederix V. Palliative bile duct drainage: a new endoscopic method of introducing a transpapillary drain. Endoscopy. 1980;12:8.
10. Vitale GC, Stephens G, Wieman TJ, Larson GM. Use of endoscopic retrograde cholangiopancreatography in the management of biliary complications after laparoscopic cholecystectomy. Surgery. 1993;114(4):806–12.
11. Inoue H, Minami H, Kobayashi Y, Sato Y, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42(4):265–71.

2. Endoscopic Tools: Instruments

Michael Paul Meara and Vimal K. Narula

Introduction

As a prelude to any focused discussions of endoscopic procedures, one must be familiar with the instrumentation necessary to complete those tasks. This chapter provides a cursory overview of endoscopic instrumentation and creates a basis for tools which are available to an endoscopist. This chapter is not meant to be exhaustive, but provides a framework from which to draw upon as one begins to perform endoscopic techniques within their practice. Each instrument discussed provides a description of the instrument as well as a brief overview of potential applications. Images are provided to assist in the reader's familiarity with the instrument, but will vary from manufacturer to manufacturer. Many of the procedures and techniques mentioned will be discussed in-depth in chapters later in the handbook. As endoscopic procedures continue to evolve, the instrumentation will continue to change and adapt to meet the endoscopist's specific needs.

Channel Sizes

Prior to embarking on a discussion about instruments available for the endoscopy, a brief discussion is required as to the sizes of channels available on an endoscope and instruments which they will accommodate. Smaller endoscopes, such as those utilized in choledochoscopy, may have working channels as small as 1.2 mm in size. This will significantly limit the size of instruments which the endoscope can utilize. In these instances, specific instruments and pre-packaged kits are available. Diagnostic channel sizes are normally 2.8 mm in size and size increases as the need for additional therapeutics increases. Channel sizes as large

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as 6.0 mm can be utilized for foreign body removal as well as evacuation of blood and other semiliquid substances. Knowledge of the standard channels sizes being utilized within the endoscopy suite will help you tailor those tools you most frequently use [1].

Standard Instruments

Forceps

The most basic and common instrument utilized in endoscopy is forceps. This device has been augmented over time and from company to company, but in its basic design is comprised of two teethed jaws which close upon the object of interest. This is achieved by an extension and closure mechanism at the handle. The object of interest may be a foreign body requiring removal/manipulation or tissue which it is necessary to sample or remove (Figs. 2.1, 2.2, and 2.3).

Biopsies can be performed in a variety of ways. These include cold biopsies, which are extracted by a simple, sharp withdrawal of the closed device with hemostasis reliant on the body or subsequent endoscopic

Fig. 2.1. A typical forceps handle mechanism. This specific forceps has a connection for electrocautery should it be desired.

Fig. 2.2. An open forceps instrument.

Fig. 2.3. An open forceps instrument with a barb to allow for repeat samples without needing to remove the forceps.

intervention. Biopsy forceps have been augmented to include a single barb in the center of the jaws which allow for a second, repeat biopsy to be performed prior to complete withdrawal of the forceps. Other biopsy forceps may include a connection for the application of electrocautery. Care should be taken with the decision to apply electrocautery as this has the possibility to distort anatomy and pathology as well as cause various degrees of injury, including perforation [2, 3].

Snare

Another commonly utilized tool in endoscopy is the endoscopic snare. This instrument is comprised of a metal wire, either in a single loop or multiple loops, used for extraction or biopsy. The composition of the loops varies based on manufacturer, and the conductive metal may either be braided or monofilament in nature. The loops are transmitted via the channel in a closed fashion in a protective plastic insulating tube. Snares are made in a variety of loop sizes and configurations. The amount of loop extended from the protective sheath is controlled by an extension and closure mechanism at the handle (Figs. 2.4, 2.5, and 2.6).

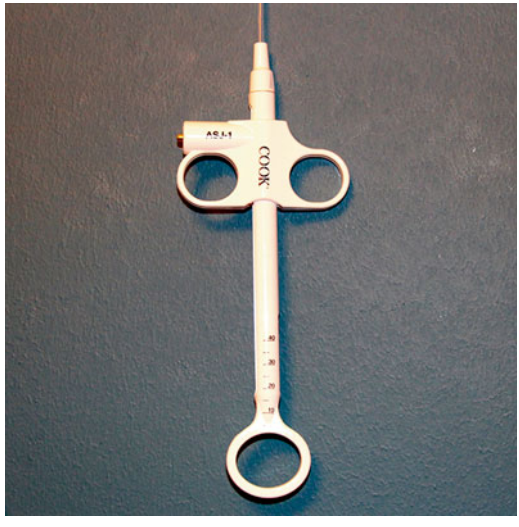

Fig. 2.4. A representation of a standard snare handle. This specific snare has a connection for electrocautery should it be desired.

Fig. 2.5. A snare protected in the protective plastic sheath. This is representative of the protective sheaths used in a wide variety of instrumentation.

Fig. 2.6. A typical snare open with the ability to ensnare a target lesion.

Like the forceps, biopsies can be performed in a variety of ways utilizing snare devices. These include cold snares for resection of flat or polypoid lesions of small size. Hemostasis can be reliant on the patient's coagulation mechanisms or by the application of an endoscopic clip. Larger lesions may require the application of electrocautery to the snare for coagulation of the base of the lesion as the snare is tightened. Dependent on the configuration of the lesion, larger, flat lesions may require a saline lift technique, where saline is injected under the mucosa to raise the lesion and to help prevent the potential of perforation.

Once lesions have been separated from the mucosa via this variety of techniques, the tissue must be retrieved. Small lesions can be suctioned through the scope and collected at the connection of the suction device and the endoscope. For larger lesions, other devices such as a mesh net may be used to retrieve these lesions, but necessitate withdrawal of the scope in its entirety [2, 3].

Injection Catheter

A common tool with multiple possible applications is the endoscopic injection needle. This instrument is comprised of a needle which is encased by a protective outer plastic sheath. The amount of needle extended from the protective sheath is controlled by an extension and closure mechanism at the handle. At the end of the device a syringe can be attached and a wide array of substances can be transmitted via the device.

There are multiple applications of the injection needle. The needle may be utilized for a submucosal injection to lift an area of suspicion, making it more easily and safely accessed by other instruments. This application has become quite useful in the setting of endoscopic mucosal resection (EMR) and per oral endoscopic myotomies (POEM). It can be loaded with dye and utilized for preoperative marking, making localization intraoperatively more straightforward. In the setting of bleeding, vasoactive medications can be injected around the area of concern with the intention of inducing vasospasm [4, 5].

Endoscopic Cutting Tools

Endoscopic cutting tools are derived from the same basic configuration of a protective plastic sheath that shields the underlying cutting tool. Vast arrays of cutting tools have been fashioned for endoscopic uses.

These range from sharpened needles that may be used to make pinpoint incisions to larger, more complex tips which include sharpened triangles. Frequently these cold knives are combined with electrocautery to assist in sharp dissection and to improve hemostasis of incisions.

Cutting devices have become an essential tool in multiple procedures that will be discussed later in this text. They have become commonly used in endoscopic mucosal resection when a target lesion has been identified and is being prepared for liberation from the mucosa. They are also utilized in per oral endoscopic myotomies for entry into the submucosal plan of the esophagus, for the dissection, and for the myotomy [2, 3].

Retrieval Devices/Net

Retrieval devices and nets are all primarily designed with a protective plastic sheath and the net contained within the sheath. Nets share the basic design of a snare with a netting component stretched across the snare. Nets are provided in a variety of sizes to allow for retrieval of different sizes of objects (Figs. 2.7 and 2.8).

Nets can be used for many retrieval possibilities. In the event of an ingested or inserted foreign body, a net can be utilized to retrieve the

Fig. 2.7. An open US Endoscopy Roth Net Retrieval Device. Nets come in a variety of sizes for retrieval of various sizes of devices.

Fig. 2.8. A captured specimen in a US Endoscopy Roth Net. The Net and endoscope must be withdrawn in its entirety for retrieval and cannot be withdrawn via the channel.

object. Likewise, nets can be used to retrieve larger tissue samples which have been removed by snare removal or endoscopic mucosal resection. Unfortunately, because of the size of objects being retrieved, the scope must be completely removed from the patient to retrieve the target [2].

Endoscopic Wires

Wires are provided in a wide range of materials and rigidity dependent on their needed application. Wires are essential to endoscopic procedures as they provide a guide for the delivery of other devices. Wires may also be utilized to traverse tight stenoses and allow for further dilation (Fig. 2.9) [6, 7].

Balloon Catheters

Dilating balloons are available in two varieties, but both operate under the same principle. A balloon of varying length and size is attached to a catheter which can be delivered via a working channel or

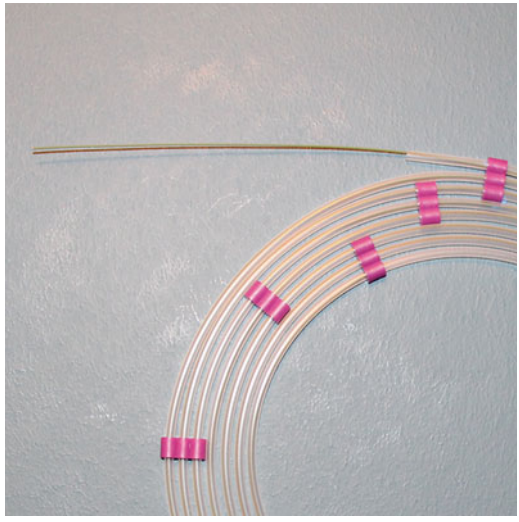

Fig. 2.9. A single example of an endoscopic wire, which may be passed via an instrument or directly into a channel. There are multiple different types of wires made from different compositions dependent on the specific application.

over an endoscopically placed wire. The external portion of the catheter is comprised of two ports, one for inflation of the balloon itself and the other to pass a wire through or for injection of contrast. Balloons can be made from different materials, ranging from compliant balloons which inflate and conform to the luminal wall to non-compliant balloons which retain the pre-formed shape of the inflated balloon despite the configuration of the lumen being dilated (Figs. 2.10, 2.11, and 2.12).

A balloon is delivered via the working channel of the endoscope and traversed across a lesion under direct visualization or delivered fluoroscopically via a pre-placed wire and placed across a lesion. The balloon port itself is connected to a pneumatic inflation device which allows for a balloon to be inflated to a specific atmospheric pressure. Care must be taken to appropriately size the balloon as to mitigate the risk of potential perforation. Recently, dilation balloons have been used in endoscopic retrograde cholangiopancreatography to help dilate the channel when delivery of a foreign body or stone is required [6, 7].

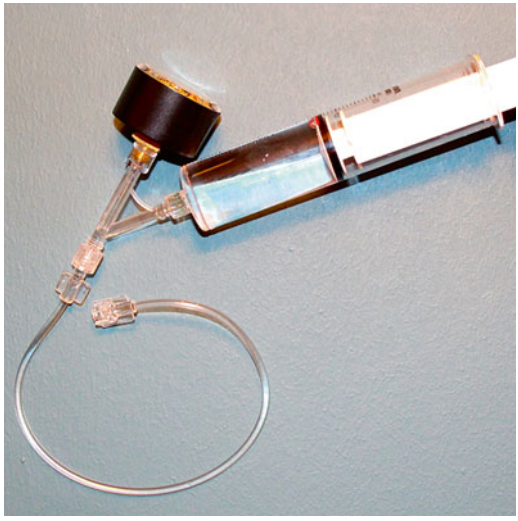

Fig. 2.10. The dilating balloon is connected to a balloon inflating device to bring the balloon to the appropriate pressure to provide dilation of the stenosis or lesion.

Fig. 2.11. A typical dilating balloon prior to insufflation. An unused balloon will traverse the working channel without difficulty if appropriate sized.

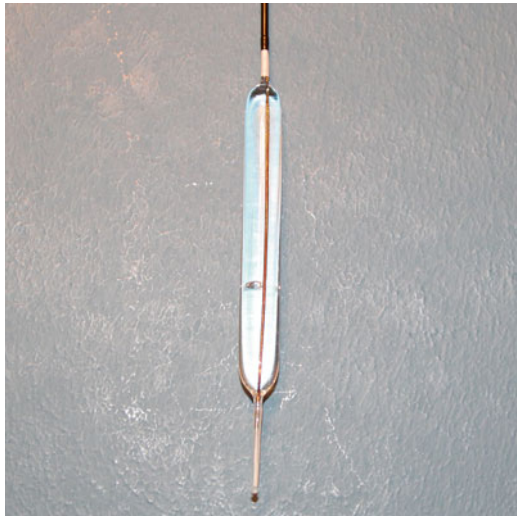

Fig. 2.12. A typical dilating balloon brought to pressure which could be used to dilate a lesion.

Hemostasis

Clips

Like many endoscopic instruments, endoclips have undergone multiple iterations. The basic design includes the plastic delivery sheath similar to previously described instruments. Once extended from the sheath, the clips are comprised of two jaws which interlock to grasp mucosa and approximate this tissue. Some manufactured clips rotate on their axis to allow for more targeted application of the clip. Once the jaws are locked, the clip and head are deployed and remain located within the patient. Some devices are able to open and close, while other manufactures are a single-closure and deployment system (Fig. 2.13).

The purpose of approximating the mucosa has multiple possibilities. It may be to occlude an underlying bleeding vessel. These devices can also be utilized after snare resection of an endoluminal lesion to control bleeding or ensure the resection site does not become a full thickness perforation. Endoclips are radiopaque and can be used in conjunction with endovascular interventions to help control bleeding and identify specific feeding vessels for thrombin injection or coiling. Endoclips are

Fig. 2.13. This specific clip allows for repeat open and closure prior to firing of the clip. Other clip types allow for easy rotatability prior to deployment.

also utilized extensively to close mucosal tunnels created in per oral endoscopic myotomies and approximate tissue defects created after an endoscopic mucosal resection [4, 5].

Band Ligation

An endoscopic band ligation device is unique among many of the previously discussed instruments. As opposed to traditional devices which are introduced through the channel of the endoscopic, the endoscopic band ligation device is a transparent cap which fits over the end of the endoscope. It protrudes slightly over the field of view and comes pre-loaded with endoscopic rubber bands. The lesion in question is brought into the cap by suction and the band is deployed via a deployment wheel which is placed through the working channel (Figs. 2.14, 2.15, and 2.16).

Endoscopic band ligation has a wide variety of uses. These include the prophylactic treatment of esophageal varices as well as therapy for active bleeds. Band ligation devices have also been used in combination with saline lifts and endoscopic snares for endoscopic mucosal resections

Fig. 2.14. The band ligation firing component which has been passed via the working channel and attached to the handle for firing.

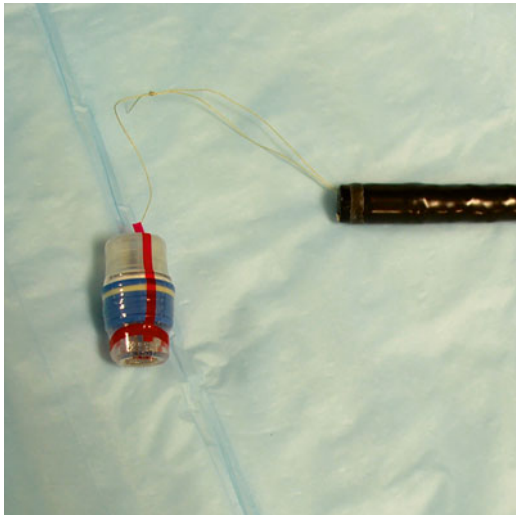

Fig. 2.15. A band ligation device that has been attached to the firing mechanism via the working channel, but not placed upon the end of the endoscope.

Fig. 2.16. A band ligation device that has been attached to the end of the endoscope with a deployed band.

(EMR). The procedure involves suctioning the lesion of interest into the endoscopic band ligation cap and deploying the band. The lesion is then raised and is amenable to resection [4, 5].

Energy Delivery

Electrocautery/Thermocoagulation Probes

Hemostatic probes are comprised of a long shaft introduced into the working port. The tip of the instrument contains a metallic probe capable of conducting bipolar or monopolar cautery dependent on the manufacture specifications.

These probes work by a combination of both coaptive coagulation and mechanical pressure. Mechanical pressure is applied with the intention of collapsing the vessel and approximating the vessel edges. The application of energy is to provide coagulation and long-standing hemostasis. Some manufacturers have designed probes which have been combined with injection catheters to provide two modalities which can be used to aid in hemostasis. A combination of electrical control and vasospasm can be used by these devices to assist in hemostasis [4, 5].

Argon Plasma Coagulation Catheters

Some lesions are more amenable to superficial cautery application as opposed to physical contact and compression. Argon plasma coagulation (APC) catheters are designed with a central lumen which passes a stream of argon gas into the operative field. A monopolar tip at the end of the catheter provides an electrical spark which creates a ring of cauterization, but with a low depth of tissue penetrance.

APC hemostatic control may be useful when coagulation is required for a broad number of lesions or those lesions which are superficial in nature. Certain disease states such as radiation proctitis, gastric antral vascular ectasia, and angiodysplasia are amenable to such therapy [4, 5].

Radiofrequency Ablation Catheters

Currently there is a single FDA-approved system for delivery of bipolar radiofrequency energy. The system includes a balloon catheter which is placed separately and independent of the endoscope. Other modalities include an ablation catheter that is placed over the end of the endoscope and is provided in varying lengths and sizes.

The radiofrequency ablation (RFA) plate is deflected against the luminal mucosa and a pre-set amount of energy is delivered. The end of the other-the-scope plate is used to scrap off the treated mucosal slough and the area of interest is treated a second time. Large, circumferential lesions may be better addressed by the circumferential balloon catheters which are placed independently of the endoscope over a pre-placed wire [8].

Over-the-Scope Control

Over-the-scope clips (OTSC) have been developed as large clips mounted on a cap which accesses the area of concern via scope suction. Once on top of the target tissue, the clip is deployed via direct plunger-push or string-wench mechanisms and spring shut on the tissue resulting in hemostasis or closure of a visceral opening.

Endoscopic suturing has been facilitated by over-the-scope devices which have evolved to pass a needle and suture in similar fashion as a sewing machine in unidirectional orientation. These devices are also mounted on endoscopic cap platforms and are controlled via wire cables

running to the operator's hand controls. Bleeding or perforated tissue is penetrated by a running needle/thread and sutures are commonly deployed in simple or figure-Z fashion resulting in closure of the perforation and hemostasis.

Specialty Instruments: ERCP/EUS

Sphincterotome

A sphincterotome is a specialized catheter used in side-viewing endoscopes to traverse the major or minor papilla during endoscopic retrograde cholangiopancreatography. Configurations vary between manufacturers, but the generic design includes a catheter which is comprised of a flexible tip connected to a deflection wire at the handle which allows the catheter to deflect in a single direction. Wires may be utilized to assist in cannulation and are passed via the catheter, or the tip of the catheter can be utilized for injection of contrast medium. The deflection wire can be connected to an electrocautery generator which enables the endoscopist to perform a biliary or pancreatic sphincterotomy when necessary.

The sphincterotome is essential to therapeutic modalities performed via the side-viewing endoscope and to endoscopic retrograde cholangiopancreatography. The ability to deflect the tip in conjunction with the elevator lever on the endoscope enables reliable cannulation. Once cannulated, a wire can be left and a multitude of instruments can be delivered to perform varies therapeutic procedures [9].

Brush

Endoscopic brushes are fashioned in a similar mechanism to snares. The brush tip is made of firm bristles similar to that of a pipe cleaner. The brush is protected from the channel and facilitates passage to the end of the endoscope via a plastic insulating tube. Commonly utilized in examination of biliary lesions, some endoscopic brushes can be passed over a wire to help guide the brush and protective sheath into position for the optimal sample (Figs. 2.17 and 2.18).

Once in position, the brush is extended and withdrawn from the plastic tube multiple times over the area of interest in an attempt to obtain cells from the lesion. The brush is provided to pathology in its entirety where the cells are plated and examined [9].

Fig. 2.17. An example of a typical endoscopic brush handle. The brush is exposed and retracted across the target lesion to obtain a cellular sample.

Fig. 2.18. An endoscopic brush that can be placed across a lesion of interest for recovery of a cellular sample.

Endoscopic Retrieval Balloons

Endoscopic retrieval balloons can be utilized after a sphincterotomy for the extraction of common bile duct stones. The catheter is comprised of a single cannulation of introduction into the bile duct, most commonly over a wire. The end of the catheter contains an 8 Fr balloon which can be inflated to a variety of sizes commonly ranging from 9 to 18 mm. An injection port is frequently available on the end of the balloon, which allows for injection of contrast medium during stone extraction (Fig. 2.19).

Using fluoroscopy, the catheter is placed past the targeted lesion and the balloon is inflated. The balloon is then brought retrograde, capturing the stone and delivering the stone via the sphincterotomy. The balloon can be adjusted to size to help with traversing the sphincterotomy if it is smaller in nature. Completion cholangiograms can be performed via the catheter injection mechanism to ensure that the common bile duct has been cleared of debris [9].

Fig. 2.19. An example of an endoscopic retrieval balloon inflated for the removal of common bile duct or pancreatic duct debris.

Endoscopic Baskets

Endoscopic retrieval baskets are an additional therapy that can be utilized after a sphincterotomy for the extraction of common bile duct stones. The catheter is comprised of a protective sheath and a series of wires (coming in different configurations ranging from oval to crescent and hexagon), which can be delivered to the common bile duct via a wire.

Under fluoroscopy, the catheter is placed proximal to the stone and the basket is opened exposing the wire components of the basket. The instrument is rotated and moved rapidly inward and outward until the stone is captured in the basket. The basket is then closed snuggly around the stone. If possible, the stone is brought under direct vision out of the sphincterotomy. If unable to traverse the sphincterotomy, the basket can be closed tightly around the stone with intentions of completely crushing the stone. A balloon catheter can then be used to remove the smaller components of the stones [9].

EUS Fine-Needle Aspiration Biopsy

Similar to that of an injection needle, needle biopsy instruments include a hollow-bore needle covered in a protective plastic sheath. The device can be un-sheathed and re-sheathed once guided into position. This technique is frequently used during endoscopic ultrasound to allow for optimal localization of lesions and to obtain tissue samples for diagnosis.

Once the needle is located within the lesion, the syringe can be placed to vacuum suction, or simply negative pressure applied by a syringe. The aspirate is then provided to pathology where the cells are plated and examined [9].

References

1. Marks J, Dunkin B. Principles of flexible endoscopy for surgeons. 1st ed. New York: Springer; 2013.
2. Diehl D, Adler D, Conway J, Farraye F, Kantsevoy S, Kaul V et al. Endoscopic retrieval devices. Gastrointestinal endoscopy [Internet]. 2009 [4 Sep 2014];69(6):997–1003. http://dx.doi.org/10.1016/j.gie.2009.01.005.
3. von Renteln D, Vassiliou M. Endoscopic tools/techniques for tissue sampling. In: Marks J, Dunkin B, editors. Principles of flexible endoscopy for surgeons. 1st ed. New York: Springer; 2013. p. 63–78.

4. Conway J, Adler D, Diehl D, Farraye F, Kantsevoy S, Kaul V et al. Endoscopic hemostatic devices. Gastrointestinal endoscopy [Internet]. 2009 [4 Sep 2014];69(6): 987–96. http://dx.doi.org/10.1016/j.gie.2008.12.251.
5. Ahad S, Mellinger J. Tools and techniques for gastrointestinal hemostasis. In: Marks J, Dunkin B, editors. Principles of flexible endoscopy for surgeons. 1st ed. New York: Springer; 2013. p. 79–90.
6. Pauli E, Marks J. Endoscopic tools and techniques for strictures and stenoses. In: Marks J, Dunkin B, editors. Principles of flexible endoscopy for surgeons. 1st ed. New York: Springer; 2013. p. 105–18.
7. Siddiqui U, Banerjee S, Barth B, Chauhan S, Gottlieb K, Konda V et al. Tools for endoscopic stricture dilation. Gastrointestinal endoscopy [Internet]. 2013 [4 Sep 2014]; 78(3):391–404. http://dx.doi.org/10.1016/j.gie.2013.04.170.
8. Dunkin B. Endoscopic tools and techniques for tissue removal and ablation. In: Marks J, Dunkin B, editors. Principles of flexible endoscopy for surgeons. 1st ed. New York: Springer; 2013. p. 91–104.
9. Pearl J. Techniques of endoscopic retrograde cholangiopancreatography. In: Marks J, Dunkin B, editors. Principles of flexible endoscopy for surgeons. 1st ed. New York: Springer; 2013. p. 215–26.

3. Operating Platforms for Surgical Endoscopy

Andrew C. Storm and Christopher C. Thompson

Introduction

Platforms for endolumenal therapy can be categorized in several ways. The system we use in this review broadly divides platforms into two categories, namely access platforms and task-specific platforms. Access platforms, many of which were developed for use in natural orifice translumenal endoscopic surgery (NOTES), provide the capability for a host of interventional therapies. These all-purpose platforms attempt to address the basic needs of the endoscopic surgeon: exposure, an appropriate field of view, and delivery of various instruments for tissue manipulation, dissection, and remodeling, all while maintaining a minimal footprint by way of the natural orifice. In contrast, task-specific platforms are typically focused on a more narrow set of specific tasks, such as defect closure, suturing, and cutting [1].

Access Platforms

Standard Endoscopes

Standard commercially available endoscopes are currently the most commonly used platform for endolumenal procedures. Several limitations exist with these standard platforms:

- Standard working channel size: 3.7 mm (or 6 mm in large-channel therapeutic scope).
- A maximum of two working channels are available on commercially available models.

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- Ancillary channels for insufflation, suction, and irrigation are limited in size and quantity.
- Views are limited by the light source (25 lumens) and visual orientation.

These limitations have led to new platforms which aim to improve upon the basic flexible endoscopic paradigm (Table 3.1).

NOTES Scope

One of the first platforms used in the development of NOTES was the R-scope later named the NOTES scope (Olympus, Tokyo, Japan). It uses a traditional endoscopic paradigm as a dual-channel endoscope with a second bending segment controlled by a second steering wheel further down the handle. The primary bending segment may be locked. Two, 2.8 mm working channels are outfitted with lifting gates positioned to allow simultaneous lifting and dissection of target tissue. Versions of this endoscope are commercially available in Asia and have demonstrated clinical utility, specifically for endoscopic submucosal dissection (ESD) (Fig. 3.1).

TransPort™

Previously known as the Incisionless Operating Platform (I-OP), the TransPort platform (USGI Medical, San Capistrano, CA) appears similar to a traditional endoscopic platform, but is larger (18 mm diameter) with steerable shaft and four working (a 7 mm, 6 mm, and two 4 mm) channels. A slim 6 mm scope may be used through this platform and is freely rotatable allowing for adjustment of the horizon. Several tools have been developed specifically for this platform including a 2.5 cm grasping jaw and plicator device, discussed later in this chapter. Much like the laparoscopic paradigm, visualization is maintained by an assistant, allowing the primary operator more freedom for instrument exchange and performing highly technical interventions. This platform is commercially available, with the most extensive experience in Europe where it is used primarily for bariatric interventions (Fig. 3.2).

Table 3.1. Access platform specifications.

Platform	Paradigm	Length (cm)	Channels (mm)	Diameter	Visualization	Positioning
EGD/colonoscope	Endoscopic	103/168	Two: 3.7, 2.8/two: 3.7, 3.2	12.6/13.7	Standard endoscopic	Standard scope
NOTES scope	Endoscopic	133	Two: 2.8 (2)	14.3	Standard endoscopic	2 bending segments
TransPort	Endoscopic	110	Four: 7, 6, 4, 4	18	N-scope	Built-in shaft-stiffening system
EndoSAMURI	Flexible-laparoscopic	103	Three: all 2.8	15.7	Endoscopic	Stiffening overtube
Direct Drive	Flexible-laparoscopic	55	Three: 7, 4.2, 4.2	16×22	N-scope	Articulating guide sheath

From Shaikh SN and Thompson CC, WJGS, 2010

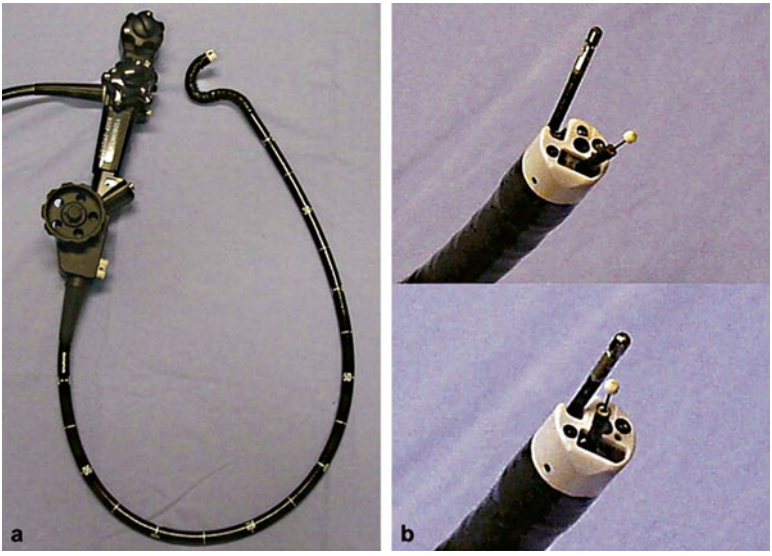

Fig. 3.1. Notes scope.

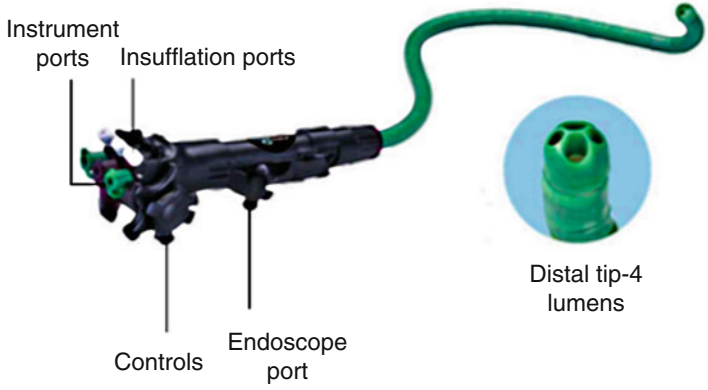

Fig. 3.2. TransPort™.

EndoSAMURAI™

Also known as the multi-tasking endoscope system, the EndoSAMURAI™ (Olympus, Tokyo, Japan) was designed to operate with a "flexible-laparoscopic" paradigm using a specialized endoscope

Fig. 3.3. EndoSAMURAI™.

with remote working station and locking overtube system. The distal end of the scope has two robotic independent arms which open at elbow joints once in position. The arms have 5 degrees of freedom and triangulation capability, allowing for tying sutures and various other effectors may be placed through the arm channels for tissue manipulation and remodeling. A third channel, exiting between the arms, allows for another effector or suction/irrigation of the operating field. The locking overtube does allow for more freedom of the primary operator as maintenance of field of view may be performed by an assistant. The fixed camera carries the same issue of image-perspective limitation as the previously mentioned platforms. This system has not been approved for clinical use (Fig. 3.3).

Direct Drive Endoscopic System

The direct drive endoscopic platform (Boston Scientific, Natick, MA) is another flexible multi-tasking laparoscopic paradigm platform consisting of a 16 mm diameter guide sheath housing three channels. The N-scope (Olympus, Tokyo, Japan) is used for visualization and may be freely rotated for change of horizon. Specialized tools may be inserted through the remaining two 4 mm channels including graspers, scissors, needle pushers, and cautery. The platform is controlled using a rail-based platform with two drive handles. Seven degrees of freedom are achieved and complex laparoscopic techniques of cutting, grasping, suturing, triangulation, and knot tying may be performed. View limitations are similar to other platforms described as instruments and optics approach the field from the same direction. Additionally, no channel is dedicated to suction/irrigation which limits the scope of procedures that may be performed with this platform. This system has not been approved for clinical use (Fig. 3.4).

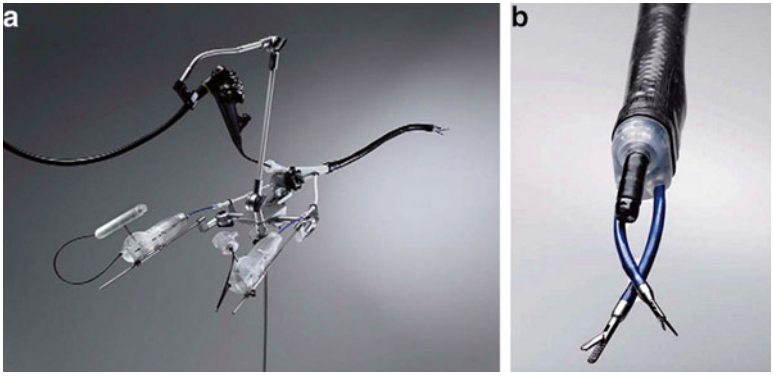

Fig. 3.4. Direct drive system.

Endoscopic Ultrasound

One of the most promising and evolving technologies in surgical endoscopy is EUS. Both radial (360° ultrasound) and linear (linear field of view) EUS is available depending on the intended intervention and angle of approach. EUS was initially developed and used for diagnostic purposes including lymph node biopsy and staging of gastrointestinal malignancies. More recently, use of EUS has grown to include a vast host of therapeutic procedures including necrosectomy for the management of walled off pancreatic necrosis, EUS-guided anastomosis for pancreaticobiliary disease, entero-enteral anastomosis in the management of obesity and diabetes, and angiotherapy for the injection of glue and/or embolization coils to achieve hemostasis of variceal and other bleeding lesions within the GI tract [2–4] (Fig. 3.5).

Task-Specific Platforms

Many tools have been developed over the past decade allowing for an increased breadth of endoscopic interventions. General categories include those for tissue resection (including several varieties of needle knives) and tissue remodeling (including large over-the-scope clips, suturing, and stapling devices).

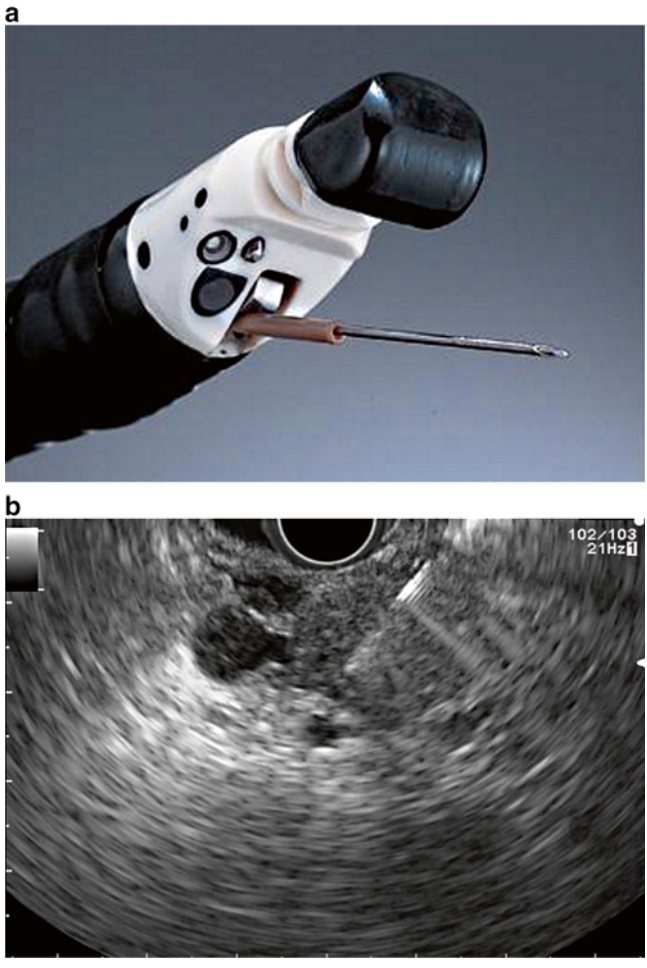

Fig. 3.5. Linear EUS: (**a**) tip of the EUS scope with needle, (**b**) EUS view of needle in vivo.

Tissue Dissection: Knives, Scissors, and Balloons

All commercially available endoscopic knives utilize a bare diathermy wire which dissects tissue through use of electrocautery and a free-hand technique. Efficacy and rate of complications are highly operator dependent and proficient use of endoscopic knives has a long learning curve.

There are three basic knife configurations available: standard non-insulated tip knives, various insulated tip knives, and hook-tip knives. The standard tip is used for initial access into the submucosal plane and "pre-cut" biliary access techniques, and the insulated tips aid in tissue dissection while preventing deeper penetrating cuts that may lead to perforation, making these useful for ESD, electroincision of complex strictures, peroral endoscopic myotomy (POEM), pyloromyotomy, cricopharyngeal myotomy, and Zenker's septotomy.

Use of endoscopic scissors has also been applied to various clinical applications including removal of sutures and foreign material, cricopharyngeal myotomy, and resection of superficial invasive cancers. Endoscopic scissors have not seen widespread adoption for applications other than foreign body removal.

Balloons have a variety of roles in endoscopic therapy, and their use is covered in detail elsewhere in this text. They have been most extensively utilized for stricture dilation and removal of biliary stones. However, as intraoperative hemorrhage is a leading concern in therapeutic endoscopy, when possible, balloons may also be used to perform blunt tissue dissection. This has been well described in some POEM and pyloromyotomy techniques (Fig. 3.6).

Suturing and Plication Devices

Endoscopic suturing has proven to be a game changer in the development of novel minimally invasive procedures of the GI tract. The technology was first FDA approved in 2000 with the EndoCinch (CR BARD Endoscopic technologies, Massachusetts, USA) system which has since left the market. LSI solutions produced a similar endoscopic suturing prototype which is also no longer commercially available. Today, the G-Prox™ plication device (USGI Medical, San Capistrano, CA) and Overstitch (Apollo Endosurgery, Austin, TX) are commercially available and gaining more widespread use [5].

The g-prox device is more of a tissue plication system that consists of a tissue grasping jaw which closes at a 45° angle to the axis of the device shaft, a hollow needle housed within the device that is passed through tissue grasped in the jaw, and polyester mesh tissue anchors that are deployed through the needle. It requires a 7 mm working channel and is typically used with the TransPort access platform. The device is fully reloadable without removal from the TransPort platform.

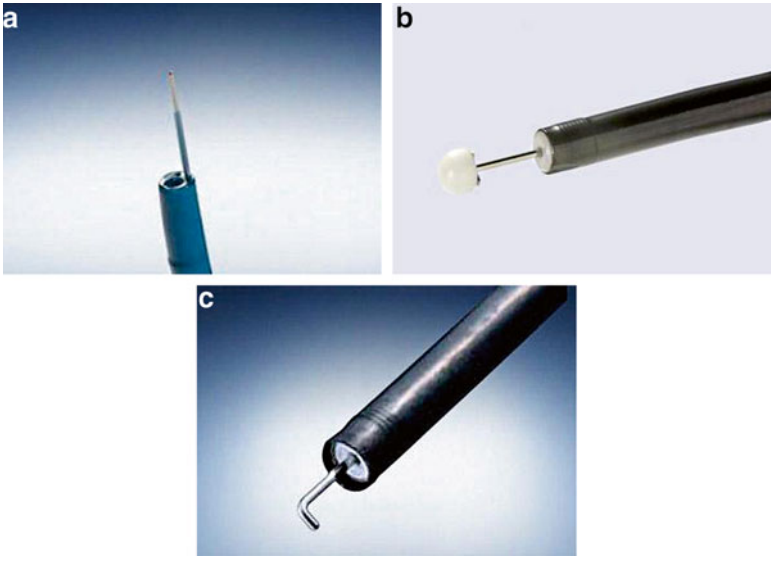

Fig. 3.6. Needle knives: (**a**) needle knife, (**b**) insulated tip knife, (**c**) hook knife.

The Overstitch device, FDA approved in 2008, is a single-use, disposable suturing platform which is mounted exclusively on Olympus double-channel therapeutic endoscopes and allows for a variety of suturing techniques, including running, figure-of-eight, mattress, and interrupted stitch patterns. The platform consists of a scope cap with curved needle driver, a needle driver handle that is attached adjacent to the accessory channel ports, and an anchor exchange catheter that runs through the larger accessory channel. Additional components include a cinching device, a helix tissue grasping device, and an overtube. The included suture is connected to the short strait needle, which also serves as a T tag. Absorbable (polydioxanone) and nonabsorbable (polypropylene) 2-0 and 3-0 sutures are available for use with the system.

Endosopic suturing is reported to have been used successfully for closure of perforations, oversewing of ulcers, management of fistulas, anchoring of intralumenal devices such as stents, to provide directional traction in ESD, for hemostasis, and for endoscopic bariatric procedures (Fig. 3.7).

Two related devices are currently available in the USA specifically for endoscopic fundoplication in the management of gastroesophageal reflux disease; the MUSE system (Medigus, Omer, Israel) is an

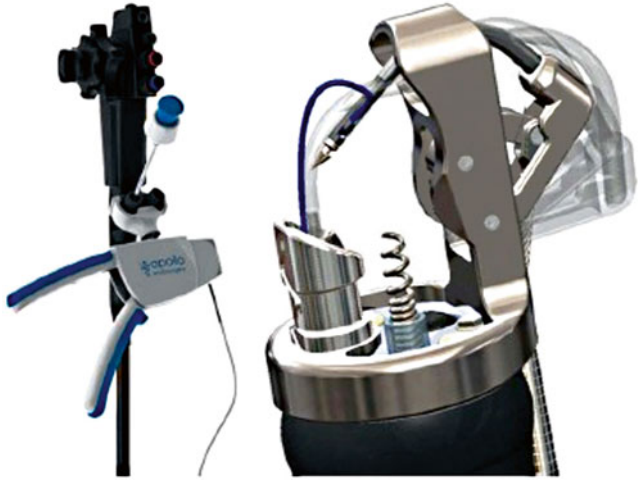

Fig. 3.7. Overstitch.

EUS-guided stapler and EsophyX (EndoGastric Solutions, San Mateo, CA) is a tissue plication device used alongside an endoscope to deliver transoral polypropylene tissue anchors.

Cap-Mounted Clips

Secure closure of surgical defects including translumenal access sites, perforations and control of bleeding may be accomplished with several devices available commercially. Both the over-the-scope clip (OTSC, Ovesco Endoscopy GmbH, Tuebingen, Germany) and Padlock-G clip (Aponos Medical, Kingston, NH) have been used in clinical practice demonstrating efficacy and safety in closure of perforations, surgical access sites, fistulas, post-polypectomy, and EMR sites as well as hemostasis. [6, 7] The OTSC clip is a double-jaw nitinol tissue grasper that closes when deployed with interlocking teeth similar to a bear trap. Assist devices are available, including a reloader for mounting sequential clips onto the applicator cap, a twin grasper used to oppose two flaps of a defect within the cap prior to clip deployment, and another grasping device which uses three retractable needle pins to pull tissue into the cap prior to clip deployment. The Padlock-G clip is a hexagonal nitinol ring with six inner needles, which grasp and approximate tissue after deployment from the Lock-It delivery system. Both platforms consist of a cap

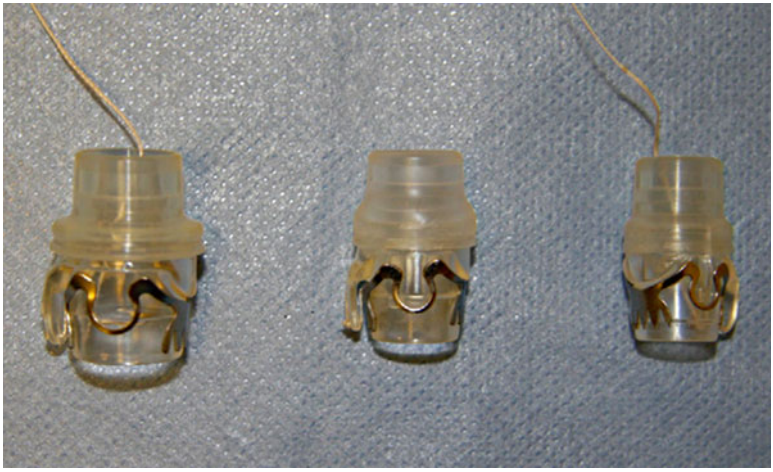

Fig. 3.8. OVESCO.

holding a single clip which is mounted on the distal tip of the scope, and attached to a firing device which may be mounted on the handle of the scope. Currently, commercially available devices only load and fire a single clip and the scope must be fully withdrawn to prepare and load a second clip (Fig. 3.8).

Lumen-Apposing Stents and Sleeves

Parallel to the development of suturing devices and EUS-guided translumenal procedures has been the development of technologies for diversion and anastomosis formation in the treatment of both gastrointestinal and extralumenal disease.

Anastomotic Stents

Stent systems, especially the AXOIS system (Xlumena, Mountain View, CA), have been designed with flanged ends specifically to allow for the creation of endoscopic anastomosis. The system is commercially available and used for opposition of two opposing lumens to bypass strictures or drain fluid collections as in trans-gastric necrosectomy or trans-duodenal choledochoduodenostomy. These covered stents also

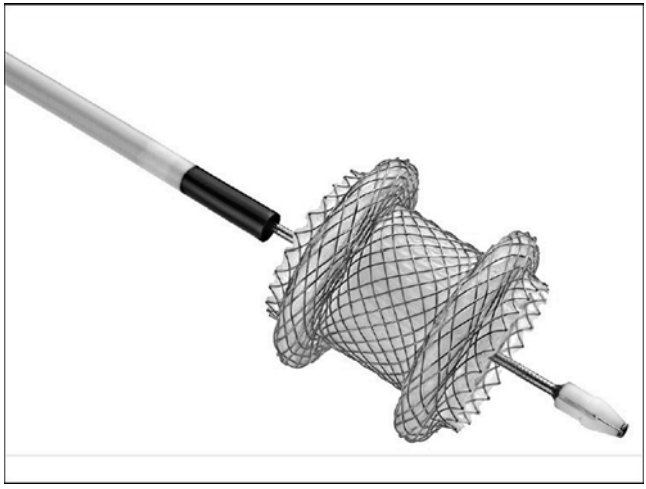

Fig. 3.9. Axios stent.

provide tamponade after dilation of the anastomosis, which may reduce bleeding complications for these minimally invasive procedures. There are also several reports of its successful use in procedures such as cholecystoduodenostomy and various bowel-to-bowel anastomosis procedures, with clinical trials for these more advanced procedures currently underway [3, 4] (Fig. 3.9).

Sleeves

Bariatric sleeves, currently available only through clinical trials across the USA, include Endobarrier (GI Dynamics, Lexington, MA) and ValenTx (ValenTx, Maple Grove, MN) which have been developed for the indication of management of type 2 diabetes. These devices, anchored in the proximal small intestine and gastroesophageal junction, respectively, attempt to mimic the mechanisms of a gastric bypass and exclude the small bowel from absorbing nutrients in a minimally invasive endoscopic procedure. The role these devices will play in the management of obesity and diabetes has yet to be determined. Although the Endobarrier is clinically available in Europe and South America, neither is yet approved for use in the USA outside of clinical trials [8].

Tissue Ablation

Application of thermal energy for hemostasis and tissue fulguration is a mainstay in endoscopic therapy. Bicap and heater-probe technology have been used traditionally, though newer technologies including argon plasma coagulation (APC) is becoming more popular and has demonstrated safety and efficacy. APC generators and catheters are offered by several commercial companies.

In the management of Barrett's esophagus, ablation technologies including Barrx (Coviden, Dublin, Ireland) and cryotherapy catheters have been developed to address the need to easily treat larger areas at one time. These systems utilize RFA (Barrx) or cryotherapy (delivered via CO_2 or liquid nitrogen) on a balloon or paddle-like through-the-scope catheter which may be applied to areas of abnormal mucosa in the esophagus. These technologies are readily available for commercial use.

Stretta (Mederi Therapeutics, Norwalk, CT) is a tissue ablation system for the management of GERD. The device acts through low frequency radiofrequency treatment of the muscularis propria at the distal esophagus, and likely results in muscle fiber proliferation resulting in increased lower esophageal sphincter tone. The device is used commercially.

Ablation within the biliary system has been studied using endoscopically applied radiofrequency including the Habib™ EndoHPB catheter (EMcision, Montreal, Canada). This system is not commercially available in the USA, but is used elsewhere for management of clogged metal biliary stents as well as palliation of obstructing hepatobiliary tumors.

Summary

The diversity of tools available to the endoscopic surgeon have grown exponentially over the past decade, and will likely continue to be refined and reimagined with safety, minimal invasiveness, and cost-effective therapy for patients as primary goals. Additionally, therapeutic endoscopy and its tools have evolved to address not only the management of gastrointestinal disease, but also systemic disease including diabetes and obesity. Several hurdles remain, including those regarding training, credentialing, and reimbursement. Nevertheless, the future of operating through the endoscope is an exciting one.

References

1. Shaikh SN, Thompson CC. Natural orifice translumenal surgery: flexible platform review. World J Gastrointest Surg. 2010;2(6):210–6.
2. Storm AC, Kumbhari V, Saxena P, Canto MI, Azola A, Messallam AA, et al. EUS-guided angiotherapy. Gastrointest Endosc. 2014;80(1):164–5.
3. Gornals JB, De la Serna-Higuera C, Sanchez-Yague A, Loras C, Sanchez-Cantos AM, Perez-Miranda M. Endosonography-guided drainage of pancreatic fluid collections with a novel lumen-apposing stent. Surg Endosc. 2013;27(4):1428–34.
4. Shah RJ, Shah JN, Waxman I, Kowalski TE, Sanchez-Yague A, Nieto J, et al. Safety and efficacy of endoscopic ultrasound-guided drainage of pancreatic fluid collections with lumen-apposing covered self-expanding metal stents. Clin Gastroenterol Hepatol. 2014;13(4):747–52.
5. Pauli EM, Delaney CP, Champagne B, Stein S, Marks JM. Safety and effectiveness of an endoscopic suturing device in a human colonic treat-and-resect model. Surg Innov. 2013;20(6):594–9.
6. Guarner-Argente C, Cordova H, Martinez-Palli G, Navarro R, Cuatrecasas M, Rodriguez de Miguel C, et al. Yes, we can: reliable colonic closure with the Padlock-G clip in a survival porcine study (with video). Gastrointest Endosc. 2010;72(4):841–4.
7. Haito-Chavez Y, Law JK, Kratt T, Arezzo A, Verra M, Morino M, et al. International multicenter experience with an over-the-scope clipping device for endoscopic management of GI defects (with video). Gastrointest Endosc. 2014;80(4):610–22.
8. Gersin KS, Rothstein RI, Rosenthal RJ, Stefanidis D, Deal SE, Kuwada TS, et al. Open-label, sham-controlled trial of an endoscopic duodenojejunal bypass liner for preoperative weight loss in bariatric surgery candidates. Gastrointest Endosc. 2010;71(6):976–82.

4. Endoscopic Energy Sources

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Energy Sources in Endoscopy

Endoscopy has evolved to include dissection, ablative, and destructive techniques that use a variety of devices. These devices have various energy sources including electrocautery, contact probes, argon plasma coagulator, light sources in photodynamic therapy, radiofrequency ablation, and laser devices.

Electrocautery

Electrocautery uses electrical circuitry with electrodes that generate heat from resistance within tissues when the electrical current passes through the target tissue. This is an indirect thermal method of tissue ablation [1]. This may be a single monopolar electrode requiring the patient be grounded, or a bipolar which does not require grounding. The probe is passed through the working channel of the upper or lower scope and is fitted with an irrigation port. An electrocautery probe with injection needle is also available which allows injection of saline or epinephrine without removal of the probe.

The depth of tissue penetration is dependent on the power, duration of application and, in the case of bipolar/multipolar devices, the pressure applied. A light pressure with 2-s duration can achieve a tissue penetration depth of 1 mm [2]. As the tissue desiccates the electrical conductivity decreases and limits the maximum temperature to 100 °C. These devices (Table 4.1) are easy to use with power setting standard at 20 W and maximum of up to 50 W [3].

Clinical application of this technology in endoscopy includes treatment of mucosal bleeding, polypectomy, sphincterotomy in ERCP, ablations, endoscopic mucosal resection (EMR), and dissection or cutting

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Table 4.1. Contact energy devices.

Manufacturer	Device name	Catheter French size	Catheter length (cm)	Special features
Multipolar electrocautery probe				
Boston Scientific (Natick, MA)	Gold Probe	7, 10	300, 350	
	Injection Gold Probe	7, 10	210	25-gauge injection needle
Cook Medical (Winston-Salem, NC)	Quicksilver Bipolar Probe	7, 10	350	
ConMed Endoscopic Technologies (Utica, NY)	BiCap Superconductor Multi-electrode Bipolar Probe	5, 7, 10	200, 300, 350	
Olympus America (Center Valley, PA)	BiCOAG Bipolar Hemostasis Probe	7, 10	350	
US Endoscopy (Mentor, OH)	Bipolar Hemostasis Probe	7, 10	350	
Hemostatic grasper				
Olympus America	Coagrasper Hemostatic Forceps	7	165, 230	Rotatable
Heater probe				
Olympus America	HeatProbe	7, 10	230, 300	Reusable
Radiofrequency ablation				
Covidien GI Solutions (Sunnyvale, CA)	Barrx 360 RFA Balloon Catheter (formerly HALO360+)		85	18, 22, 25, 28, 31 mm diameter
	Barrx 90 RFA Focal Catheter (formerly HALO90)		160	20 × 13 mm electrode
	Barrx 60 RFA Focal Catheter		160	15 × 10 mm electrode

(continued)

Table 4.1. (continued).

Manufacturer	Device name	Catheter French size	Catheter length (cm)	Special features
	Barrx Ultra Long RFA Focal Catheter		160	40×13 mm electrode, articulated platform moves in three axes to assure tissue contact
	Barrx Channel RFA Endoscopic Catheter	7	135	15.7×7.5 mm electrode, fits through the working channel of a flexible endoscope
Radiofrequency energy delivery for GERD				
Mederi Therapeutics Inc. (Norwalk, CT)	Stretta			

techniques in natural orifice surgery. Complications are rare, including perforation and bleeding. Treatment of peptic ulcers ironically can lead to bleeding reported as high as 18 % [4]. Colonic perforation in the right colon after angiodysplasia treatment with monopolar electrocautery is reported at 2.5 % [5].

Hemostatic Grasper

This is a newer combination entity that utilizes both an energy source and mechanical force. The structural configuration of the grasper is similar to the biopsy forceps, except that the jaws are flat instead of cupped, and the device is rotatable. The grasper holds the tissue with the flat jaw surface and subsequently allows delivery of a monopolar current which desiccates the tissue in the jaws of the grasper. This device (Table 4.1) is currently investigational and it has been used in natural orifice transluminal endoscopic surgery cholecystectomy in porcine animals [6].

Hemostatic graspers are often used in endoscopic submucosal dissection and per-oral endoscopic myotomy procedures for definitive hemostasis of larger submucosal vessels.

Contact Probes

Endoscopic thermal coagulation with contact probes was introduced over 20 years ago. Contact probes, such as the heater probe, are a thermal contact energy source that can be applied directly to tissue. The heater probe is a Teflon-coated aluminum cylinder that generates heat as current is transmitted through thermal coupling from the metal coil at the tip. The tip of the probe maintains a constant temperature. The heater probe offers good vessel sealing with coagulation combining the effects of heat and direct pressure to aid in vessel coaptation. This makes it useful for directed therapy during active bleeding, delivering standard energy over set time with constant temperature.

The heater probe (Table 4.1) passes through the working channel of the scope and the tip is focused in direct vision of the target lesion. An irrigation port on the probe allows irrigation and better visualization of the target. Application of the trigger results in delivery of a preset amount of energy. Once initiated the delivery of energy cannot be stopped.

Heater probe uses include peptic ulcer disease, angiodysplasia, Dieulafoy lesions, radiation induced proctitis and post polypectomy bleeding. The heater probe, electrocautery, and APC have revolutionized the treatment of bleeding complications of peptic ulcer disease. The heater probe is comparable in regard to initial hemostasis, recurrent bleeding and 30 day mortality to APC [3, 7–9]. With the coupled use of epinephrine or sclerosis agents, these energy devices have reduced the need for surgery for gastrointestinal bleeding [10, 11]. Numerous studies are available comparing electrocautery and heater probes with other modalities such as epinephrine or sclerosant with results showing significant success in initial hemostasis, while reducing re-bleeding rates, transfusion requirements, and the need for surgery [3]. The best modality, however, involves the use of combination therapy. Wong et al. confirmed a hemostasis rate of 98.6 % in 1144 patients with recurrent bleeding of only 8.2 % with epinephrine and heater probe [12]. The heater probe has stood the test of time and in 1991, Chung et al. showed that the heater probe was effective for initial hemostasis in 85.7 % of

peptic ulcer bleeding with the mean number of applications 6.7 pulses at a setting of 25–30 J. Perforation rates vary from 1.8 to 3 % with precipitation of bleeding in up to 5 % [13, 14].

Argon Plasma Coagulation

Argon plasma coagulation (APC) is another thermal non-contact form of tissue coagulation that requires grounding. It offers directed coagulation without significant loss of energy to the surrounding fluids and limits collateral injury. The depth of tissue coagulation depends on the flow rate of the Argon gas, the power of the generator setting, the duration of the application, and the distance from the target tissue. Argon, a relatively inert gas, is forced through a tiny flexible catheter (Table 4.2) with a tungsten electrode at the tip. Trigger with a foot pedal releases the argon gas simultaneously with ionization of the electrode. Argon flow over the tip of the ignited tungsten wire ionizes the gas, producing a flow of electrons which is confined to the stream of gas. If the tip is in close proximity to tissue, then it will allow the current to flow as an arc of ionized gas. If the catheter is too far, then the resistance is too great and no arc of flow results. The tip of the probe can be controlled and directed to a localized area, desiccating the tissue at the surface of contact. The electrical resistance rises as a result of the tissue desiccating, and the electrical current then flows to the adjacent conductive tissue limiting the depth of injury [3, 15].

APC is commonly used to treat gastric vascular ectasia (GVE). APC is also commonly used for peptic ulcer disease, angiodysplasia, and radiation-induced angioectasias. A retrospective study of 30 patients showed treatment of bleeding GVE was efficient and safe in cirrhotic and non-cirrhotic patients in more than 80 % of cases; non-cirrhotic patients required significantly more APC sessions to achieve a complete treatment [16]. However, most patients do not achieve full long-term resolution [17]. APC is very useful in the treatment of hemorrhagic radiation proctitis with Swan et al. showing success rates of 96 % with a short term complication rate of 34 % and long term complication rate of 2 % [18].

Complications are rare but unique to APC. Abdominal distension with the argon gas, submucosal emphysema, pneumomediastinum, and pneumoperitoneum have all been described [3, 7, 19, 20]. Perforation has been described in the duodenum and colon [3]. The most feared complication is intra-colonic gas explosion which has been reported. The explosion occurred in patients with presumed incomplete bowel

Table 4.2. Noncontact energy devices.

Manufacturer	Device name	Catheter French size	Catheter length (cm)	Fire direction	Special features
Argon plasma coagulation					
US Medical Innovations (Takoma Park, MD)	Canady Plasma GI Probe	7	230, 340	Straight, side	
ConMed Endoscopic Technologies	Beamer Argon Probe	5, 7, 10	160, 230, 320	Straight	
	Beamer Argon Snare Probe	7	160, 230	Straight	Combination APC probe and snare
	ABCFlex Argon Beam GI Probe	7	220, 270	Straight	
ERBE USA (Marietta, GA)	APC Probe	5, 7, 10	150, 220, 300	Straight, side, circumferential	
	FiAPC Probe	5, 7, 10	150, 220, 300	Straight, side, circumferential	Filter integrated
Photodynamic therapy					
Biolitec US Inc (East Longmeadow, MA)	980 nm Diode Laser				
	810 nm Diode Laser				
Excel Lasers Limited (Suffolk, UK)	Medlight SA	3	250, 300	Straight, circumferential	Diffusing balloon catheter system

preparation or when malabsorbed carbohydrates were used as bowel preparation, wherein the accumulated methane or oxygen was ignited [21, 22]. The listed complications may be related to the power setting, duration of application and distance from the target tissue [15].

Photodynamic Therapy

Photodynamic therapy (PDT) is an ablative therapy that uniquely uses a light source to target dysplastic or malignant tissue. The underlying mechanism of this treatment is that some chemicals have a photoexcitatory property when exposed to light of particular wavelengths. These chemicals have the propensity to be absorbed by abnormal tissues. These photosensitizing drugs are administered followed by the application of a specific wavelength of light leading to photocoagulation and cellular injury of targeted abnormal cells. On light exposure reactive chemical radicals and singlet oxygen cause local cellular damage and vascular thrombosis resulting in tissue necrosis [23].

Porfimer is the most widely used photosensitizing agent for gastrointestinal diseases and is the only agent widely available for systemic use. Photoactivation occurs at wavelengths of 630–515 nm. It is usually cleared from most cells in 40–72 h but retained in tumor and skin cells for longer. Porfimer is contraindicated with other potentially photosensitizing agents such as sulfonylurea hypoglycemic, thiazide diuretics, phenothiazines and antibiotics such as fluoroquinolones, griseofulvin, tetracycline, and sulfonamides.

Dosages are usually 2 mg/kg given as boluses over 3–5 min. Overdose toxicity is not well documented. Generally 48 h is allowed for the normal tissues to clear the agent. The Diomed 630PDT laser (Table 4.2) was previously marketed as a portable light source cleared by the FDA for esophageal treatments. Light is generated from a semiconductor diode and automated for delivery of 300 J/cm for esophageal carcinoma or 130 J/cm for esophageal dysplasia. Total dose of 400 mW/cm should not be exceeded to prevent thermal injury. An even distribution of the light to the targeted area is ensured with the use of cylindrical balloons that allow for the centering of the delivery fiber tips. The lengths of these tips are available between 10 and 50 mm. The centering balloon has a working length of 75 cm providing even light source distribution of 3, 5, and 7 cm lengths of coverage. Some of Diomed's operating assets were acquired by Biolitec (East Longmeadow, MA) in 2008, while continued support of Diomed equipment is also provided by Excel

Lasers Limited (Suffolk, UK). Both companies offer their own product lines of medical lasers for PDT as well.

PDT is currently approved by the FDA for the palliative treatment of obstructing esophageal cancer and ablation of esophageal dysplasia not undergoing surgery [24]. Complications associated with these PDT procedures are usually related to the local inflammatory effects. A frequent occurrence is odynophagia or chest pain post procedure. Nausea, vomiting, and asymptomatic pleural effusions are not uncommon. The more common complication which usually develops weeks after treatment is that of esophageal stricture with quoted rates of 15–55 %, but these are usually amenable to stricture dilation at endoscopy.

Unique to this energy source is the cutaneous phototoxic effects in up to 30 % of patients with severe sunburn in 5–7 % [25]. The recommendation is for patients to avoid bright lights and be fully covered when venturing outside. These restrictions are at minimum 1 month. There are no documented serious overdose complications of porfimer. Rare toxicities include constipation and allergic reactions.

Another photosensitizing agent available but only for topical use is 5-aminolevulinic acid. This has less limited photosensitivity duration lasting to 1–2 weeks compared to porfimer which lasts 5–6 weeks. However, the depth of penetration of 2 mm does not compared to the 4–6 mm reached with standard porfimer therapy.

One major drawback to ablative therapies for Barrett's esophagus or high grade dysplasia is the lack of pathological examination. Endoscopic mucosal resection obtains mucosa and submucosa for histological assessment and therefore may offer more pathways for treatment and staging. Several new studies have proven the safety of combination endoscopic mucosal resection and ablative therapies.

Radiofrequency Ablation

Radiofrequency ablation (RFA) has emerged as a safe and effective method of endoscopic eradication of Barrett's esophagus [26]. Although there is great heterogeneity between the studies available, there is undoubtedly a low complication rate across these studies with substantial rates of complete eradication of dysplasia and intestinal metaplasia and decreased progression to cancer [27]. A systematic review and meta-analysis found RFA resulted in complete eradication of dysplasia in 91 and 78 % of intestinal metaplasia. RFA uses standard energy resulting in uniform depth of tissue destruction [28]. The current energy

device used is the Barrx 360 RFA Balloon Catheter (Covidien GI Solutions) which circumferentially ablates the mucosa of the esophagus. It has a balloon with 60 separate 250 μm electrodes [29]. Adjacent electrodes function as bipolar devices and cause superficial destruction up to a length of 3 cm. Maximum ablation depth using energy of 12 J/cm^2 and two applications does not involve the submucosa [29–31]. The Barrx 90 system is also available, which is a rectangular platform mounted on the tip of the endoscope where the catheter runs alongside the scope and not through the working channel. This platform has 24 electrodes and is useful for focal lesions. This is very safe with one of the largest studies (UK RFA registry) reporting one perforation in 335 patients. Stricture is the most common risk with rates of 9 % in the UK RFA registry [32]. A systematic review and meta-analysis reported stricture rates of 5 %, pain complications of 3 % and bleeding in 1 % [28]. Further studies are needed to better investigate the recurrence of dysplasia or metaplasia below squamous regrowth.

Another RFA esophageal application which utilizes minimally invasive endoluminal delivery is the Stretta procedure for gastroesophageal reflux disease (GERD). GERD is a very common chronic disease with up to 20 % of patients having breakthrough or uncontrolled heartburn with optimal medical therapy. The Stretta procedure was introduced in 2000, which uses a flexible catheter with a balloon-basket assembly and nickel–titanium needle electrodes to deliver the radiofrequency energy into the esophageal wall and LES complex, while irrigating the balloon contacting the overlying mucosa to prevent thermal injury [33]. Stretta significantly improves GERD symptoms and patient satisfaction, and reduces PPI use with proven durability at 10 years and no serious complications in a series of 109 patients [34].

Lasers

Lasers are high energy light sources that cause tissue destruction via coagulation and vaporization, via noncontact or contact energy transmission. They have been largely replaced by other energy sources. However, light sources transmitted through thin flexible fibers may enable future increased use in natural orifice transluminal endoscopic surgery [35]. There are several types of lasers available including Nd:YAG, KTP:YAG, carbon dioxide, neodymium-holmium, and diode lasers. Therapeutic interventions are dependent on the wavelength, with thermal effects causing coagulation or vaporization. Non-contact application of

wavelengths in the near infrared spectrum cause deep optical penetration, and energy is absorbed mainly by tissue water resulting in a thermal effect of protein denaturation and thus coagulation and destruction of tissue. Precise cutting of tissue on the other hand is achieved with direct contact application of wavelengths with higher frequencies. This results in rapid absorption of energy directly by the tissue, and thus tissue vaporization. The observed tissue effects are grooves and craters with coagulated tissue borders and surrounding small vessel occlusion, essentially incisions with reduced or no bleeding. Potential applications of laser technology for transluminal access, tissue destruction, and tissue sealing are under experimental and clinical research and look promising [35].

Lasers have also been applied in lithotripsy of common bile duct stones. Common bile duct stones occur in about 7–12 % of patients who undergo cholecystectomy [36]. Removal of large stones poses a particular challenge for the endoscopist and may not be amenable to conventional techniques. Laser lithotripsy can be useful in these cases. It is typically performed perorally under cholangioscopic or fluoroscopic guidance and can result in resolution of common bile duct stones [37]. Hochberger et al. in a study of 60 patients showed that using a rhodamine 6G dye laser with an optical stone tissue detection system was able to clear 87 % with 5 patients having complications all managed conservatively. Laser lithotripsy has been demonstrated to be more effective than extracorporeal shock wave lithotripsy (ESWL) in terms of stone clearance rate and more rapid stone fragmentation with a shorter duration of treatment leading to a significant reduction in cost [38].

Summary

While some energy sources like electrocautery and APC are widely available and in current use with good results for treating bleeding lesions, most have had mixed results in treating neoplastic lesions and still require further investigation to confirm safety and efficacy in more than a few large series. Other energy sources have waxed and waned in use over the years, but are finding new applications like radiofrequency ablation, photodynamic therapy for palliation of other malignancies, and lasers applied to newer transluminal access and excisional techniques. The future of energy sources in endoscopy is likely going to expand to include exciting new applications in tissue ablation, cutting, and sealing for natural orifice surgery.

References

1. American Society for Gastrointestinal Endoscopy. Mucosal ablation devices. Gastrointest Endosc. 2008;68:1031–42.
2. Laine L, Long GL, Bakos GJ, et al. Optimizing bipolar electrocautery for endoscopic hemostasis: assessment of factors influencing energy delivery and coagulum. Gastrointest Endosc. 2008;67:502–8.
3. American Society for Gastrointestinal Endoscopy. Endoscopic hemostatic devices. Gastrointest Endosc. 2009;69:987–96.
4. Laine L. Multipolar electrocoagulation in the treatment of peptic ulcers with non-bleeding visible vessels. A prospective, controlled trial. Ann Intern Med. 1989;110: 510–4.
5. Foutch PG. Angiodysplasia of the gastrointestinal tract. Am J Gastroenterol. 1993;88:807–18.
6. Meining A, Wilhelm D, Burian M, et al. Development, standardization, and evaluation of NOTES cholecystectomy using a transsigmoid approach in the porcine model: an acute feasibility study. Endoscopy. 2007;39:860–4.
7. Cipolletta L, Bianco MA, Rotondano G, et al. Prospective comparison of argon plasma coagulator and heater probe in the endoscopic treatment of major peptic ulcer bleeding. Gastrointest Endosc. 1998;48(2):191–5.
8. Hui WM, Ng MM, Lok AS, et al. A randomized comparative study of laser photocoagulation, heater probe, and bipolar electrocoagulation in the treatment of actively bleeding ulcers. Gastrointest Endosc. 1991;37:299–304.
9. Lin HJ, Wang K, Perng CL, et al. Heater probe thermocoagulation and multipolar electrocoagulation for arrest of peptic ulcer bleeding. A prospective, randomized comparative trial. J Clin Gastroenterol. 1995;21:99–102.
10. Chung SS, Lau JY, Sung JJ, et al. Randomised comparison between adrenaline injection alone and adrenaline injection plus heat probe treatment for actively bleeding ulcers. BMJ. 1997;314:1307–11.
11. Lin HJ, Tseng GY, Perng CL, et al. Comparison of adrenaline injection and bipolar electrocoagulation for the arrest of peptic ulcer bleeding. Gut. 1999;44:715–9.
12. Wong SK, Yu LM, Lau JY, et al. Prediction of therapeutic failure after adrenaline injection plus heater probe treatment in patients with bleeding peptic ulcer. Gut. 2002;50:322–5.
13. Chung SC, Leung JW, Sung JY, et al. Injection or heat probe for bleeding ulcer. Gastroenterology. 1991;100:33–7.
14. Cook DJ, Guyatt GH, Salena BJ, et al. Endoscopic therapy for acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. Gastroenterology. 1992;102:139–48.
15. Watson JP, Bennett MK, Griffin SM, et al. The tissue effect of argon plasma coagulation on gastric and esophageal mucosa. Gastrointest Endosc. 2000;52:342–5.
16. Lecleire S, Ben-Soussan E, Antonietti M, et al. Bleeding gastric vascular ectasia treated by argon plasma coagulation: a comparison between patients with and without cirrhosis. Gastrointest Endosc. 2008;67(2):219–25.

17. Boltin D, Gingold-Belfer R, Lichtenstein L, et al. Long-term treatment outcome of patients with gastric vascular ectasia treated with argon plasma coagulation. Eur J Gastroenterol Hepatol. 2014;26(6):588–93.
18. Swan MP, Moore GT, Sievert W, et al. Efficacy and safety of single-session argon plasma coagulation in the management of chronic radiation proctitis. Gastrointest Endosc. 2010;72(1):150–4.
19. Johanns W, Luis W, Janssen J, et al. Argon plasma coagulation (APC) in gastroenterology: experimental and clinical experiences. Eur J Gastroenterol Hepatol. 1997;9: 581–7.
20. Wahab PJ, Mulder CJ, den Hartog G, et al. Argon plasma coagulation in flexible gastrointestinal endoscopy: pilot experiences. Endoscopy. 1997;29:176–81.
21. Ladas SD, Karamanolis G, Ben-Soussan E. Colonic gas explosion during therapeutic colonoscopy with electrocautery. World J Gastroenterol. 2007;13:5295–8.
22. Manner H, Plum N, Pech O, et al. Colon explosion during argon plasma coagulation. Gastrointest Endosc. 2008;67:1123–7.
23. Wang KK, Kim JY. Photodynamic therapy in Barrett's esophagus. Gastrointest Endosc Clin N Am. 2003;13(3):483–9.
24. American Society of Gastrointestinal Endoscopy. Technology status evaluation update. Gastrointest Endosc. 2006;63:927–32.
25. Wolfsen HC, Ng CS. Cutaneous consequences of photodynamic therapy. Cutis. 2002;69:140–2.
26. Spechler SJ, Sharma P, Souza RF. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. Gastroenterology. 2011;140:1084–91.
27. Shaheen NJ, Sharma P, Overholt BF. Radiofrequency ablation in Barrett's esophagus with dysplasia. N Engl J Med. 2009;360:2277–88.
28. Eric SO, Nan L, Nicholas JS. Efficacy and durability of radiofrequency ablation for Barrett's esophagus: systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11:1245–55.
29. Ganz RA, Utley DS, Stern RA. 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.
30. Dunkin BJ, Martin J, Bejarano PA. Thin-layer ablation of human esophageal epithelium using a bipolar radiofrequency balloon device. Surg Endosc. 2006;20: 125–30.
31. Smith CD, Bejarano PA, Melvin WS. Endoscopic ablation of intestinal metaplasia containing high grade dysplasia in esophagectomy patients using a balloon-based ablation system. Surg Endosc. 2007;21:560–9.
32. Haidry RJ, Dunn JM, Butt MA, et al. Radiofrequency ablation and endoscopic mucosal resection for dysplastic Barrett's esophagus and early esophageal adenocarcinoma: outcomes of the UK National Halo RFA Registry. Gastroenterology. 2013;145(1): 87–95.
33. Franciosa M, Triadafilopoulos G, Mashimo H. Stretta radiofrequency treatment for GERD: a safe and effective modality. Gastroenterol Res Pract. 2013;2013:783–815.

34. Noar M, Squires P, Noar E, Lee M. Long-term maintenance effect of radiofrequency energy delivery for refractory GERD: a decade later. Surg Endosc. 2014;28(8): 2323–33.
35. Stepp H, Sroka R. Possibilities of lasers within NOTES. Minim Invasive Ther Allied Technol. 2010;19(5):274–80.
36. Freitas ML, Bell RL, Duffy AJ. Choledocholithiasis: evolving standards for diagnosis and management. World J Gastroenterol. 2006;12:3162–7.
37. McHenry L, Lehman G. Difficult bile duct stones. Curr Treat Options Gastroenterol. 2006;9:123–32.
38. Neuhaus H, Zillinger C, Born P, et al. Randomized study of intracorporeal laser lithotripsy versus extracorporeal shock-wave lithotripsy for difficult bile duct stones. Gastrointest Endosc. 1998;47:327–34.

5. Training in Advanced Endoscopic Procedures

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Abbreviations

ABS	American Board of Surgery
ACGME	Accreditation Council for Graduate Medical Education
ACS	American College of Surgeons
APDS	Association for Program Directors in Surgery
ASGE	American Society for Gastrointestinal Endoscopy
EGD	Esophagogastroduodenoscopy
ERCP	Endoscopic retrograde pancreatography
EUS	Endoscopic ultrasonography
FEC	Flexible Endoscopy Curriculum
FES	Fundamentals of Endoscopic Surgery TM
FNA	Fine needle aspiration
GAGES-C	Global assessment of gastrointestinal endoscopic skills—colonoscopy
GAGES-UE	Global assessment of gastrointestinal endoscopic skills—upper endoscopy
GIS	Gastrointestinal surgery
HPB	Hepatobiliary
LGIB	Lower gastrointestinal bleeding
MIS	Minimally invasive surgery
NOTES	Natural Orifice Transluminal Endoscopic Surgery
PEG	Percutaneous Endoscopic Gastrostomy
RRC-S	Residency Review Committee for Surgery
UGIB	Upper gastrointestinal bleeding

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Introduction

Initially developed as a method for simple visualization, endoscopy has evolved into one of the most influential tools in modern day medicine. While initially developed by surgeons, this invaluable tool was refined by, and is principally used, by gastroenterologists. However, with the increased use of minimally invasive techniques, flexible endoscopy has become a more vital tool for surgeons. Flexible endoscopic training for surgical residents has, likewise, evolved significantly over the years, with controversy arising as to the number of cases required and the methods of determining competence. To meet the demands of increased need and utilization of endoscopy, educational and clinical collaboration between surgeons and gastroenterologists is required, as this will greatly impact patient outcomes and experience with this great tool.

Brief History of Endoscopy

A Collaborative Effort

Endoscopy began as a method for general surgeons to adapt to both the diagnostic and management challenges at that time. The origins of endoscopy were initially developed and driven by general surgeons, urologists, gynecologists, and gastroenterologists. In 1806, a German army urologist, Phillip Bozzini, developed the *lichtleiter or* "light conductor," an instrument that is now considered the ancestor of modern endoscopy. It was not until years later in 1877 that Maximilian Carl-Friedrich Nitze developed the first usable endoscope that was safe, inexpensive, and clinically relevant. This marked an era of specific operative procedures, demonstrating an important transition from diagnostic to therapeutic endoscopy [1]. In 1880, Jan Mikulicz-Radecki, a junior professor under Theodor Billroth in Vienna, was able to successfully use his instrument as a gastroscope in order to visualize the stomach. This officially marked the beginning of gastrointestinal endoscopy [2, 3]. In 1895, Howard Kelly, a former surgical resident of the well-known general surgeon William Halsted, was the first to describe sigmoidoscopy [4]. Known as the "Father of Gastroscopy," Rudolf Schindler was the first

to describe the instrumentation and techniques of gastroscopy in his published atlas *Lehrbuch und Atlas der Gastroskopie* in 1923. He began the first dedicated group to gastroscopy called The American Gastroscopic Club in 1941, with Schindler as the first president. This club would later become the American Gastroscopic Society in 1961 [5]. The gastroenterologist, Basil Hirschowitz, used a prototype endoscope, passing it down his own esophagus, ushering in the era of modern flexible endoscopy. He introduced the flexible fiber-optic gastroscope at the American Gastroscopy Society in 1957, a society that would later be called the American Society of Gastrointestinal Endoscopy (ASGE). Significant changes in the treatment of upper GI bleeding were implemented by studies performed by both Hirschowitz himself, and Stephen Hedberg, a surgeon from Massachusetts General Hospital [6–8]. The first complete endoscopic colonic visualization came in 1965 by Provenzale and Revignas, two gastroenterologists who were able to biopsy the colon for the first time using endoscopic techniques [9]. In 1965, Harold Hopkins and manufacturer Karl Storz collaborated with the help of George Berci, a general surgeon, to create the new generation of endoscopes with a proximal light source transmitted through glass fibers along a shaft. Utilizing the techniques of upper endoscopy, William McCune, a surgeon from George Washington University, performed the first endoscopic retrograde cholangiopancreatography (ERCP) in 1968 using a fiber-optic gastroduodenoscope [10]. Later on, a gastroenterology fellow in London, Peter Cotton, collaborated with Leslie H. Blumgart, a surgeon, and published a series of 87 ERCPs at three hospitals. This marked the beginning of the workup and endoscopic management of patients presenting with jaundice [11, 12]. It was in 1973 that the first sphincterotomy was performed endoscopically by Kawai and colleagues in Japan, removing gallstones in two patients without any complications. Two other gastroenterologists, Classen and Safrany, described the endoscopic extraction of biliary stones using the basket-like Dormia catheter [13]. In the 1960s, Hiromi Shinya, a surgeon training at Beth Israel Medical Center, developed some of the fundamental principles of colonoscopy [14–16]. Shinya and Wolff went on to publish the follow-up and pathology results of 410 colonoscopies with 42 revealing colon cancer, marking the initial push towards utilizing this method as a means to diagnose and screen for colon cancer [17]. A collaborative effort between Jeffrey Ponsky, a surgical resident, and James King, a gastroenterologist, pro-

duced the ability for marking colon lesions in colonoscopy for further monitoring or removal [18].

Advancements continued in the field of upper endoscopy. Choichi Sugawa, a surgeon from Wayne State reported his experience with using upper endoscopy to diagnose upper GI bleeding [19]. In 1971, the first endoscopic cauterization was performed by Blackwood and Silvis, two gastroenterologists from the University of Minnesota, Minneapolis [20]. The advances in management of upper GI bleeding continued to be made by both surgeons and gastroenterologists during this time period. John Papp, a gastroenterologist from Michigan State University reported an additional case series of 245 upper endoscopies with UGIB with control of bleeding by electrocautery successfully done in 95 % of cases [21]. The double balloon endoscopy was developed by Yamamoto, a gastroenterologist from Japan [22]. The concept of NOTES was also a collaborative effort by both gastroenterologists and surgical endoscopists [23].

This brief overview of the advancement of endoscopy demonstrates the major influence that both the surgical and gastroenterology specialties had in the development of endoscopy. In its origin, endoscopy was introduced as a method of surgical planning and has since evolved into not only a screening method, but as an independent therapeutic agent. Despite its complex evolution, endoscopy remains a substantial tool in the surgical armamentarium. In each specific area of endoscopy itself, the role of both general surgery and gastroenterology is overlapped, and collaboration is vital. The development of multidisciplinary approaches to endoscopy was paramount in its advancement, and will continue to rely on collaboration in order to continue its vitality.

General Surgery

Training a Surgical Endoscopist

A general surgical residency focuses on the diagnosis and management of surgical disease throughout the entire body, with an emphasis on gastrointestinal disease and treatment. Since its origin, a general surgeon's scope of practice has undergone significant changes as the breadth of surgical knowledge and techniques have expanded. This

inevitably translates into adjustments in surgical training in order to accommodate newly required skillsets. Training has drastically changed in the face of an increased prevalence of minimally invasive surgery, technological advances, the growth of nonoperative management, as well as the significant growth of endoscopic procedures. For many procedures, laparoscopic and endovascular surgeries have nearly replaced their open surgery predecessors [24]. Surgical residency began placing much more emphasis on less invasive procedures, with trends towards minimally invasive procedures in the fields of vascular, biliary, and especially advanced endoscopy. As the demand for more minimally invasive procedures began to increase, the interest in improving training curricula involving surgical education in the USA in the past few decades also increased. With regard to endoscopy, in 1980, the American Board of Surgery (ABS) issued a statement mandating that all graduating surgeons perform a variety of endoscopic interventions such as bronchoscopy, esophagoscopy, gastroscopy, colonoscopy, and choledocoscopy [25]. At that time, it was recommended that 29 endoscopic procedures be performed during the 5-year experience. After that, surgical programs made a conscious effort towards providing necessary experiences in endoscopy to surgical residents, with the mentorship from both general surgeons and gastroenterologists. Despite initial skepticism, many surgical programs were able to legitimize the demand for further endoscopic experience at their training program, confirming the notion that a university program has sufficient clinical material to provide adequate training to surgical residents [26, 27]. It was not until 2009 that the Residency Review Committee for Surgery (RRC-S) increased the total requirement of flexible endoscopic experience from 29 to 85 total cases, with 35 upper endoscopies and 50 lower endoscopies required for graduation for resident training [28]. Despite skepticism once again to meet case requirements, surgical institutions were able to remain compliant with these new guidelines. To provide more supervisor availability, some surgical training programs relied on non-surgical subspecialties, like gastroenterology, to provide the necessary service time to train surgical residents in endoscopy. This increased requirement led to significant debate amongst gastroenterologists and surgeons, and is discussed later in this chapter.

The Accreditation Council for Graduate Medical Education (ACGME) closely monitors and evaluates each surgical residency to ensure the highest level of training. The ACGME Review Committee

also assesses the technical competence of each resident by requiring each resident to perform a minimum of 750 major operative cases, with 150 in the resident's chief year. In the area of endoscopy, ACGME guidelines state that a program should "ensure that residents have required experience with a variety of endoscopic procedures, including esophagastroduodenoscopy, colonoscopy, and bronchoscopy, as well as experience in advanced laparoscopy" [29]. In the midst of an ever-growing subspecialty, there has been a push towards developing a much more standardized method of surgical curriculum, aimed at assessing both cognitive and technical skills. This was initiated by the Surgical Skills Curriculum Task Force and aimed at improving the overall clinical experience for residency training. The task force, which consists of the American College of Surgeons and the Association for Program Directors in Surgery, was aimed at a standardization of all aspects of curricula for surgical residents. One of their main areas of focus was the development the Flexible Endoscopy Curriculum (FEC) to establish a standardized longitudinal training program for residents to ensure competency in basic endoscopy (see Overview below). This program not only consists of technical skills milestones, but also cognitive milestones to better prepare surgical residents for scenarios involving endoscopy in practice [30]. The ABS Flexible Endoscopy Curriculum's purpose statement says, "Upon completion of this curriculum, a general surgery residency will have the knowledge and technical skills to manage commonly encountered gastrointestinal disease and conditions using flexible endoscopy." Interestingly, the program requires expert teachers for the residents, which may consist of general surgery endoscopists or gastroenterologists. The goal over time is that surgical endoscopists will be able to train each other, and will remain self-reliant within the surgical community. The proposed curriculum consists of both technical and cognitive milestones for completion. These various milestones are split up into each residency year, allowing for gradual improvement. The implementation of FEC also requires a sole endoscopy rotation for residents to allow for achievement of required operative procedural numbers. The specific cognitive and technical skills examination (Fundamentals of Endoscopic Surgery (FES)) was validated recently in various studies. FES contains a high stakes written exam as well as a virtual reality-based technical assessment tool. The successful passing of FES has been mandated by the ABS for all surgical residents completing residency in 2018.

In addition, a clinical assessment tool known as GAGES-UE (global assessment of gastrointestinal endoscopic skills—upper endoscopy) and GAGES-C (global assessment of gastrointestinal endoscopic skills—colonoscopy) was created [31]. GAGES was developed by both expert upper and lower endoscopists as a method to expand on measuring the proficiency of a training endoscopist. With the notion that mere numbers of procedures performed was not a satisfactory method to measure competency, GAGES was developed as a method of scoring various skillsets, in an effort to objectify clinical performance more accurately. This was proposed and validated initially in 2010 by Vassilliou et al., who performed the test during 2007–2009 on gastroenterology fellows, surgical residents, attending surgeons, and gastroenterologists at 11 institutions. Their areas of skill measurement for upper endoscopy included: intubation of the esophagus, scope navigation, keeping a clear endoscopic field, instrumentation, and quality of assessment. For colonoscopy, the areas consisted of: scope navigation, use of strategies, ability to keep clear endoscopic field, instrumentation, and quality of examination. This method of technical skills evaluation was successfully found to be a reliable method to objectively assess skills [6]. FEC recommends that GAGES be implemented in the surgical curricula starting in their post-graduate year (PGY)-2 or PGY-3 years, consisting of knowledge-based learning, in addition to technical skills. Further on in the PGY-4 year, residents are expected to achieve GAGES scores that are considered "experienced" endoscopists, as shown in the previously stated studies [7]. These significant advancements in developing objective methods for evaluating training endoscopists have sparked a great deal of excitement amongst the endoscopic community.

Overview of Flexible Endoscopy Curriculum for General Surgery Residents (Adapted from [31])

Level I

Cognitive Milestones: Basic understanding of GI diseases and endoscopic GI anatomy

T*echnical Milestones*: Simulation or clinical tutorial exposure with an emphasis on basic scope manipulation including one-handed

wheel deflection, control of suction, irrigation, and insufflation, and passage of instruments through the working channel.

Level II

Cognitive Milestones: Basic understanding of flexible endoscope function.

Technical Milestones: Simulation or clinical exposure with demonstration of proper endoscope setup and function, troubleshooting of common problems, and a continued emphasis on basic scope manipulation.

Level III

Cognitive Milestones: Indications and contraindications of upper and lower flexible endoscopy, periprocedural patient management.

Technical Milestones: Simulation exposure or clinical tutorial, dedicated endoscopy experience, intraoperative endoscopy, ICU endoscopy.

Level IV

Cognitive Milestones: Image differentiation of normal/abnormal pathology, understanding intraoperative and postoperative GI anatomy, appropriate use of endoscopy.

Technical Milestones: Intraoperative endoscopy, ICU endoscopy, continued endoscopic experience.

Level V

Cognitive Milestones: Tools/adjuncts for therapeutic endoscopy.

Technical Milestones: Intraoperative endoscopy, ICU endoscopy, continued endoscopic experience. In this module any skills listed under the description of a ***surgical endoscopist*** that have not been mastered should be performed until a GAGES score of 18 or greater is achieved.

Advanced Surgical Fellowships

With the increasing demand for both laparoscopic and endoscopic trained surgeons, and an overall feeling of unpreparedness of residents at the conclusion of residency, the creation of an advanced laparoendo-

scopic fellowship was inevitable [33]. Despite initial hesitancy from the general surgery community, fearing that the core of general surgery was GI surgery, many non-accredited fellowship programs began training surgical residents in advanced laparoscopy as well as surgical endoscopy. Less than 10 programs for advanced minimally invasive surgery (MIS) and gastrointestinal surgery (GIS) existed in 1993, and 13 years later in 2006, at least 120 programs existed [34]. Initially, these fellowships lacked structure, curriculum and accreditation. So much so that the American Surgical Association Blue Ribbon Committee issued a report in 2004, stating these programs are "unregulated, unsupervised, non-uniform, and uncertified" [35]. During that time, three main GI surgical societies (The Society of American Gastrointestinal and Endoscopic Surgeons, the American Hepato-Pancreato-Biliary Association, and the Society for Surgery of the Alimentary Tract) came together in partnership as the Fellowship Council, a joint institution representing the MIS/GIS programs throughout North American, and developed a formalized match process with published fellowship guidelines. A joint agreement was approved by the ACGME to allow for review and accreditation for institutions interested in providing such fellowships [34, 36, 37]. As it stands, the field of MIS continues to grow exponentially, providing advanced experience to general surgeons. The number of programs has increased from 80 in 2004 to 126 in 2008, to 156 in 2013 [34]. Under the main fellowship category of Advanced GI Surgery, there are subsets for directed training, including Minimally Invasive Surgery, Bariatric Surgery, Hepatobiliary Surgery, and Flexible Endoscopy. The specific curriculum of Flexible Endoscopy is divided into six major units, which includes mastery of the endoscopic intervention associated with each individual unit.

Flexible Endoscopy Fellowship Curriculum [35]

- Unit 1—Acid-peptic disease
- Unit 2—Biliary tract diseases and pancreatic disorders
- Unit 3—Gastrointestinal malignancy
- Unit 4—Motility
- Unit 5—GI Pathology
- Unit 6—Endoscopy

The Fellowship Council has provided recommended guidelines (see Table 5.1) for the number of endoscopic procedures necessary for pro-

Table 5.1. Flexible endoscopy fellowship procedural recommendations [35].

Procedures	Minimum number of cases
EGD	130
Non-variceal bleeding	25 (10 active bleeding)
Variceal bleeding	20 (5 active bleeding)
Colonoscopy	140
With polypectomy and hemostasis	30
ERCP[a]	200
EUS	150
Pancreaticobiliary	75
EUS-guided FNA pancreatic	25
EUS-guided FNA non-pancreatic	25

EGD esophagogastroduodenoscopy, *ERCP* endoscopic retrograde cholangiopancreatography, *EUS*+ endoscopic ultrasonography, *FNA* fine needle aspiration

[a]Minimum 80 % successful cannulation

cedural competence, though they do point out that it is still unclear as to the actual number of flexible endoscopic procedures necessary to attain competence. These numbers are based off of American Society for Gastrointestinal Endoscopy (ASGE) recommendations, and coincide with similar recommendations put forth by the advanced procedures track for gastroenterology fellowship [37].

An additional general surgical fellowship that is becoming much more popular and competitive is colon and rectal surgery. This remains a 1-year fellowship, and all ACGME accreditation requirements must be met within that year. For successful completion of a colorectal fellowship, the ACGME Review Committee mandates the minimal number of colonoscopies to be 140, with 30 of these consisting of interventional procedures. Interestingly, similar to other advanced fellowships, the ACGME is adopting a milestone performance evaluation to monitor the progress of colon and rectal fellows as well [38].

With an ever-increasing need for endoscopic knowledge and skill, surgical residency and fellowship governing bodies will continue to push forth curricula that promote the goals of safety and utilization of flexible endoscopy. While most general surgeons will not be dedicated surgical endoscopists in practice, many will utilize various features of endoscopy throughout their career. Thus, minimal endoscopic training requirements will not only be ever-present for the duration of surgical training, but will likely keep increasing in scope as more procedures and future surgical equipment relies on flexible endoscopic means of therapy for patients.

Gastroenterology

Training a Medical Endoscopist

Due to the growing demand of endoscopic procedures, the field of gastroenterology has rapidly grown to satisfy the demand for what are classified as advanced endoscopic procedures, with further emphasis on sub-specialization [39]. These advanced procedures mostly include endoscopic retrograde pancreatography (ERCP), endoscopic ultrasonography (EUS), endoscopic mucosal resection, esophageal and enteric stent placement, endoscopic drainage of pancreatic pseudocysts, and removal of neoplasms endoscopically. To satisfy both the increasing complexity and sub-specialization of gastroenterology, GI fellowship training time has increased from 2 to 3 years in 1996. This allowed for increasing sub-specialization within the field of gastroenterology, including hepatology, interventional endoscopy, small bowel imaging, inflammatory bowel disease, motility disorders, and gastrointestinal oncology. As it stands, gastroenterology training consists of a 36-month long fellowship after performing at least 3 years of internal medicine training. Of these 36 months, 18 of these are dedicated to core curriculum, which involves patient care experience and inpatient and outpatient consultation. This is focused on core competency, consisting of obtaining experience in medical management of various gastroenterology diseases. Furthermore, most programs include 3–6 months dedicated to research. The remaining 12 months is utilized for specialization into

various fields. Each fellow is assessed by a standardized ACGME objective document for credentialing. The specific areas of competency consist of patient care, medical knowledge, practice based learning, interpersonal and communication skills, professionalism, and system based practice [40].

With regard to technical skills, the minimal requirement of endoscopic procedures has continued to evolve over the years [40]. In 1987, the American College of Physicians had initially proposed a minimum of 50 colonoscopies with 15 polypectomies, and 50 upper endoscopies to achieve competency for hospital privileges [41]. This was changed in 1991, when the ASGE proposed a minimal experience of 100 supervised colonoscopies with a mandatory 20 polypectomies, and 100 upper endoscopies. These recommendations were based on a study by Cass et al., who looked at seven gastroenterology fellows and five surgical residents and their experience with both upper and lower endoscopies. They concluded that cecal intubation was successful in 84 % of patients after 100 endoscopies, and esophageal intubation was successful in 90 % after 100 procedures [42]. This was again changed in 2002, when the ASGE requirements for gastroenterology fellowship were a minimal of 140 colonoscopies and 130 upper endoscopies. These changes were based on one study of nine participants, and a study published only in abstract form [43, 44]. At this time, all fellows are required to complete these requirements, and all must be able to provide routine screening endoscopy and common therapeutic procedures such as polypectomies and hemostasis techniques. These requirements are similar to those demonstrated in the Overview of Flexible Endoscopy Curriculum for General Surgery Residents above, with the addition of 15 Percutaneous Endoscopic Gastrostomy tubes (PEG), and 25 capsule endoscopy procedures. There are two various training tracks that can be chosen by each fellow, Level 1 and Level 2. A Level 1 gastroenterologist is one trained in "… performing routine gastrointestinal endoscopic and non-endoscopic procedures as part of the practice of gastroenterology and gastroenterologists specializing in non-endoscopic aspects of gastroenterology, including but not limited to, the study of liver diseases, motility, nutrition, and basic science research." Level 2 trained gastroenterologists focus on advanced endoscopic procedures, such as ERCP, EUS, EMR, endoscopic GERD therapy, and may require an additional fourth year of training. Interestingly, the numbers of procedures necessary for graduation are minimal requirements. Establishing competency for these pro-

cedures has remained, and will likely continue to be, a heavily debated topic. The requirements are similar to the ERCP and EUS requirements stated in Overview of Flexible Endoscopy Curriculum for General Surgery Residents. The curriculum outline states, "Endoscopic competence is difficult to define and quantify. Evaluation remains largely subjective." As it stands, endoscopic competence relies on the discretion of the program directors. There is, however, an objective documentation requirement set forth by the American Board of Internal Medicine for each program director to keep track of, to provide substantiality for competence. These areas of are adapted from the Principles of Training, published by ASGE. There is, however, a section in training devoted to surgical education. As stated in the Core Curriculum, "Surgery is the primary and preferred method of management for some gastrointestinal disorders." One of the paramount goals of gastroenterology fellowship remains in the understanding of the surgical management of patients. They are required to learn operative indications, surgical steps, and postoperative outcomes. This area of education, however, is mainly taught through lectures and didactics, with no surgical operative experience outside of observation. A surgical rotation during the fellowship is encouraged, but is optional [40].

Gastroenterology and General Surgery

A Comparison

In the past 50 years, there has been a great deal of controversy regarding the milestones required to train a physician to perform endoscopy proficiently. In a field overlapped by both gastroenterologists and general surgery, it is not surprising that areas of contention would ensue. Controversy over the definition of competence, procedural numbers, and training curriculum has continued to remain a topic of debate for the past decade and will continue as more advanced GI surgical endoscopists begin practicing and training junior residents. Despite collaborative advancements and contributions to endoscopy, general surgeons and gastroenterologists are at the center of a global discussion regarding determining the best method to train a skilled endoscopist. Both general surgeons and gastroenterologists seek to reach the goal of achieving both cognitive

and motor competency in endoscopy, yet their training pathways are completely different. A great deal of resources has focused on developing various objective tools for assessing competence, and to attempt to objectify a previously subjective measurement. The significance of this issue directly affects privileging and credentialing at various hospitals, placing substantial financial implications on such an issue.

One of the initial areas of controversy came from a position paper published in 2011. Four of the largest gastrointestinal societies (The American Society for Gastrointestinal Endoscopy, the American Association for the Study of Liver Diseases, the American College of Gastroenterology, and the American Gastroenterological Association) released a controversial position paper stating their concern with creating an arbitrary number to define competency [45]. The paper, written in response to the recent change in surgical residency requirements for endoscopic procedures to 85 (50 colonoscopies and 35 upper endoscopies), mentions a concern regarding the "quality of endoscopic training, especially when the surgical residents are required to perform only a fraction of procedures necessary to achieve competency." The paper went on to mention an inevitable increased burden on gastroenterologists, who train surgical residents at some programs. The main concern was in the area of achieving "competency," which they defined as "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." Their recommendations followed the ASGE guidelines, proposing a total of 140 colonoscopies and 130 upper endoscopies as benchmarks. They cited two major studies to support their claims. The first, by Spier et al. professed a competency baseline of 200–300 procedures [46]. They also cited a study by Rabeneck et al. which concluded an increased risk of missed colorectal cancer in patients who had their procedures performed by "non-intensely trained" physicians, which included internists, family medicine practitioners and general surgeons in a single group [45, 47].

It is no surprise that this sparked a great deal of discord in the surgical community. The American Board of Surgery initiated a rebuttal statement on February 24, 2011, regarding the article's conclusions, stating that the general surgeon's role in endoscopic management of patient's is paramount to patient care, and that maintaining surgical involvement in endoscopy is necessary to provide "effective and comprehensive care and to serve the public need." One area of focus remained on the issue

of competency. The ABS stated that they "do not maintain that any numerical standard defines competence in any procedure," and "counting the number of cases is an inadequate surrogate for measuring safety and competence during training or afterwards." They also noted the significance of providing endoscopy to rural regions, areas that are underserved by gastroenterologists. These two position papers ignited a great deal of research focused on improving residency training, defining competency, and questioning hospital privileges to physicians who perform endoscopy [48]. One article quoted in the ABS paper was a study by Wexner et al., who prospectively studied the safety and efficacy of surgeons performing colonoscopies, while incorporating the current credentialing guidelines at that time. Their study demonstrated a safety completion rate of 92 %, and complication rate of 0.074 %. Their conclusions were based on the review of 21 additional studies that demonstrated a mean completion rate of 81.9 %, studies consisting of both general surgeons and gastroenterologists [49].

The question of competency is a hotly debated topic. There are multiple areas of deviation from both general surgery and gastroenterology regarding their definitions of "competence" in each endoscopic procedure. For ERCP, it was originally defined as the ability to achieve cannulation of the biliary and pancreatic ducts, and to perform a successful sphincterotomy. Multiple studies have attempted to determine the number for competency, including a study by Jowel et al., who stated that at least 180 ERCPs needed to be performed for competency [50]. In 1999, the definition of proficiency was redefined by the ASGE, defining it as the ability to achieve cannulation of the desired duct, perform a successful sphincterotomy, to achieve biliary or pancreatic decompression, and to gather the desired imaging or pathology to conclude a diagnosis and treatment plan. Because of the difficulty of the procedure and need for focused study, ERCP training has been relegated to a subspecialty of interventional gastroenterology fellowships. As it stands, there are currently over 70 programs that provide HPB training spanning from 12 months to 24 months, depending on the requirement for transplant surgery. The current recommendations for general surgery residency require at least 80 endoscopic procedures, with no minimum number of ERCPs. While these recommendations include upper endoscopy alone, a recent survey reports that only 24 % of the total upper endoscopies consisted of an ERCP [51]. It is postulated that this is directly related to referrals of these operations to gastrointestinal specialists. As the focus

of HPB surgery progresses more towards noninvasive procedures, the number of endoscopic opportunities continues to increase, creating a higher demand for the subspecialty.

The concept of colonoscopy has been around since the late nineteenth century, and has undergone significant changes in the past century. It is a routinely performed procedure throughout the world and serves as an established method for diagnosis and management of an abundance of colorectal pathology. It continues to remain the most accurate intervention for diagnosing colorectal cancer [49]. Despite initially introduced by surgeons, the general surgeon's role in colonoscopy has been an intense topic of discussion over the past two decades. The implications of this topic affect residency training, hospital credentialing, and fellowships, all of which have significant financial consequences. As it stands, there are a variety of studies both published and ongoing that attempt to define competency and success rates with regard to colonoscopy. The debate has sparked a plethora of retrospective and prospective studies analyzing the outcomes of surgeons and gastroenterologists in the attempt to determine if there remains a disparity between outcomes between these two specialties. One of the first studies to look at surgical endoscopists was performed by Wexner et al., which retrospectively looked at 2069 colonoscopies performed by surgeons from 1992 to 1995, demonstrating a rate of completion of 96.5 %, bleeding of 0.097 %, and perforation in 0.14 % [52]. These favorable results sparked a follow-up prospective study discussed earlier looking at 13,580 colonoscopy cases with the outcomes of both efficacy and safety of performed the interventions. They concluded that surgeons are capable of successfully performing safe and effective colonoscopies, demonstrating a completion rate of 92 % with minimal bleeding and perforation rates. Regarding proficiency, their data also demonstrated increased completion time with increased annual experience, specifically that participants who had a minimum of 50 colonoscopies with 100 annual procedures had high rates of completion. Interestingly, they concluded that there was no minimum number of colonoscopies that could be mandated for credentialing to perform safe colonoscopies [49].

There are a great deal of studies that attempt to define the definition of competency, and attempt to disclaim surgeons as safe endoscopists. However, surgeons have the benefit of performing routine manual tissue manipulation and three-dimensional anatomical evaluation, both of

which aid in evaluating and treating patients with endoscopic techniques. It can be said that, while they perform significantly more endoscopies in training, gastroenterologists may be limited by insufficient experience with tissue planes, texture, and overall anatomic architecture during complex endoscopic procedures. There are no sufficient data supporting this notion, but many surgeons would argue that their overall experience with a multitude of other skillsets, including laparoscopic surgery, would ensure their competency in endoscopic procedures.

Over the years, advancements in endoscopy have drastically improved the ability to manage, stage, and surgically plan disease management. While endoscopy has improved the use of noninvasive techniques and decreased the need for urgent surgical intervention, the necessity for surgery still exists. The diagnostic advantages of endoscopy are generally used to plan surgical procedures. In addition to this, while complications from endoscopic procedures are rare, surgical management is often required in the event of endoscopic complications. Relying on general surgeons to provide the continuity of care and safety net for complications is paramount in providing quality patient care. It is apparent that, despite the significant growth of endoscopy, surgical management and understanding of three-dimensional anatomy still remains an essential aspect of patient care.

Rural and Urban Endoscopy

Geographical Disparity

As described earlier in this chapter, one of the main arguments for continuing to keep general surgeons directly involved in endoscopic training is the significant disparity between urban and rural resources. In the USA, there are approximately 56 million people living in rural locations, accounting for 20 % of the total population [53]. A significant gap exists between the rural and urban surgical force, finding a ratio of 4.48 rural surgeons to 100,000 patients compared to 6.36 surgeons per 100,000 people in the urban setting. Decreased availability has also led to procedural differences between urban and rural surgeons. A study by Heneghan et al. found a higher volume of endoscopic, gynecological, obstetrics, and urological procedures performed by rural surgeons. Endoscopy itself makes up approximately 40 % of

rural surgical procedures, with some general surgeons shifting their practice to 86 % endoscopic procedures [54]. Within rural communities themselves, smaller community surgeons demonstrate a substantially higher number of endoscopic procedures compared to larger community based surgeons, simply because the general surgeon is the only accredited practitioners who can performed endoscopy at the hospital. A survey published by Valentine et al. in 2011 determined that urban surgeons performed significantly less endoscopic procedures than their rural surgical counterparts, where endoscopy made up the highest percentage of their total procedures. Rural surgeons performed over 200 endoscopies a year, well above the average of urban surgeons. Interestingly, their study found a rural physician density of gastroenterologists of 0.39 per 100,000 patients, compared to 4.8 per 100,000 patients of general surgeons [55]. The American Board of Surgery argued that limiting the credentialing criteria for surgeons to perform endoscopy would undoubtedly restrict access to care in already underserved regions. This will, inevitably, continue to remain as the demand for general surgeons continues to increase. With the high demand for rural endoscopists, endoscopic training in surgical residency remains paramount to train rural based surgeons. A recent study by Aboagye et al. looked at the rural access to colorectal cancer care in the USA, showing the significant disparity between access to urban and rural general surgeons [56]. The evidence suggests a true demand for endoscopists in rural communities, a demand mostly met by a supply of general surgeons. As endoscopic interventions continue to improve, the need for any invasive surgery inevitability will continue to decline, but will undoubtedly remain. While most surgical specialists and gastroenterologists agree in the management of upper GI bleeding, there still remains a territorial debate at each institution. Significant endoscopic advancements have led to a successful management of upper GI bleeding by endoscopic means to 94 %. While major academic institutions have the necessary resources to provide a gastroenterology service, these services are less available at community based, rural hospitals [56]. As it stands, a general surgeon successfully trained in endoscopy remains the sole management option in many rural communities. While gastroenterology as a subspecialty continues to grow and more gastroenterologists will undoubtedly move their practice into these regions, the current environment relies on community general surgeons to provide endoscopic interventions.

The Future of Endoscopy

Collaboration

Endoscopy is an invaluable technology invented by surgeons and matured by gastroenterologists over the last century. Its use has increased dramatically, with its ability to not only diagnose but to treat a wide variety of gastrointestinal diseases. Minimally invasive techniques continue to evolve for the treatment of patients, and nowhere is this seen more than in the endoscopic realm. Such evolution will force surgeons to become more facile and proficient using the endoscope as another tool in the armamentarium for treating disease as endoscopy's role increases. While there continues to be debate about how many specific endoscopic procedures should be performed by trainees, more focus should be on qualitative proficiency rather than just a quantitative statistic of numbers performed. Regardless of this debate, what is known is that there is an ever-present overlap of surgical and gastroenterological disciplines for the treatment of many gastrointestinal diseases, thus requiring collaboration and partnership in order to foster the next evolution of endoscopic therapy.

References

1. Morgenthal CB, Richards WO, Dunkin BJ, Forde KA, Vitale G, Lin E, et al. The role of the surgeon in the evolution of flexible endoscopy. Surg Endosc. 2007;21(6): 838–53.
2. Kuczkowski J, Stankiewicz C, Kopacz A, Narozny W, Mikaszewski B, Drucis K. Jan Mikulicz-Radecki (1850-1905): pioneer of endoscopy and surgery of the sinuses, throat, and digestive tract. World J Surg. 2004;28(10):1063–7.
3. Berci G, Forde KA. History of endoscopy: what lessons have we learned from the past? Surg Endosc. 2000;14(1):5–15.
4. Kelly HA. VI. A new method of examination and treatment of diseases of the rectum and sigmoid flexure. Ann Surg. 1895;21(4):468–78.
5. Schäfer PK, Sauerbruch T. Rudolf Schindler (1888–1968)—"father" of gastroscopy. Z Für Gastroenterol. 2004;42(6):550–6.
6. Hirschowitz BI. Endoscopic examination of the stomach and duodenal cap with the fiberscope. Lancet. 1961;1(7186):1074–8.
7. Hirschowitz BI, Balint JA, Fulton WF. Gastroduodenal endoscopy with the fiberscope—an analysis of 500 examinations. Surg Clin North Am. 1962;42:1081–90.

8. Hirschowitz BI. Photography through the fiber gastroscope. Am J Dig Dis. 1963;8:389–95.
9. Provenzale L, Revignas A. An original method for guided intubation of the colon. Gastrointest Endosc. 1969;16(1):11–7.
10. McCune WS, Shorb PE, Moscovitz H. Endoscopic cannulation of the ampulla of Vater: a preliminary report. Ann Surg. 1968;167(5):752–6.
11. Cotton PB. Cannulation of the papilla of Vater by endoscopy and retrograde cholangiopancreatography (ERCP). Gut. 1972;13(12):1014–25.
12. Salmon PR. Endoscopic retrograde choledochopancreatography in the diagnosis of pancreatic disease. Gut. 1975;16(8):658–63.
13. Classen M, Safrany L. Endoscopic papillotomy and removal of gall stones. Br Med J. 1975;4(5993):371–4.
14. Shinya H, Wolff WI. Morphology, anatomic distribution and cancer potential of colonic polyps. Ann Surg. 1979;190(6):679–83.
15. Sircus W. Milestones in the evolution of endoscopy: a short history. J R Coll Physicians Edinb. 2003;33(2):124–34.
16. Sivak MV. Polypectomy: looking back. Gastrointest Endosc. 2004;60(6):977–82.
17. Wolff WI, Shinya H, Geffen A, Ozaktay SZ. Colonofiberoscopy. A new and valuable diagnostic modality. Am J Surg. 1972;123(2):180–4.
18. Ponsky JL, King JF. Endoscopic marking of colonic lesions. Gastrointest Endosc. 1975;22(1):42–3.
19. Sugawa C, Werner MH, Hayes DF, Lucas CE, Walt AJ. Early endoscopy: a guide to therapy for acute hemorrhage in the upper gastrointestinal tract. Arch Surg. 1973;107(2):133–7.
20. Blackwood WD, Silvis SE. Electrocoagulation of hemorrhagic gastritis. Gastrointest Endosc. 1971;18(2):53–5.
21. Papp JP. Endoscopic electrocoagulation of upper gastrointestinal hemorrhage. JAMA. 1976;236(18):2076–9.
22. Yamamoto H, Kita H, Sunada K, Hayashi Y, Sato H, Yano T, et al. Clinical outcomes of double-balloon endoscopy for the diagnosis and treatment of small-intestinal diseases. Clin Gastroenterol Hepatol. 2004;2(11):1010–6.
23. Moris DN, Bramis KJ, Mantonakis EI, Papalampros EL, Petrou AS, Papalampros AE. Surgery via natural orifices in human beings: yesterday, today, tomorrow. Am J Surg. 2012;204(1):93–102.
24. Eckert M, Cuadrado D, Steele S, Brown T, Beekley A, Martin M. The changing face of the general surgeon: national and local trends in resident operative experience. Am J Surg. 2010;199(5):652–6.
25. Patel NM, Terlizzi JP, Trooskin SZ. Gastrointestinal endoscopy training in general surgery residency: what has changed since 2009? J Surg Educ. 2014;71(6):846–50.
26. Smale BF, Reber HA, Terry BE, Silver D. The creation of a surgical endoscopy training program—is there sufficient clinical material? Surgery. 1983;94(2):180–5.

27. Dasmahapatra KS, Najem AZ, Cheung NK. Surgical endoscopy training in a university program. Am Surg. 1986;52(6):287–90.
28. Bittner IV JG, Marks JM, Dunkin BJ, Richards WO, Onders RP, Mellinger JD. Resident training in flexible gastrointestinal endoscopy: a review of current issues and options. J Surg Educ. 2007;64(6):399–409.
29. ACGME Program Requirements for Graduate Medical Education in General Surgery [Internet]. https://www.acgme.org/acgmeweb/Portals/0/PFAssets/ProgramRequirements/440_general_surgery_07012014.pdf.
30. Bittner JG, Marks JM, Dunkin BJ, Richards WO, Onders RP, Mellinger JD. Resident training in flexible gastrointestinal endoscopy: a review of current issues and options. J Surg Educ. 2007;64(6):399–409.
31. Flexible Endoscopy Curriculum for General Surgery Residents [Internet]. http://www.absurgery.org/xfer/abs-fec.pdf.
33. Rattner DW, Apelgren KN, Eubanks WS. The need for training opportunities in advanced laparoscopic surgery. Surg Endosc. 2001;15(10):1066–70.
34. Park A, Kavic SM, Lee TH, Heniford BT. Minimally invasive surgery: the evolution of fellowship. Surgery. 2007;142(4):505–13.
35. Debas HT, Bass BL, Brennan MF, Flynn TC, Folse JR, Freischlag JA, et al. American Surgical Association Blue Ribbon Committee Report on Surgical Education: 2004. Ann Surg. 2005;241(1):1–8.
36. Hunter JG. The case for fellowships in gastrointestinal and laparoendoscopic surgery. Surgery. 2002;132(3):523–5.
37. Fellowship Council—Program Guidelines [Internet]. [cited 19 Oct 2014]. https://fellowshipcouncil.org/about/program-guidelines/.
38. ACGME Program Requirements for Graduate Medical Education in Colon and Rectal Surgery [Internet]. https://www.acgme.org/acgmeweb/Portals/0/PFAssets/ProgramRequirements/060_colon_rectal_surgery_07012014.pdf.
39. Elta GH. GI training: where are we headed? Am J Gastroenterol. 2011;106(3):395–7.
40. The Gastroenterology Core Curriculum [Internet]. http://www.gastro.org/2007_Version_Core_Curriculum.pdf.
41. Golden E, William A. Reynolds, and James S. Roberts. Clinical competence in diagnostic esophagogastroduodenoscopy. Ann Intern Med. 1987;107(6):937–9.
42. Cass OW, Freeman ML, Peine CJ, Zera RT, Onstad GR. Objective evaluation of endoscopy skills during training. Ann Intern Med. 1993;118(1):40–4.
43. Cass O, Freeman M, 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(4):308.
44. Marshall JB. Technical proficiency of trainees performing colonoscopy: a learning curve. Gastrointest Endosc. 1995;42(4):287–91.
45. ASGE, AASLD, ACG, and AGA Statement Regarding the ABS Mandate for Surgery Resident Training in Endoscopy [Internet]. http://www.asge.org/uploadedFiles/Pressroom/JointSocietyABSTrainingStatement2011.pdf.

46. Spier BJ, Benson M, Pfau PR, Nelligan G, Lucey MR, Gaumnitz EA. Colonoscopy training in gastroenterology fellowships: determining competence. Gastrointest Endosc. 2010;71(2):319–24.
47. Rabeneck L, Paszat LF, Saskin R. Endoscopist specialty is associated with incident colorectal cancer after a negative colonoscopy. Clin Gastroenterol Hepatol. 2010;8(3):275–9.
48. ABS Statement on GI Endoscopy|American Board of Surgery [Internet]. [cited 9 Aug 2014]. http://www.absurgery.org/default.jsp?newsgiresponse.
49. Wexner SD, Garbus JE, Singh JJ, SAGES Colonoscopy Study Outcomes Group. A prospective analysis of 13,580 colonoscopies. Reevaluation of credentialing guidelines. Surg Endosc. 2001;15(3):251–61.
50. Jowell PS, Baillie J, Branch MS, Affronti J, Browning CL, Bute BP. Quantitative assessment of procedural competence: a prospective study of training in endoscopic retrograde cholangiopancreatography. Ann Intern Med. 1996;125(12):983–9.
51. Chang Y-J, Mittal VK. Hepato-pancreato-biliary training in general surgery residency: is it enough for the real world? Am J Surg. 2009;197(3):291–5.
52. Wexner SD, Forde KA, Sellers G, Geron N, Lopes A, Weiss EG, et al. How well can surgeons perform colonoscopy? Surg Endosc. 1998;12(12):1410–4.
53. Williams TE, Satiani B, Thomas A, Ellison EC. The impending shortage and the estimated cost of training the future surgical workforce. Ann Surg. 2009;250(4):590–7.
54. Heneghan SJ, Bordley J, Dietz PA, Gold MS, Jenkins PL, Zuckerman RJ. Comparison of urban and rural general surgeons: motivations for practice location, practice patterns, and education requirements. J Am Coll Surg. 2005;201(5):732–6.
55. Valentine RJ, Jones A, Biester TW, Cogbill TH, Borman KR, Rhodes RS. General surgery workloads and practice patterns in the United States, 2007 to 2009: a 10-year update from the American Board of Surgery. Ann Surg. 2011;254(3):520–5. Discussion 525–526.
56. Aboagye JK, Kaiser HE, Hayanga AJ. Rural-urban differences in access to specialist providers of colorectal cancer care in the united states: a physician workforce issue. JAMA Surg. 2014;149(6):537–43.

Part II
Managing Surgical Complications

6. Endoscopic Management of Bleeding

Kathryn E. Fong and Kevin El-Hayek

Introduction

Gastrointestinal (GI) bleeding is a commonly occurring medical emergency, frequently associated with peptic ulcer disease. A 1991 study in the USA reported that 59 % of acute upper GI bleeding is caused by peptic ulcer disease, with a range of 28–59 % when examining other Western countries such as the UK, Scotland, France, and Greece [1]. Though morbidity and mortality have improved due to improvements in medical and interventional therapies, there still exists mortality from GI bleeding. Studies from the 1990s report an all-cause mortality rate of 3–14 %. This is similar to the 3.5 % mortality reported in a retrospective Canadian registry of non-variceal upper GI bleeding [1, 2]. Furthermore, it continues to represent a significant amount of healthcare expenditure. In studies from 1998 and 2004, the mean cost of peptic ulcer hemorrhage was between USD 1883 and 17,933 [3]. A 1997 study evaluating the epidemiology and outcomes of patients with lower GI bleeding demonstrated an incidence of 22 people per 100,000 adults that were hospitalized for lower GI bleeding [4].

This chapter will review the presentation, assessment, and endoscopic management of upper, lower, and occult GI bleeding.

Clinical Presentation

Depending on location and volume of blood loss, GI hemorrhage can manifest quite variably. The appearance of hematemesis—bright red blood or the oft described "coffee ground emesis" suggests a location proximal to the ligament of Treitz. Brighter blood can suggest a more

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rapid or more recent bleed, while darker "coffee ground" characteristic suggests blood that has been partially digested by gastric acid. A nasogastric tube aspirate can be used to better elucidate the character of the hemorrhage. Melena refers to dark, tarry stools that result from the degradation of heme as it travels through the GI tract, and often signals an upper GI source. However, a rapid or massive upper GI hemorrhage can also manifest itself as hematochezia—the appearance of bright blood from the rectum. Failure to recognize the upper gastrointestinal tract as a potential source of bleeding must be avoided, as it can have potentially fatal results. Lower GI bleeding often presents as bright red blood per rectum, although blood from the right colon may have a darker, more melenotic appearance. The less common etiology, known as obscure GI bleeding, is defined as bleeding from an unknown source that persists or recurs following a negative endoscopic evaluation [5]. Traditionally, this includes an esophagoduodenoscopy and colonoscopy with examination of the terminal ileum. This entity can present *overtly*, with visible evidence of bleeding stigmata, or *occultly*, without visible evidence but with signs or symptoms of blood loss, including anemia and/or positive fecal occult blood.

A thorough patient history should be obtained, and can often provide important information with regard to location and/or etiology. Weight loss, change in bowel habits, medications, alcohol use, history of malignancy, diverticulosis, or prior colonoscopy are all examples of important questions that should be addressed with the patient.

With regard to exam, the patient may have a completely benign abdominal exam as may occur in slow upper, or obscure GI bleeding. Conversely, colicky abdominal pain and loose stools may be elicited due to the cathartic effect of blood in the lower gastrointestinal tract. A rectal exam should always be performed in cases of suspected GI bleeding; occult blood testing should accompany exams without gross evidence of hemorrhage. Furthermore, attention must be paid to signs of liver disease including ascites, jaundice, spider angiomata, and gynecomastia. In a patient with GI hemorrhage, these should raise the suspicion for variceal bleeding, both from the upper and lower GI tract.

Initial Assessment

Proper evaluation and assessment is critical in patients with upper GI hemorrhage. A full set of vital signs should be obtained, including orthostatic vital signs, as aberrations such as tachycardia or postural hypotension can be the first signs of impending hypovolemic shock (Table 6.1).

Table 6.1. Classification of hypovolemic shock.

	Class I	Class II	Class III	Class IV
Blood loss (mL)	≤750	750–1000	1500–2000	
Blood loss (%)	≤15	15–30	30–40	
Heart rate (beats/min)	<100	≥100	>120	
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal or increased	Decreased	Decreased	Decreased
Mental status	Slightly anxious	Mildly anxious	Anxious/confused	Confused/lethargic
Fluid replacement	Crystalloid	Crystalloid	Crystalloid, blood	Crystalloid, blood

A focused history and review of systems should be performed to elicit important comorbid or concomitant conditions that may affect medical or endoscopic management. Patients presenting with hematemesis should be evaluated for airway compromise, and if present, a secure airway established. Complete blood count, complete metabolic panel with liver function tests, assessment of coagulation with prothrombin time and partial thromboplastin time, and blood type and crossmatch should be obtained with blood work.

Fluid Resuscitation

Much of the literature on resuscitation in hypovolemic, or hemorrhagic, shock is applied from trauma and critical care literature. Two large-bore peripheral intravenous lines should be obtained and resuscitation undertaken. Classical teaching supports early resuscitation with infusion of crystalloid fluid, such as 0.9 % normal saline or lactated Ringer's solution in order to restore intravascular circulating volume from ongoing losses, and prevent inadequate tissue perfusion [6]. Recent years have seen controversy over type of fluid, colloid versus crystalloid, used for resuscitation in shock. A 2012 Cochrane Database Review of randomized controlled trials examining resuscitation with crystalloid versus colloid solutions demonstrated no survival benefit to colloids. Given the increased cost of colloid solutions–coupled with its failure to provide a survival benefit and an increased mortality associated with hydroxyethyl starch—the authors recommend use of crystalloid solution in resuscitation [7].

Correction of Coagulopathy

Any clinical or laboratory evidence of coagulopathy should be quickly corrected to assist in controlling the hemorrhage. Care should be taken in those patients with blood loss requiring massive transfusion of red blood cells, (greater than 10 units) as these patients are at risk of developing a concomitant dilutional coagulopathy. The massive transfusion of red blood cells results in a relative deficit in platelets and clotting factors, which unless corrected with transfusions of platelets and plasma will further exacerbate any existing coagulopathies [8].

Nasogastric Tubes

Nasogastric (NG) tube use in the assessment and management of upper GI hemorrhage is controversial. As alluded to earlier, placement of an NG tube can facilitate localization of bleeding with the presence of "coffee grounds" or fresh blood in the NG aspirate. However, it should not be used in lieu of a careful history and physical, as up to 15 % of true upper GI sources of bleeding may be missed if the NG aspirate is falsely clear [9]. An NG tube may also be used to lavage the stomach in preparation for endoscopic intervention, which will be covered later in the chapter. Care must also be taken in the insertion of NG tubes, especially if the etiology of the GI hemorrhage is unknown. Bleeding from esophageal varices or Mallory–Weiss tears may be exacerbated by a careless insertion technique.

Risk Stratification

Many GI hemorrhages resolve spontaneously or with medical management, and never require endoscopic or surgical intervention. In contrast, patients with massive GI hemorrhage may require admission to an intensive care unit for close monitoring and aggressive resuscitation with multiple transfusions and interventions. Thus, a way to stratify these patients into low-risk and high-risk groups is useful for developing management strategies, allocating resources, and predicting prognosis and outcomes.

One of the most common ways to classify UGIB into low and high-risk patient populations is by using endoscopy to assess for stigmata of

Table 6.2. Forrest classification.

Forrest class	Lesion
1A	Arterial spurting
1B	Active oozing
2A	Ulcer with nonbleeding visible vessel
2B	Ulcer with adherent clot on surface
2C	Ulcer with red or dark blue flat spot
3	Ulcer with clean base

Table 6.3. Rockall score.

	Score			
Variable	**0**	**1**	**2**	**3**
Age (years)	<60	60–79	≥80	
Shock	None	Tachycardia	Hypotension	
	Systolic blood pressure ≥ 100	SBP ≥ 100	SBP < 100	
	Pulse < 100	Pulse ≥ 100		
Comorbidity	None		Cardiac failure	Renal failure
			Ischemic heart disease	Liver failure
			Any major comorbidity	Disseminated malignancy
Diagnosis	Mallory–Weiss	All other diagnoses	Malignancy of upper GI tract	
	No lesion			
	No SRH			
Major of stigmata recent hemorrhage (SRH)	None		Blood visible in upper GI tract	
	Dark spot		Adherent clot	
			Visible or spurting vessel	

active or recent bleeding. In 1974, Forrest et al. developed a classification system for these characteristics (Table 6.2).

The most extensively validated scoring models are the Blatchford and Rockall scores. The Rockall scoring system uses age, presence and severity of hemodynamic compromise, diagnosis, and stigmata of recent hemorrhage to calculate a risk score. While the score is easy to calculate, it does require endoscopy for diagnosis and assessment of stigmata of hemorrhage [10] (Table 6.3).

Table 6.4. Blatchford score.

Admission Risk Marker			Score component value	
BUN (mmol/L)	6.5–8		2	
	8–10		3	
	10–25		4	
	>25		6	
Hemoglobin (g/dL)	*Men*	*Women*	*Men*	*Women*
	12–13	10–12	1	1
	10–12	<10	3	6
	<10		6	
Systolic blood pressure	100–109		1	
	90–99		2	
	<90		3	
Other markers	Pulse > 100 beats/min		1	
	Melena		1	
	Syncope		2	
	Hepatic disease		2	
	Cardiac failure		2	

The Blatchford score was developed out of the desire to predict and identify which patients need treatment. Using variables such as hemoglobin, blood urea levels, pulse, and systolic blood pressure, combined with presenting features of syncope or melena and medical history including liver disease or cardiac failure, the authors created a screening score that can be used at initial presentation (Table 6.4).

Patients who were identified as low-risk of needing clinical intervention for upper GI hemorrhage had a blood urea level less than 6.5 mmol/L, hemoglobin greater than 13 g/dL and 12 g/dL for men and women, respectively, systolic blood pressure greater than 110 mmHg, and heart rate less than 100 bpm [11].

Upper Gastrointestinal Tract

One of the most common causes of acute upper GI hemorrhage is gastric and duodenal ulcers. Gastric ulcers can occur anywhere in the stomach. They are classified into five categories, using criteria such as location and causative factors. Type I ulcers are the most common; they make up approximately 60 % of gastric ulcers. They are located on the lesser curvature, often near the incisura angularis. These ulcers are often associated with normal gastric acid secretion. Contrasting these are type

II ulcers. These ulcers are more often located in the body of the stomach. They comprise approximately 15 % of gastric ulcers and are often seen in conjunction with excess acid secretion. Type II ulcers are also commonly seen in conjunction with duodenal ulcers. Type III ulcers are typically found in the pre-pyloric region of the stomach. They account for approximately 20 % of ulcers. Like type II ulcers, these are also often seen in states with elevated acid levels. Type IV ulcers occur near the gastroesophageal junction, high along the lesser curvature. They account for less than 10 % of ulcers and tend not to have an association with excess acid secretion. Type V ulcers are considered relatively new to the classification schema. Their location is variable, and they are associated with chronic nonsteroidal anti-inflammatory use, rather than elevated acid levels.

Ulcers that are noted to have pulsatile or arterial bleeding, adherent clot, or a visible vessel are considered high-risk for bleeding and should undergo endoscopic intervention (Fig. 6.1).

With the increased use of endoscopy, the development of endoscopic therapies for the conditions diagnosed by endoscopy also developed and evolved. They can be classified into broad categories: injection therapy, thermal therapy, mechanical devices, or a combination of all the above.

Injection therapy is one of the most common modalities utilized for bleeding peptic ulcers. Endoscopists use a vasoconstricting solution, most commonly epinephrine, in order to stem hemorrhage. Twenty to forty milliliters of a diluted solution of 1:10,000 in normal saline is injected circumferentially around and under the ulcer base [12, 13]. Injection therapy is most often used in conjunction with other therapies for hemostasis.

Thermal therapy, which includes bipolar electrocautery and heater probes, is another endoscopic modality used to control GI hemorrhage. Heater probes are used to both tamponade and direct thermal energy to coagulate a bleeding vessel.

Clips, endoloops, and rubber bands are also part of the endoscopic arsenal used to achieve hemostasis from gastrointestinal bleeding. Though it is slightly different for each device, the primary mechanism relies on the sustained compression of a bleeding vessel. With respect to ulcer disease, clips are more commonly used than bands or endoloops due to the anatomy of ulcers (Fig. 6.2).

The above modalities are often used in combination to improve efficacy. There are multiple studies that evaluate the efficacy of varying combinations of injection, thermal, and mechanical devices in providing hemostasis, with the majority demonstrating that combination therapy is

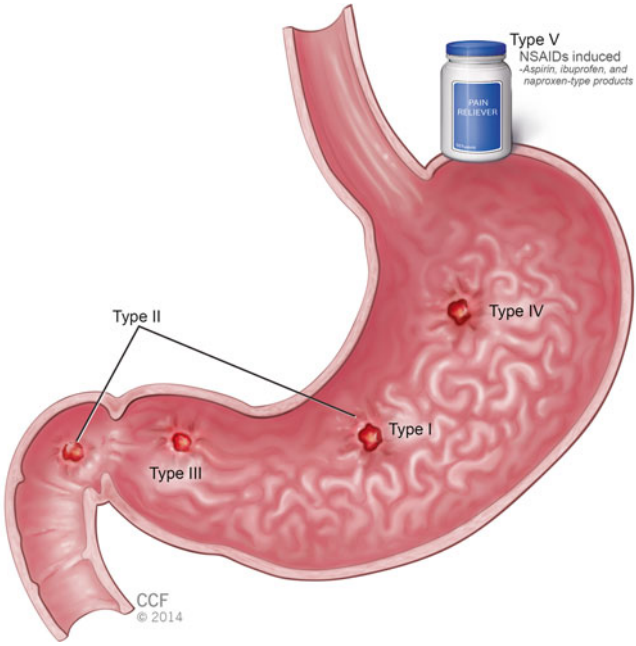

Fig. 6.1. Ulcer types. Type I ulcers occur in the gastric antrum, near the incisura. Type II ulcers occur in the gastric body, often in conjunction with duodenal ulcers. Type III ulcers are pre-pyloric in location, and along with type II ulcers, are associated with elevated gastric acid levels. Type IV ulcers occur near the gastroesophageal junction. Type V ulcers are NSAID induced, and can occur anywhere in the stomach. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014. All Rights Reserved.

superior to monotherapy, regardless of which therapies are chosen [14–16]. Chung et al. compared epinephrine injection alone versus combined with heater probe in patients with actively bleeding ulcers. Patients with active arterial bleeding fared better and ultimately were less likely to require surgical intervention than those without active bleeding (29.6 % vs. 6.5 %) [16]. Lo and colleagues demonstrated that combination therapy using injection and clips were superior to injection of epinephrine alone in reducing rebleeding (3.8 % vs. 21 %, $P=0.008$) and the need for urgent surgery (0 % vs. 9 %, $P=0.023$). Furthermore, among patients who had recurrent bleeding, repeat combination therapy was more effective in achieving hemostasis than repeat injection therapy alone (100 % vs. 33 %, $P=0.02$) [15].

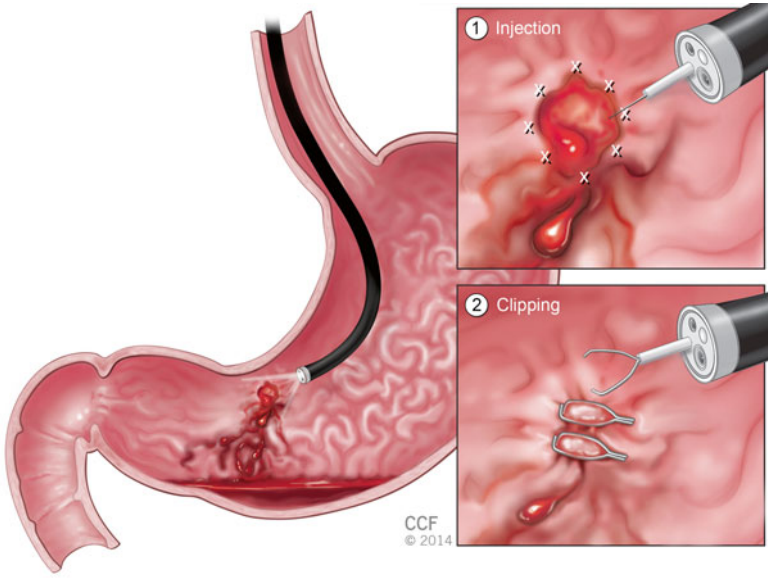

Fig. 6.2. Injection therapy and endoscopic clip therapy. Panel 1 illustrates injection therapy, where a dilute solution of epinephrine in saline is injected around and under the ulcer base. It is used most often in conjunction with other hemostatic modalities. Endoscopic clipping, as illustrated in panel 2, provides sustained compression of the bleeding vessel, leading to hemostasis. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014. All Rights Reserved.

A meta-analysis of 16 studies including 1673 patients by Calvet et al. compared epinephrine injection versus epinephrine injection in combination with a second method. Combination therapy had lower rates of rebleeding by approximately 8 %, decreased the need for surgical intervention by approximately 4 %, and decreased mortality by approximately 3 %. Furthermore, the risk of rebleeding decreased as long as a second modality was used, regardless of type [17].

Though this chapter focuses on endoscopic techniques for hemostasis, medical therapy remains an important adjunctive therapy in the treatment of peptic ulcers. A large, double-blind randomized trial examining the use of omeprazole versus placebo in patients who underwent endoscopic therapy for bleeding ulcers demonstrated decreased rates of recurrent bleeding at 30 days (6.7 % vs. 22.5 %), with a statistically significant relative risk reduction of 70 % [18].

Esophageal and gastric varices are another common cause of upper GI bleeding. Resulting from increased pressures in the portal venous, system, physiologic collateral venous plexuses between the portal and systemic venous systems enlarge in an attempt to decompress the portal system. Portal hypertension is usually categorized based on the location of increased pressure as it relates to the position of the liver. Pre-hepatic causes include portal or splenic vein thrombosis, which elevate the portal venous pressures prior to reaching the liver. When the elevated pressure is caused at the level of the liver, this is termed hepatic portal hypertension and most commonly is caused by cirrhosis. Post-hepatic portal hypertension occurs when the elevated pressures occur distal to the liver, and includes such entities such as inferior vena cava obstruction, or cardiac failure (Fig. 6.3). Cirrhosis is the most common cause of portal hypertension in the Western world, accounting for ~90 % of the cases [19]. Other less common causes of portal hypertension include portal vein or splenic vein thrombosis, nodular regenerative hyperplasia of the liver, congenital hepatic fibrosis, or myeloproliferative disorders.

Like peptic ulcer disease, endoscopic therapy for varices is complemented by pharmacologic therapy to lower the portal pressures. Unlike with peptic ulcer disease, endoscopic therapy can be used not only for treatment of an acute hemorrhage, but also to prevent the first episode of variceal bleeding. Though endoscopic sclerotherapy can be used to prevent and treat acute esophageal variceal bleeding, it has been mostly supplanted by endoscopic variceal ligation (EVL). A randomized trial by Sarin et al. in 68 patients comparing EVL and no therapy found that EVL was superior in preventing an initial variceal bleed (8.6 % vs. 39.4 %). Another study by Lay et al. demonstrated decreased incidence and mortality when compared with no therapy [20, 21]. In addition to *preventing* initial bleeding, EVL is considered the standard therapy for treatment of bleeding varices. A banding device at the tip of the endoscope is used to apply a rubber band over a varix, causing strangulation and subsequent thrombosis and necrosis (Fig. 6.4).

Sclerotherapy is another modality that can be employed to control acute variceal bleeding. It is accomplished by the injection of a sclerosing agent into or adjacent to varices. Ethanolamine oleate, polidocanol, and absolute alcohol have all been used as sclerosing agents. A needle is passed through the operating channel of the endoscope and sclerosant is injected. It has been shown that endoscopic sclerosant injections can stop acute esophageal variceal bleeding in approximately 95 % of cases. However, data exists that demonstrates the superiority of EVL in control

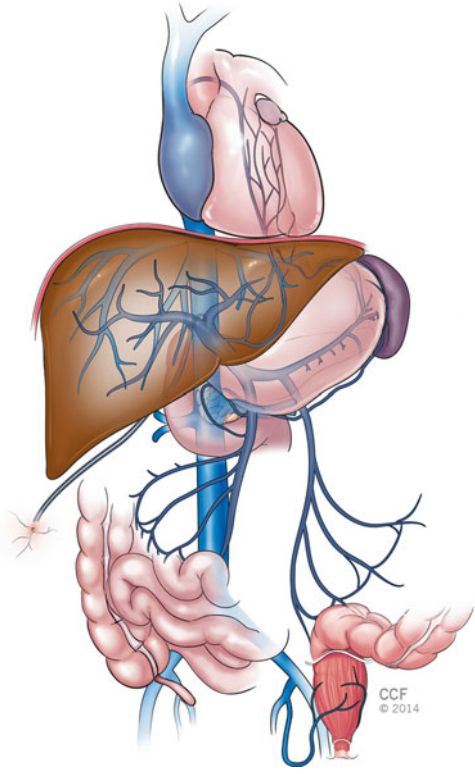

Fig. 6.3. Portal hypertension. Obstruction of blood flow through the portal venous system results in elevated portal venous blood pressure, which forces blood through portosystemic collaterals. Collaterals in the esophagus, stomach, and rectum are common causes of gastrointestinal tract bleeding. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014. All Rights Reserved.

of an initial acute variceal bleed, and is associated with better mortality and fewer adverse effects [22].

If endoscopic therapy fails to arrest the bleeding from esophageal varices, balloon tamponade is another option. However, due to its high rate of complications, balloon tamponade is often used as a last resort if endoscopic therapy and pharmacotherapy have failed [23].

Gastric variceal bleeding can also be managed effectively through the endoscope. Though bleeding from gastric varices occurs less often than esophageal varices, it can often present more severely and carries

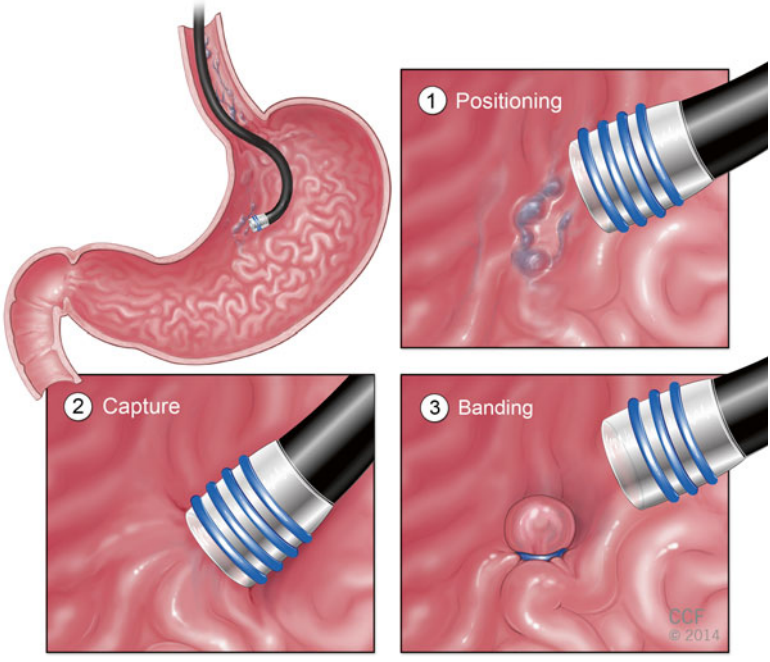

Fig. 6.4. Endoscopic variceal ligation. In endoscopic variceal ligation, an endoscope is positioned over a varix. Suction is used to draw the varix into the applicator, and a band is then deployed at the varix base, leading to thrombosis and subsequent necrosis. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014. All Rights Reserved.

with it a high mortality rate (10–30 %). EVL is indicated in actively bleeding varices, with hemostasis obtained at rates ranging from 83 to 100 %. Sclerotherapy is also used for gastric variceal bleeding, however like with esophageal varices, has largely been supplanted by EVL due to lower complication and rebleeding rates [24].

Tissue adhesives can also be injected through the endoscope to treat gastric variceal bleeding with good effect. One of the popular tissue adhesives is cyanoacrylate, which is a monomer that rapidly polymerizes when in contact with ionic substances, like blood or tissue fluids. The monomer is injected via a needle in the operating channel. If the procedure is effective, the varix will harden, effectively obliterating it [24]. Sarin et al. compared cyanoacrylate to absolute alcohol in the management of gastric varices. They found cyanoacrylate to be superior in

the control of bleeding (89 % vs. 62 %) and obliteration of the varix (100 % vs. 44 %) [25]. Additionally, Lo et al. compared cyanoacrylate with EVL and found higher rates of initial hemostasis (45 % vs. 87 %) and lower rates of rebleeding (54 % vs. 31 %) in the cyanoacrylate group, demonstrating the superiority of tissue adhesive compared to EVL [26].

Mallory–Weiss tears are another common cause of upper GI bleeding. Though they are initially thought to be a rather rare clinical entity, the increasing use of endoscopy demonstrated that they are responsible for 5–15 % of upper GI hemorrhages. These tears are caused most often by forceful retching or vomiting, which propels the gastric cardia into the thorax, resulting in longitudinal mucosal tears at the gastroesophageal junction and lesser curvature. Hiatal hernia and alcohol ingestion commonly accompany Mallory–Weiss tears [27] (Fig. 6.5).

Studies examining endoscopic injection, clipping, and banding has shown that endoscopic therapy is effective in managing bleeding from Mallory–Weiss tears. Laine et al. demonstrated the superiority of

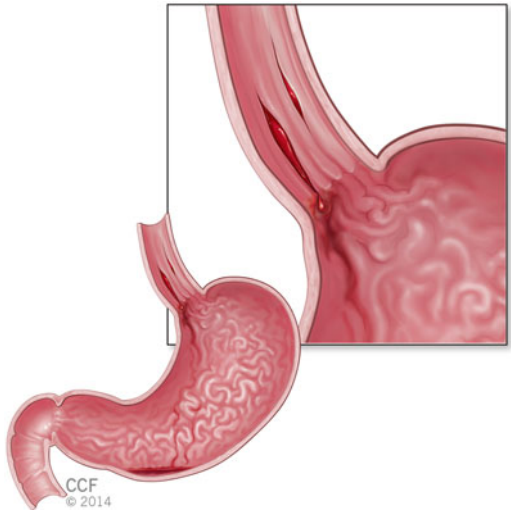

Fig. 6.5. Mallory–Weiss lesion. Forceful retching or vomiting is the most common cause of these longitudinal tears in the esophageal mucosa. The gastric cardia is propelled into the thorax by the increased intra-abdominal pressure, which results in tears at the gastroesophageal junction and along the lesser curvature. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014. All Rights Reserved.

multipolar thermal therapy to medical treatment in achieving hemostasis in Mallory–Weiss bleeding [28]. Cho and colleagues examined EVL and clip placement for patients with actively bleeding Mallory–Weiss lesions. Primary hemostasis was obtained for all 41 patients who underwent endoscopic therapy. No differences were noted in rates of primary hemostasis, recurrent bleeding or permanent hemostasis. The authors concluded that EVL and hemoclip placement were equally safe and effective in the management of bleeding secondary to Mallory–Weiss lesions [29].

Dieulafoy's lesion, also known as a caliber persistent artery, is an uncommon, though it is a potentially devastating and morbid cause of upper GI hemorrhage. It is believed to account for approximately 1–2 % of acute GI bleeding, although an incidence as high as 5.8 % has been reported [30]. First described by Gallard in 1884 as "miliary aneurysms of the stomach," its description was later amended by Georges Dieulafoy in 1898 to "exulceratio simplex," which reflected the belief that the lesion represented a precursor to peptic ulcers. Today, the term Dieulafoy's lesion describes a large caliber arteriole within the gastric submucosa that protrudes into the gastric lumen via a mucosal defect, with fibrinoid necrosis as the lesion's base. The suspected pathogenesis of bleeding is erosion of the mucosa due to compression from the larger than normal vessel, which then bleeds into the gastrointestinal tract lumen [31]. A 1993 study demonstrated approximately 60 % of lesions occur at the gastroesophageal junction as classically described, but also noted 14 % of lesions occurring in the duodenum [30].

Monotherapy with injection of epinephrine or sclerosing agents, and thermal coagulation have both been shown to be effective in the treatment of Dieulafoy's lesions. However, similar to endoscopic therapies of peptic ulcer disease, combination therapy appears to be more effective than monotherapy at providing hemostasis. In a Mayo Clinic series, 19 of 1124 consecutive patients with UGIB were found to have Dieulafoy's lesions and underwent combination therapy with epinephrine injection and thermal therapy. They demonstrated a 100 % rate of initial hemostasis, with evidence of only one patient with rebleeding in the follow-up period [32]. Endoscopic band ligation is also an effective means of treating Dieulafoy's lesions. Matsui et al. compared band ligation with bipolar electrocautery in patients with acute UGIB. There were 27 patients with Dieulafoy's lesion who underwent endoscopic therapy. Matsui's group demonstrated 100 % hemostasis in band ligation with only 86 % in the electrocautery group [33]. Park et al. compared band ligation with clip placement for Dieulafoy's lesions and were able to achieve 100 %

hemostasis in both groups with one episode of rebleeding in each group. The authors concluded that both band ligation and clip placement were safe and effective therapies for bleeding Dieulafoy's lesions [34].

Lower Gastrointestinal Tract

Diverticula of the colon represent a common cause of lower GI bleeding. These frequently occur in the elderly and represent approximately 10–30 % of GI bleeds. Diverticulosis is mostly a condition of the elderly, as the overall prevalence is reported at less than 10 % in people under the age of 40 years; however, it is noted to be 50–66 % in ages 80 or older. More prevalent in industrialized, and/or "Westernized" societies, diverticulosis is notably absent in sub-Saharan Africa, and as low as 0.5 % and 1.7 % in China and Korea, respectively. Remarkably, an increase in diverticular disease has been reported as countries become more industrialized and the "Westernized" diet becomes more popular [35, 36]. The pathogenesis of diverticular bleeding is directly related to the anatomy of the colonic wall. Diverticulum form where the vasa recta, which provide blood supply to the colon wall, penetrate the circular muscle of the colon wall at the anti-mesenteric border. This results in an inherent weakness in the colonic wall, through which colonic mucosa and submucosa herniate. In cases of diverticular bleeding, intimal thickening of the vasa recta in the direction of the diverticular lumen, combined with a disruption of the overlying mucosa, results in intraluminal bleeding (Fig. 6.6). Blood loss related to diverticular bleeding has the potential to be severe and was noted to occur in 3–5 % of patients with diverticular disease. Though left-sided colonic diverticula occur most commonly; 90 % of diverticula occur in the left colon, diverticular bleeding can occur in the right colon up to 50 % of the time [35]. Furthermore, diverticular bleeding tends to recur over time. Longstreth reported recurrence rates of 9 % at 1 year, 10 % at 2 years, 19 % at 3 years, and 25 % at 4 years [4]. This is consistent with literature showing increasing diverticula with increasing age.

Obtaining hemostasis from diverticular bleeding with colonoscopy has been well described using epinephrine injection, clip placement, band ligation, and thermal therapy. Jensen et al. examined 121 patients with severe hematochezia and diverticulosis. One group received medical therapy with or without surgical intervention, while the other underwent colonoscopy with hemostatic therapy (epinephrine injection and/or bipolar coagulation). The group that underwent colonoscopic hemostatic

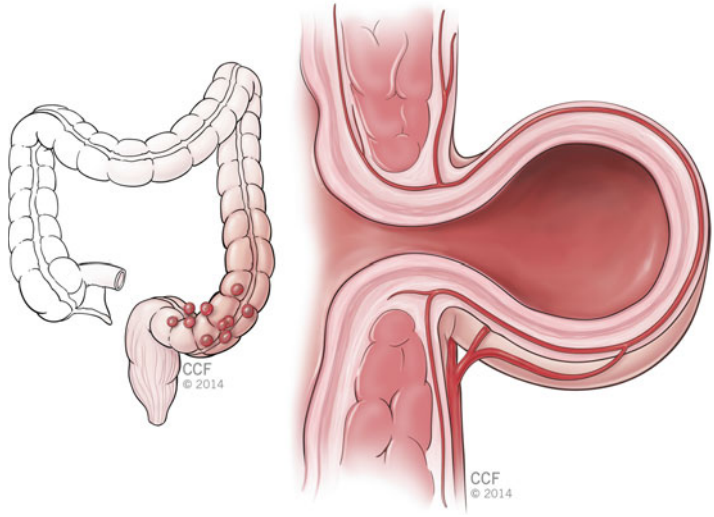

Fig. 6.6. Colonic diverticulum. The entrance of the vasa recta along the antimesenteric border of the colonic wall results in an inherent area of weakness, through which the submucosa and mucosa herniate. Intra-luminal bleeding arises from the disruption of the colonic mucosa overlying the nearby vasa recta. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014. All Rights Reserved.

therapy had a 0 % rebleed rate and none of the patients required subsequent surgical intervention. Contrastingly, 35 % of the group treated medically and without colonoscopic intervention required emergency hemicolectomy. The authors submitted that colonoscopic intervention for severe diverticular bleeding may both prevent recurrent bleeding and decrease the need for emergency surgical intervention [37]. A study through the University of California at San Francisco examined 11 patients with hematochezia and evidence of acute LGIB, who underwent colonoscopy and hemostatic therapy with epinephrine injection (only 7 of 11 patients) and clip placement (11 of 11 patients). The authors describe a technique of clip placement on the diverticulum lip when bleeding was localized to the lip, and over the area of hemorrhage catching the diverticulum lip when the bleeding appeared to originate from the dome of the diverticulum. Immediate hemostasis was obtained and patients were discharged from the hospital within 3 days of therapy. The authors concluded that use of clips to control diverticular bleeding was

an effective modality to achieve immediate hemostasis and may obviate the need for more invasive surgical therapy [38].

Inflammatory colitis is a less common cause of lower GI bleeding, and often times the episodes resolve with medical management of the inflammatory state; however, colonoscopic therapy has also been used to achieve hemostasis. In a series of Mayo Clinic patients, 28 of 31 patients who developed lower GI bleeding suffered from Crohn's disease. In their series, endoscopy was often utilized for diagnostic purposes; however, only 3 of 31 patients had lesions that were amenable to endoscopically directed therapy (epinephrine injection or bipolar coagulation). None of the patients who underwent endoscopic therapy for GI bleeding required re-intervention. Of the 27 patients that were treated medically, only 4 ultimately required surgical treatment [39].

In the era of colonoscopy, post-polypectomy bleeding is the most frequently observed complication of colonoscopy and represents another cause of lower GI bleeding that must be recognized. Immediate bleeding after polypectomy has been noted to be 0.5–2.2 % for small polyps (less than 10 mm) and ranges from 1 to 10 % for larger lesions (greater than 10 mm). Delayed bleeding occurs less frequently (0.3–0.6 %). It is usually mild and self-limiting, though if requiring treatment it is most often amenable to endoscopic therapy [40].

Management strategies include many of the same modalities previously described, including epinephrine injection, thermal coagulation therapy, clips and endoloops, or band ligation [40, 41]. Chou and Yen detail the use of clip and endoloop placement to treat a delayed post-polypectomy hemorrhage [42]. Additionally, studies have examined whether some of these modalities can be used to prophylactically to prevent post-polypectomy bleeding. Though a 2003 study by Shioji et al. demonstrated that prophylactic clip placements do not decrease the rate of post-polypectomy bleeding, there are nevertheless, studies examining whether the application of various endoscopic hemostatic modalities is useful for preventing or decreasing post-polypectomy bleeding [43]. For example, a study by Paspatis in 2006 saw decreased rates of bleeding when snare polypectomy was augmented with epinephrine injection and detachable snare placement was compared with snare polypectomy alone (2.3 % vs. 10.6 %, $P=0.04$) [44].

Perhaps one of the most common causes of lower GI bleeding is secondary to hemorrhoids. It is often described as bright red blood that is noticed when wiping with tissue or coating the stool. Bleeding is usually mild and self-limiting and manageable with diet modification and medical therapy to soften the stools. Endoscopic therapy is most often

used when the hemorrhoids are refractory to the above methods. The most common methods employed in endoscopic treatment of hemorrhoids are sclerotherapy and band ligation. Bipolar electrocautery can be used, but has mostly been supplanted by band ligation.

In a 2013 study from Germany that examined sclerotherapy in grade 1 hemorrhoidal disease, the authors randomized 130 patients to receive foam or liquid sclerotherapy. They found that more patients who received foam sclerotherapy were successfully treated after one session when compared to the liquid sclerotherapy group (88 % vs. 69 %, $P=0.01$). Furthermore, while the satisfaction for both groups was high, there was a statistically significant difference between the two groups, with the foam group rating their satisfaction higher [45].

The American Society for Gastrointestinal Endoscopy (ASGE) reports on the use of band ligation either with or without an endoscope. Very similar to the banding of esophageal varices, the hemorrhoid is suctioned into the colonoscope tip and a band applicator at the tip of the colonoscope then releases a band around the base of the hemorrhoidal tissue (Fig. 6.7).

A 1997 meta-analysis out of Canada demonstrated the superiority of band ligation compared to sclerotherapy for all grades of hemorrhoids with fewer required treatment sessions, and without differences in complication rates. The authors recommended band ligation as first-line therapy for grades 1 and 2 hemorrhoids or grade 3 hemorrhoids that are unresponsive to medical therapy or lifestyle modifications [46].

Obscure Gastrointestinal Bleeding

Obscure GI bleeding is defined as persistent or recurrent bleeding from an unknown source in spite negative evaluation by endoscopy. It represents approximately 5 % of all GI bleeding. Common causes include vascular ectasia, which are typically found in the small bowel, but can also be found in the stomach, varices, and small bowel ulcers and neoplasms, both benign and malignant [47]. A negative endoscopic evaluation includes esophagogastroduodenoscopy (EGD) and colonoscopy, and radiologic evaluation of the small bowel [48].

Though obscure bleeding can be caused by lesions anywhere in the GI tract, in approximately 75 % of patients, the responsible lesions are detected in the small bowel. Vascular ectasia represents one of the most common causes, especially in the elderly population. Small bowel neoplasms tend to predominate as causes in the younger population. Ulcers

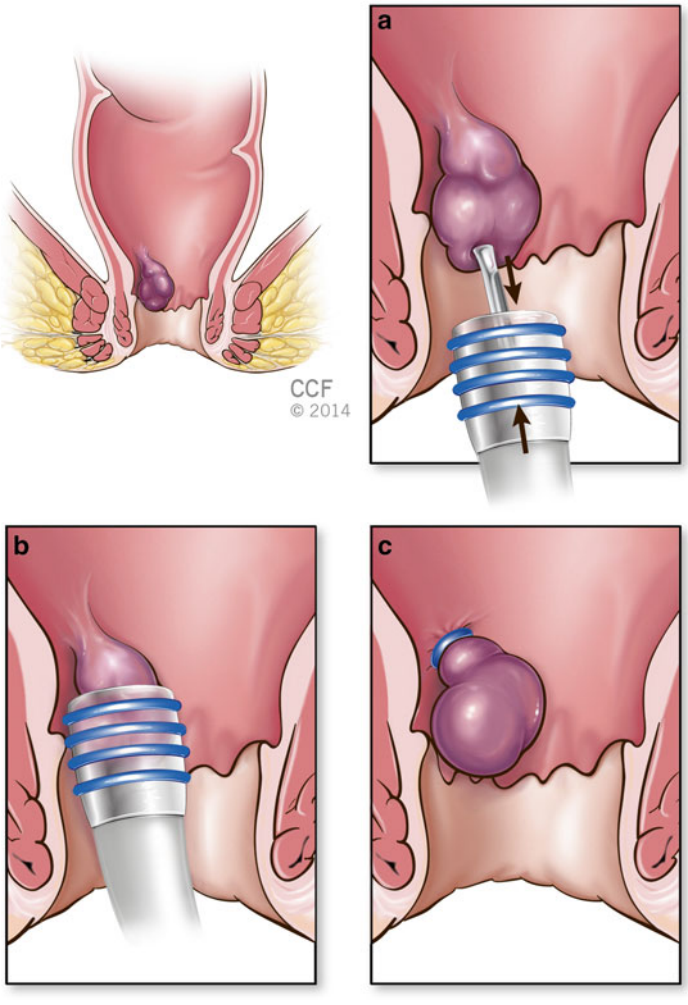

Fig. 6.7. Endoscopic band ligation for hemorrhoids. Banding of hemorrhoids is performed similarly to gastric varices. The colonoscope is positioned over the hemorrhoid (**a**), which is then suctioned or pulled into the applicator (**b**). A band is then released from the applicator around the base of the hemorrhoidal tissue, which thromboses and then necroses (**c**). Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014. All Rights Reserved.

such as those caused by nonsteroidal anti-inflammatory drugs are becoming increasingly recognized as causes of obscure bleeding [47, 48]. As such, modalities like capsule endoscopy and double balloon enteroscopy (DBE) are often employed to evaluate the small bowel under direct visualization.

Capsule endoscopy uses a capsule endoscope composed of a light source, lens, imager, battery, and wireless transmitter. The capsule is swallowed and records images of the lumen of the GI tract as it is moved from mouth to anus via peristalsis [49]. In spite of its ease of use, capsule endoscopy is limited mainly due to its diagnostic but not therapeutic capabilities. The main complication related to capsule endoscopy is capsule retention.

First described in 2001 by Yamamoto, DBE utilizes an endoscope fitted with an overtube and two balloons. The endoscope is advanced into the small bowel, and using a "push and pull" technique, the small bowel is telescoped onto the endoscope, allowing the ability to visualize the entirety of the small bowel. The endoscope is pushed ahead of the overtube. The balloon at the tip of the endoscope is inflated, and the intestine is then telescoped over the overtube. The overtube balloon is inflated, holding the bowel in place, and the endoscope balloon is deflated. The process is repeated until the entire small bowel has been examined [50]. DBE can be performed in an antegrade fashion (per oral), or retrograde fashion (per rectum), depending on the suspected location of the lesion. Unlike capsule endoscopy, DBE is both diagnostic and therapeutic, allowing for biopsies and tattooing of lesions for later surgical resection.

The American Gastroenterological Association (AGA) released a literature review on obscure GI bleeding and found that DBE yielded successful diagnostic data in 40–80 % of cases, with diagnostic or treatment success in 43–76 % of cases [48]. Limitations are notable for length of procedure, skill of endoscopist, need for separate days of per oral and per rectum approach to adequately visualize the entire small bowel, which also increases the time the patient is under anesthesia or sedation.

Operative Endoscopy

Intraoperative enteroscopy (IOE) has been utilized as early as the 1950s using a rigid sigmoidoscope through an operative enterotomy or colostomy. In 1980, Bowen and colleagues described intraoperative

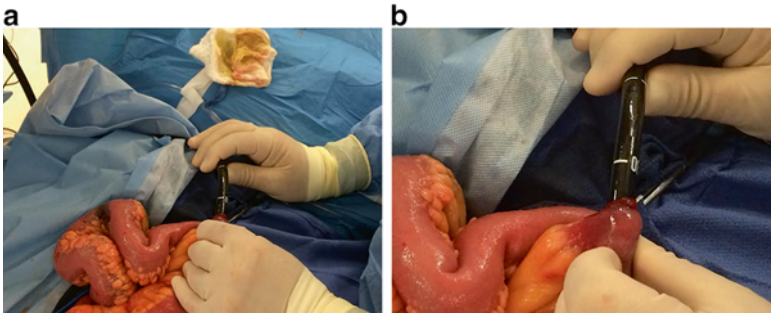

Fig. 6.8. Intraoperative endoscopy: open approach. Utilizing an open surgical approach, a laparotomy is made to expose the small bowel. A controlled enterotomy allows entry of an endoscope. The bowel is then manually telescoped over the endoscope in order to visualize the entirety of the small bowel (**a**); panel (**b**) depicts a magnified view of the endoscope through the enterotomy.

enteroscopy by placing a colonoscope per oral and per rectum, while the surgeon manually telescoped the bowel over the endoscope through a laparotomy [48] (Fig. 6.8). Small bowel endoscopy can also be employed by using a laparoscopic technique. A controlled enterotomy is made and a 15 mm port is introduced through the enterotomy. The bowel is elevated using stay sutures. The endoscope is introduced into the small bowel through the port. This method allows for a small bowel lesion to be identified and intervened upon laparoscopically and does not rely upon the larger and more invasive midline incision (Figs. 6.9 and 6.10).

Developing Modalities

Newer modalities for control of hemorrhage such as the OVESCO OTSC® (Over-The-Scope Clip) System and the Apollo OverStitch™ are two systems that are becoming more popular for endoscopic interventions.

The OTSC System aims to provide better strength and tissue capture compared to conventional clips that are delivered through the endoscope's working channel. The use of the OTSC System has been described in case reports for the closure of perforations and obtaining hemostasis. Kirschniak et al. report a series of 11 patients with gastric and colonic bleeding who were all treated with the OTSC System. The

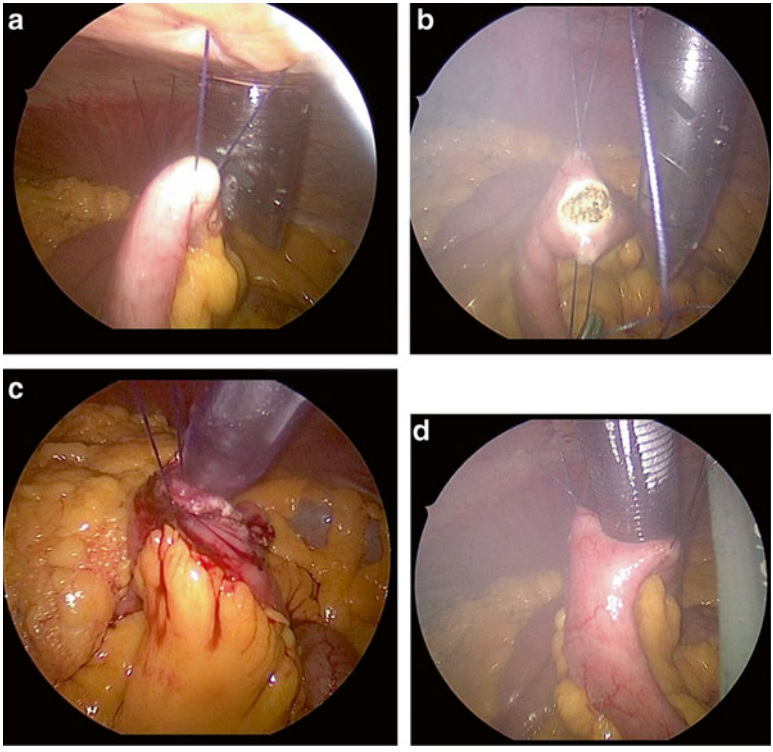

Fig. 6.9. Intraoperative endoscopy: laparoscopic approach, intra-abdominal view. Laparoscopic access to the peritoneal cavity is obtained. Two 5 mm laparoscopic ports may be used for laparoscopic instruments. A 15 mm laparoscopic port is then placed, which allows the endoscope passage into the peritoneal cavity. The bowel is elevated towards the 15 mm port using trans-fascial stay sutures (**a**). Cautery is used to create a controlled enterotomy (**b**). The trocar is guided into the enterotomy (**c**). The endoscope is passed through the trocar, into the bowel lumen (**d**). Using laparoscopic instruments, the bowel is pulled over the endoscope, allowing examination of the entire small bowel lumen, without the need for a midline laparotomy.

authors were able to achieve hemostasis and close lesions in all 11 patients, without evidence of complications [51].

The Apollo OverStitch™ endoscopic suturing system enables a physician the ability to place full thickness sutures while using an endoscope. It was trialed by Pauli and colleagues in four patients undergoing elective colectomy. The OverStitch™ device was used to place sutures in healthy colonic tissue during a 15-min time-limited period. The colectomy

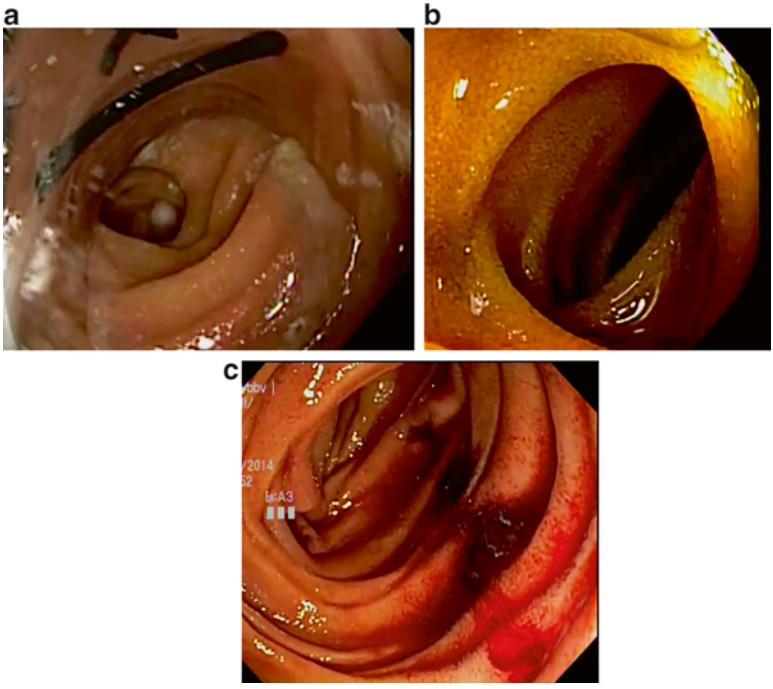

Fig. 6.10. Intraoperative endoscopy: laparoscopic approach, endoscopic view. In this endoscopic view, the trocar can be seen within the small bowel lumen (**a**). The endoscope is advanced out of the trocar, and the bowel is telescoped over the endoscope (**b**). The bleeding lesion is able to be readily identified (**c**).

specimen was then explanted and the tissue examined to determine the depth of suture penetration and effectiveness of the suture's ability to cinch down. The authors found that the sutures could be consistently placed at a subserosal depth. They reported few technical issues that prohibited the operator's ability to effectively place the sutures [52].

Kurian and colleagues published their experience using the OverStitch™ system to repair an inadvertent full thickness myotomy during per-oral endoscopic myotomy (POEM). The perforation was successfully repaired in two layers using the OverStitch™ system [53]. Though each of these devices requires more development and study, they represent advances in treatment modalities available to experienced endoscopists.

Conclusion

Though gastrointestinal bleeding is a common problem faced by patients, it can often have serious consequences if not appropriately managed. With the development of endoscopy and its increasing familiarity and use by physicians, GI hemorrhage is being increasingly diagnosed and treated by endoscopic means. It only follows naturally, that techniques to treat GI hemorrhage would soon follow. Given the many advances in endoscopy, treatment of GI bleeding is increasingly being managed by endoscopic, rather than traditional surgical interventions. This chapter highlights the importance of understanding the many etiologies of gastrointestinal bleeding, and how the etiology of bleeding drives the manner of treatment.

References

1. Van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding. Best Pract Res Clin Gastroenterol. 2008;22(2):209–24.
2. Barkun A, Sabbah S, Fallone C, et al. The Canadian Registry on Nonvariceal Upper Gastrointestinal Bleeding and Endoscopy (RUGBE): endoscopic hemostasis and proton pump inhibition are associated with improved outcomes in a real-life setting. AM J Gastroenterol. 2004;99:1238–46.
3. Barkun A, Leontiadis G. Systematic review of the symptom burden, quality of life impairment and costs associated with peptic ulcer disease. Am J Med [Internet]. 2010;123(4):358–66.e2. Elsevier Inc.
4. Longstreth G. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1997; 92(3):419–24.
5. Leighton JA, Goldstein J, Hirota W, et al. Obscure gastrointestinal bleeding. Gastrointest Endosc. 2003;58(5):650–5.
6. Kobayashi L, Costantini TW, Coimbra R. Hypovolemic shock resuscitation. Surg Clin N Am Internet. 2012;92(6):1403–23. Elsevier Inc.
7. Perel P, Roberts I, Ker K. Colloids versus crystalloids for fluid resuscitation in critically ill patients. Cochrane Database Syst Rev. [Internet] 2013(Issue 2):Art. No.: CD000567. doi:10.1002/14651858.CD000567.pub6.
8. Jairath V, Barkun AN. The overall approach to the management of upper gastrointestinal bleeding. Gastrointest Endosc Clin N Am [Internet]. 2011;21(4):657–70. Elsevier Inc.
9. Silverstein FE, Gilbert DA, Tedesco FJ, Buenger NK, Persing J. The ASGE National Survey on upper gastrointestinal bleeding. Gastrointest Endosc [Internet]. 1981; 27(2):94–102. Elsevier.

10. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet. 2000;356:1318–21.
11. Rockall TA, Logan RFA, Devlin HB, Northfield TC, Thames W, Thames SW. Risk assessment after acute upper gastrointestinal haemorrhage. Gut. 1996;38:316–21.
12. Chung SC, Leung JW, Steele RJ, Crofts TJ, Li AK. Endoscopic injection of adrenaline for actively bleeding ulcers: a randomised trial. Br Med J (Clin Res Ed) [Internet]. 1988;296(6637):1631–3.
13. Liou T-C, Lin S-C, Wang H-Y, Chang W-H. Optimal injection volume of epinephrine for endoscopic treatment of peptic ulcer bleeding. World J Gastroenterol [Internet]. 2006;12(19):3108–13.
14. 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 [Internet]. 2004;60(6):910–5.
15. Lo C-C, Hsu P-I, Lo G-H, Lin C-K, Chan H-H, Tsai W-L, et al. Comparison of hemostatic efficacy for epinephrine injection alone and injection combined with hemoclip therapy in treating high-risk bleeding ulcers. Gastrointest Endosc [Internet]. 2006;63(6):767–73.
16. Chung SSC, Lau JYW, Sung JJY, Chan ACW, Lai CW, Ng EKW, et al. Randomised comparison between adrenaline injection alone and adrenaline injection plus heat probe treatment for actively bleeding ulcers. Br Med J (Clin Res Ed). 1997;314(May): 1307–11.
17. Calvet X, Vergara M, Brullet E, Gisbert JP, Campo R. Addition of a second endoscopic treatment following epinephrine injection improves outcome in high-risk bleeding ulcers. Gastroenterology. 2004;126(2):441–50.
18. Lau JYW, Sung JJY, Lee KKC, Yung M-Y, Wong SKH, Wu JCY, et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. N Engl J Med. 2000;343(5):310–6.
19. Cárdenas A, Ginès P. Portal hypertension. Curr Opin Gastroenterol [Internet]. 2009;25(3):195–201.
20. Sarin S, Guptan R. A randomized controlled trial of endoscopic variceal band ligation for primary prophylaxis of variceal bleeding. Eur J Gastroenterol Hepatol. 1996;8(4):337–42.
21. Lay C-S, Tsai Y-T, Teg C-Y, Shyu W-S, Guo W-S, Wu K-L, et al. Endoscopic variceal ligation in prophylaxis of first variceal bleeding in cirrhotic patients with high-risk esophageal varices. Hepatology. 1997;25(6):1346–50.
22. Virk C, Coelho-prabhu N, Buttar NS. Chapter 13—Portal hypertensive bleeding [Internet]. Clinical gastrointestinal endoscopy. 2nd ed. London: Elsevier Inc.; 2012.
23. Haddock G, Garden OJ, McKee RF, Anderson JR, Carter DC. Esophageal tamponade in the management of acute variceal hemorrhage. Dig Dis Sci. 1989;34:913–8.
24. Crisan D, Tantau M, Tantau A. Endoscopic management of bleeding gastric varices—an updated overview. Curr Gastroenterol Rep [Internet]. 2014;16(10):413.
25. Sarin SK, Jain AK, Jain M, Gupta R. A randomized controlled trial of cyanoacrylate versus alcohol injection in patients with isolated fundic varices. Am J Gastroenterol. 2002;97:1010–5.

26. Lo GH, Lai KH, Cheng JS, Chen MH, Chiang HT. A prospective, randomized trial of butyl cyanoacrylate injection versus band ligation in the management of bleeding gastric varices. Hepatology [Internet]. 2001;33(5):1060–4.
27. Sugawa C, Benishek D, Walt AJ. Mallory-Weiss syndrome. A study of 224 patients. Am J Surg [Internet]. 1983;145(1):30–3.
28. Laine L. Multipolar electrocoagulation in the treatment of active upper gastrointestinal tract hemorrhage. A prospective controlled trial. N Engl J Med. 1987;316: 1613–7.
29. Cho Y, Chae H, Kim H. Endoscopic band ligation and endoscopic hemoclip placement for patients with Mallory-Weiss syndrome and active bleeding. World J Gastroenterol [Internet]. 2008;14(13):2080–4.
30. Baettig B, Haecki W, Lammer Jr F. Dieulafoy's disease: endoscopic treatment and follow up. Gut. 1993;34(4):1418–21.
31. Baxter M, Aly EH. Dieulafoy's lesion: current trends in diagnosis and management. Ann R Coll Surg Engl [Internet]. 2010;92(7):548–54.
32. Stark M, Gostout C, Balm R. Clinical features and endoscopic management of Dieulafoy's disease. Gastrointest Endosc [Internet]. 1992;38(5):545–50.
33. Matsui S, Kamisako T, Kudo M, Inoue R. Endoscopic band ligation for control of nonvariceal upper GI hemorrhage: comparison with bipolar electrocoagulation. Gastrointest Endosc [Internet]. 2002;55(2):214–8.
34. Park C, Joo Y, Kim H, Choi S. A prospective, randomized trial of endoscopic band ligation versus endoscopic hemoclip placement for bleeding gastric Dieulafoy's lesions. Endoscopy [Internet]. 2004;36(8):677–81.
35. Lewis M. Bleeding colonic diverticula. J Clin Gastroenterol [Internet]. 2008;42(10):1156–8.
36. Martel J, Raskin JB. History, incidence, and epidemiology of diverticulosis. J Clin Gastroenterol [Internet]. 2008;42(10):1125–7.
37. 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(2):78–82.
38. Yen EF, Ladabaum U, Muthusamy VR, Cello JP, McQuaid KR, Shah JN. Colonoscopic treatment of acute diverticular hemorrhage using endoclips. Dig Dis Sci [Internet]. 2008;53(9):2480–5 [cited 2014 Sep 21].
39. Pardi DS, Loftus EV, Tremaine WJ, Sandborn WJ, Alexander GL, Balm RK, et al. Acute major gastrointestinal hemorrhage in inflammatory bowel disease. Gastrointest Endosc [Internet]. 1999;49(2):153–7.
40. Anderloni A, Jovani M, Hassan C, Repici A. Advances, problems, and complications of polypectomy. Clin Exp Gastroenterol [Internet]. 2014;7:285–96.
41. Sorbi D, Norton I, Conio M, Balm R, Zinsmeister A, Gostout CJ. Postpolypectomy lower GI bleeding: descriptive analysis. Gastrointest Endosc [Internet]. 2000;51(6): 690–6.
42. Chou K-C, Yen H-H. Combined endoclip and endoloop treatment for delayed postpolypectomy hemorrhage. Gastrointest Endosc [Internet]. 2010;72(1):218–9. Elsevier Inc. [cited 2014 Sep 21].

43. Shioji K, Suzuki Y, Kobayashi M, Nakamura A, Azumaya M, Takeuchi M, et al. Prophylactic clip application does not decrease delayed bleeding after colonoscopic polypectomy. Gastrointest Endosc. 2003;57(6):691–4.
44. Paspatis GA, Paraskeva K, Theodoropoulou A, Mathou N, Vardas E, Oustamanolakis P, et al. A prospective, randomized comparison of adrenaline injection in combination with detachable snare versus adrenaline injection alone in the prevention of postpolypectomy bleeding in large colonic polyps. Am J Gastroenterol [Internet]. 2006; 101(12):2805–9.
45. Moser K-H, Mosch C, Walgenbach M, Bussen DG, Kirsch J, Joos AK, et al. Efficacy and safety of sclerotherapy with polidocanol foam in comparison with fluid sclerosant in the treatment of first-grade haemorrhoidal disease: a randomised, controlled, single-blind, multicentre trial. Int J Colorectal Dis [Internet]. 2013;28(10):1439–47.
46. Macrae HM, Mcleod RS. Comparison of hemorrhoid treatments: a meta-analysis. Surg Pract. 1997;40(1):14–7.
47. Rockey DC. Occult and obscure gastrointestinal bleeding: causes and clinical management. Nat Rev Gastroenterol Hepatol [Internet]. 2010;7(5):265–79. Nature Publishing Group.
48. Raju GS, Gerson L, Das A, Lewis B. American Gastroenterological Association (AGA) Institute technical review on obscure gastrointestinal bleeding. Gastroenterology [Internet]. 2007;133(5):1697–717 [cited 2014 Jul 9].
49. Eliakim R. Video capsule endoscopy of the small bowel. Curr Opin Gastroenterol [Internet]. 2008;24(2):159–63.
50. Yamamoto H, Sekine Y, Sato Y, Higashizawa T, Miyata T, Iino S, et al. Total enteroscopy with a nonsurgical steerable double-balloon method. Gastrointest Endosc. 2001; 53(2):216–20.
51. Kirschniak A, Kratt T, Stüker D, Braun A, Schurr M-O, Königsrainer A. A new endoscopic over-the-scope clip system for treatment of lesions and bleeding in the GI tract: first clinical experiences. Gastrointest Endosc. 2007;66(1):162–7.
52. Pauli EM, Delaney CP, Champagne B, Stein S, Marks JM. Safety and effectiveness of an endoscopic suturing device in a human colonic treat-and-resect model. Surg Innov. 2013;20(6):594–9.
53. 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.

7. Stricture Management: Interventional Options

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Esophageal Anastomotic Strictures

Definition

Esophageal anastomotic stricture is defined as any form of cervical dysphagia in the anastomotic region requiring endoscopic dilation [1], or failure of passage of a 9-mm endoscope [2]. Post-esophagectomy anastomotic strictures are the most common reason for esophageal stricturing disease seen by general surgeons and gastroenterologists [3]. In the pediatric population, strictures from esophageal atresia repairs are the most common etiology [4].

Pathophysiology

Benign esophageal strictures are the result of collagen deposition and scar tissue formation from prolonged esophageal inflammation [5]. The majority of benign strictures are the result of peptic disease; however with the advent of aggressive treatment of reflux, other causes like anastomotic strictures are becoming relatively more common [6]. The exact mechanism behind anastomotic stricturing is yet to be elicited, but a compromised blood supply and reflux of stomach acid are undoubtedly involved in the pathophysiology [7, 8].

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Incidence and Risk Factors

The incidence of anastomotic esophageal stricturing post esophagectomy ranges between 5 and 48 % [1, 2, 9–11]. Usually appearing between 3 and 6 months post-surgery [12], risk factors for stricture formation can be classified into four categories: patient factors (smaller esophagus [2, 9], increased preoperative weight [2], preoperative cardiac disease [11], diabetes mellitus [13]), surgical technique (stapled anastomosis [9, 10, 14] with smaller stapler size [12], two-layer hand-sewn anastomosis [1], cervical anastomoses [12, 15], gastroesophageal anastomosis [2]), postoperative complications (conduit ischemia [2], anastomotic leak [2, 11] anastomotic bleed [16], anastomotic infection [16]), and treatment factors (postoperative radiation [1]).

The incidence of malignant esophageal stricturing post esophagectomy ranges from 4 to 8 % [1, 10]. These strictures usually appear later than benign, fibrotic strictures [12].

In the pediatric population, the incidence of anastomotic esophageal stricture post-esophageal atresia repair ranges between 18 and 50 % [4]. Risk factors for stricture development are classified into three categories: patient factors (reflux, gap length), surgical technique (anastomosis tension, anastomosis suture material), and postoperative complications (anastomotic leak, fistula) [4].

Symptoms

The most common clinical presentation of esophageal stricturing disease is dysphagia, reported in 83 % of patients [5]. The severity of dysphagia does not correlate to the degree of stricture due to patients often adjusting their diet to more tolerable foods [17]. Esophageal complaints of reflux was also quite common (66 %), likely due to the strong correlation between reflux and stricture formation [5]. Potential extra-esophageal symptoms include chronic cough, weight loss, vomiting, chest pain, hoarseness, and asthma [5, 17].

Treatment

The mainstay of therapy for an upper gastrointestinal anastomotic stricture that is associated with a clinically significant functional impairment is mechanical esophageal dilation [18]. The goal of dilation is

centered on symptomatic relief of dysphagia [3]. Dilation can be performed with rigid or balloon dilators, with or without a guidewire to help positioning, and with or without endoscopy or fluoroscopy [19]. Esophageal anastomotic strictures generally are considered more complicated than simple peptic strictures thus often require a number of dilation sessions, with the median ranging between 2 and 9 sessions per patient. Randomized controlled trials have shown no significant difference in efficacy between the rigid versus balloon dilators [20, 21]. Additional therapies like stenting, intralesional corticosteroid injections, and electrocautery are generally reserved for refractory strictures of failed dilation, defined as clinical dysphagia despite dilation, in strictures that are unable to be mechanically dilated to 14 mm or to remain at least 14 mm dilated [8, 16].

Dilators

Rigid Dilators

Rigid dilators have been the traditional treatment for esophageal strictures, dating back to the sixteenth century. Significant evolution has occurred since, progressing from initial tools that included whalebones and tapered wax candle dilators [8]. Theses fixed rigid dilators apply both axial and radial forces as they are advanced through a stenosis [22]. Rigid fixed dilators can be quite variable in their appearance and subtleties of action, based on the design of the different companies.

The push type dilators (PTD), Hurst and Maloney, are internally weighted with mercury-free tungsten, ranging in sizes from 16 Fr to 60 Fr with their tips being rounded or tapered [19]. These dilators are best suited for simple strictures (straight, symmetric, diameter ≥12 mm) [3].

Wire-guided dilators (WGD) are polyvinyl chloride tapered tubes with a central channel that allow for a guidewire [19]. The Savary-Gilliard and American Dilation System dilators have varied length tapered tips, radiopaque markings, and external distance markings [19]. These dilators can be used for more complicated strictures (torturous, asymmetric, longer >2 cm, diameter <12 mm) [3, 8].

Rigid dilation, as a procedure, begins with an endoscopic or barium study assessment of the stricture; marking diameter, length, and any suspicious lesions for cancer-recurrence [3, 23]. A guide-wire is then placed through the instrument channel into the gastric antrum; this step is omitted for the Hurst and Maloney dilators. The endoscope is then

withdrawn and the wire position is maintained [3]. The wire is then grasped at the patient's mouth and its length noted (usually around 60 cm). The initial choice of dilator depends on the estimated diameter of the stricture. A general rule is that a 24 Fr, 30 Fr, and 36 Fr are trialed for strictures ≤6 mm, 7–10 mm, and ≥10 mm respectively [3]. The dilator is lubricated and loaded onto the guidewire and passed with a fingertip grasp through the stricture and then subsequently removed. The guide-wire length at the patient's mouth is then noted again and further dilation can take place with larger diameter bougies. The first dilator should be used is estimated endoscopically by comparing the lumen with the diameter of the endoscope. The "Rules of Three's" should be employed, stating that: during any one dilation session, a maximum of three consecutive dilators of progressively increasing size (a total of 3 mm) should be passed after the first one that meets moderate resistance [3]. Endoscopic evaluation after dilation can be performed to assess the damage to the mucosa. Subsequent dilation sessions can be repeated until the patient has relief of swallowing difficulties [3].

Both PTD and WGD can be passed blindly or under fluoroscopic control. Fluoroscopy is an aid to help determine that the bougie has passed the strictured segment of esophagus and has entered the stomach, this is advantageous in situations where direct visualization with the endoscope cannot be performed [3]. Direct visualization throughout the procedure is possible with newer, transparent bougies that fit over a standard endoscope [19].

The efficacy of rigid dilators for anastomotic strictures ranges between 78 and 100 % [19, 24]. The median number of dilations prior to achieving clinical success ranges between 2-9 dilations [24]. 50 % of patients will fail initial dilator therapy from rigid dilator therapy [20].

Balloon Dilators

First introduced by London et al. in 1981 for ctwo patients who failed the conventional, bougie rigid dilator technique, this technique has gained widespread popularity in benign esophageal stricturing disease, including anastomotic strictures, for its less traumatic effect on esophageal tissue [7, 25]. Contrary to rigid dilators, balloon dilators exert only radial forces when expanded within a stenosis. There is tremendous variability in the type of balloon dilators that exist, such as single-diameter, multi-diameter, and hydrostatic or pneumatic balloons [26].

Through the scope (TTS) balloon dilation, as a procedure, begins with an initial evaluation of the stricture via endoscopy or a barium study [23]. The balloon diameter used is once again dependent on the diameter size of the stricture [3]. A general rule is that 10 mm, 12 mm, and 15 mm balloons are used for strictures of ≤6 mm, 7–10 mm, and ≥10 mm respectively. The endoscope is placed in the stomach, distal to the stricture, and the balloon is passed through the scope to the end of the endoscope. The endoscope is then withdrawn through the stricture and the balloon is then inflated with radiocontrast or water for 30–60 s [3]. The endoscope remains in the esophagus allowing the operator to directly visualize the dilation, an advantage of balloon dilators over most, non-transparent bougies [19]. If fluoroscopy is used, the balloon is inflated until the waist deformity from the stricture disappears [23]. Fluoroscopic control has the advantages of visualizing both the proximal and distal ends of the stricture, merely not the entrance as in endoscopy, and allows visual control of the whole balloon catheter [27].

With the advent of controlled radial expansion, the same balloon can be inflated to three consecutive larger diameters rather than one balloon, one diameter [3]. The rules of three can also be applied for balloon dilators [7]. Once again, the mucosa is then evaluated by the endoscope after dilation for trauma.

The efficacy of balloon dilators for anastomotic strictures ranges between 83 and 100 % [7, 11, 13, 19, 28]. The average number of dilations prior to achieving clinical success ranges between 3 and 7 dilations [11, 28]. Studies have shown that restenosis rates after balloon dilation are approximately 50 % [7, 13].

Predictive factors that determine the success of dilation include stricture diameter >13 mm [7], stricture length <12 mm [28] and strictures without prior history of leakage [28]. Predictors of failure of dilation include interval from esophageal surgery to the first initial intervention <90 days [7] and balloon dilations to 12 mm or less [7].

Complications and Limitations of Dilators

The complexity of anastomotic strictures put them at risk for esophageal perforation or significant hemorrhage with dilation. The incidence of esophageal perforation or significant bleed is reported between 0.1 and 0.5 % [3]. There remains a paucity in the literature as to predictive factors associated with decreased or increased dilation attempts prior to clinical success [29]. The drawbacks then of these dilators are the time

and expense of repeated, indeterminate therapy sessions, with the potential adjuvant therapy interruption [29]. Ultimately, the decision to use balloon or rigid dilation is based more on preference, comfort and regional availability [19].

Other Endoscopic Procedures

Stents

Stents are usually considered as a second line treatment for patients with recurrent dysphagia, failing initial dilation attempts [30]. They have a primary role in patients with unresectable malignancy for palliation and improvement of dysphagia and are used sparingly in benign disease [31, 32].

Metal Stents

Self-expanding metal (SEMSs) stents are metal mesh cylinders usually composed of stainless steel or alloys, which are able to self-expand until they restore the lumen of hollow organs [33]. Traditionally SEMSs have been used as a palliative procedure for patients with stricturing disease from unresectable esophageal cancer, encompassing also recurrences at the anastomotic site [31, 34]. The indications for SEMSs in fibrotic anastomotic strictures are limited. The historical concern with bare metal stents focused on the increased tissue irritation leading to secondary strictures, mucosa ulcerations at contact points, esophageal obstruction, perforation and tracheoesophageal fistulas [30, 34]. In addition, due to tissue embedding, once placed, metal stents were considered permanent [34]. On the other hand, this tissue embedding does limit possible stent migration, with reported rates by Pennarthur et al. to be as low as 8.7 %.

Newer, fully covered metal stents are challenging this nonreversible notion of metal stents, as newer studies have shown that they can be removed successfully [34]. However, the results with anastomotic strictures have only modest efficacy, with studies quoting a dysphagia resolution rate between 29 and 56 % [32, 34].

Metal stents and non-metal stents are placed in a similar fashion [35]. The stricture requiring stenting is first visualized with the endoscope [33]. If the stricture is deemed to be too stenotic for the stent to traverse it, the operator might choose to perform a session of dilation

with a rigid or balloon dilator prior to stenting [33]. Most gastrointestinal SEMS require the use of a guidewire for placement [33]. A distal hemoclip is placed 2 cm distal to the stricture, the endoscope is advanced placing a guidewire into the second part of the duodenum. Upon the withdrawal of the endoscope, the guidewire remains and a proximal hemoclip is placed where the stent is planned to start. Under fluoroscopy guidance, using the hemoclips as landmarks, the stent is deployed. The endoscope is then inserted to confirm correct placement. Stents are usually left for 3 months, prior to being retrieved. Retrieval involves using foreign body forceps with a longitudinally directed force that narrows the stent for removal [30].

Non-metal Stents

Self-expanding plastic stents (SEPS) were developed to correct for some short-comings of metals stents and they have been shown to be a successful treatment tool for benign anastomotic strictures [30]. Usually made of a combination polyester and silicone, where the silicone prevents hyperplastic tissue growth and the polyester helps with anchoring, these stents are able to be removed easily due to the lack of tissue embedding [30, 34]. As a second line treatment modality for recurrent dysphagia post initial dilation, plastic stent placement has been associated with decreased median numbers of subsequent dilatations, improved dysphagia scores and improved cost-effectiveness at 15 months of follow-up. Recurrent dysphagia rates after plastic stenting ranges between 5 and 36 % [29, 30, 35]. Long-term resolution of dysphagia symptoms after the SEPS removal is poor, with high associated dysphagia recurrence rates [6]. Evrard et al. stressed that SEPS should not be used as initial therapy for anastomotic strictures but should be considered in patients with cervical anastomotic stenosis and patients with refractory dysphagia to dilations [36].

There are a few other important drawbacks of SEPS. As a result of poor mucosa embedding, SEPS migration rates are high, ranging between 6 and 69 % [37]. SEPS are also less effective than metal stents in managing esophageal perforations and leaks [37]. Lastly, they require a larger applicator compared to metal stents, therefore requiring predilation of the stricture more often [30].

Biodegradable stents (BDS) are on the horizon with small case series speaking to their efficacy [38]. BDS potentially solve the problem with stent extraction and migration, as most stents dissolved by 6 weeks. However, dedicated trials with larger patient populations are needed.

While promising theoretically, small studies have shown that dysphagia clinically improved in 33–100 % of patients, but stent migration rates continued to be quite high ranging from 8 to 77 % [39].

Corticosteroid (Kenalog) Injection

Intralesional injection of corticosteroids has been used for refractory esophageal strictures for the last 50 years. Used as an adjunct to dilation, intralesional steroids interfere with collagen synthesis and fibrosis, thereby inhibiting stricture formation. Triamcinolone, specifically, inhibits fibronectin and procollagen synthesis, reduces inhibition of collagenase and prevents scar contracture. In addition to triamcinolone, betamethasone solutions are also commonly used. The procedure itself involves radial injections of the steroid using a sclerotherapy injection needle. Optimally, injections are given prior to dilation and radial injections in 4–6 quadrants just proximal to the stricture and then distally. Studies have shown that intralesional injection of corticosteroids in conjunction with dilation for anastomotic fibrotic strictures significantly reduces stricture recurrence, the number of periodic dilations required for recurrent strictures and increases the maximum dilation diameter achieved [8, 40, 41].

Electrocautery Needle-Knife

Limited, small case series have described the use of electrocautery to treat esophageal surgical anastomotic strictures [16, 42]. A sphincterotome, under direct endoscope visualization, supplies an electrocautery current to cut circumferentially, longitudinal incisions (usually 6–12) with variable length and depth [16, 24, 42]. The limited literature available is favorable towards electrocautery as success rates are as high as 100 % for dysphagia resolution with recurrence rates of 12.5 % and without major complications [3, 42]. A randomized controlled trial comparing dilation versus electrocautery needle-knife as a primary therapy for esophageal anastomotic stricturing showed no significant difference between the two groups. The authors concluded that electrocautery needle-knife can be used a as a primary therapy in the hands of an experienced endoscopists, but in less experienced hands it should be used as a second line therapy [24].

Medical Management

Based on the theory that benign strictures can be affected by the exposure of the surgical anastomosis by the reflux of acidic stomach contents, proton pump inhibitors (PPIs) have been shown to independently reduce fibrotic stricture formation 32 % [12].

Gastric Anastomotic Strictures

Definition

Gastric anastomotic strictures are diagnosed clinically in patients with persistent vomiting and dysphagia with a history of a gastric anastomosis and endoscopically as a failure of passage of a 9-mm [43] or 9.5-mm [44] endoscope through the anastomosis [44]. Post Roux-en-Y Gastric bypass, gastrojejunostomy strictures are the most common gastric anastomotic strictures seen by general surgeons and gastroenterologists and will become increasingly more common with the rise of bariatric surgery [3, 44]. Other possible surgical etiologies include pancreaticoduodenectomy and gastrojejunostomy reconstructions as well other gastric resections [3].

Pathophysiology

The mechanism behind gastrojejunal anastomotic stricturing is not completely understood [45]. Benign gastrojejunostomy anastomotic strictures are the result of fibrosis and the inflammation response secondary to a number of factors including gastric acid secretion from the neo-pouch, anastomotic ischemia or leak, technical problems, marginal ulcerations or ingestions like NSAIDS, alcohol, or smoking [45–47].

Incidence and Risk Factors

The incidence of anastomotic gastrojejunostomy stricturing post gastric bypass ranges between 0.6 and 27 %, with no difference between open versus laparoscopic approaches [3, 44, 47].

Usually appearing as a late complication, risk factors for stricture formation can be classified into three– categories: patient factors (female

gender [3], healing capacity [44]), surgical technique (stapled anastomosis [44] with a circular stapler [3, 44, 45], 21-mm stapler size [44, 47], anastomotic tension [44], large volume gastric pouch [47], surgeon inexperience [48]), and postoperative complications (anastomotic ischemia [3, 44]).

Treatment

The mainstay of therapy for a post-gastric bypass anastomotic stricture that is associated with a clinically significant functional impairment is mechanical gastrojejunostomy dilation using balloon dilation [44]. Considered the gold standard treatment, these strictures respond favorably to dilation with efficacy rates reaching 100 % and require less dilation sessions compared to esophageal anastomotic strictures, with 55–90 % of patients requiring only one session [43, 44, 49]. TTS balloon dilation has very few complications and an acceptable perforation rate under 2 % [43]. The role for other treatments, like surgical revision and to a lesser extent endoluminal stenting and Savary-Gilliard bougies, are usually reserved for refractory strictures, defined as recurrence of stenosis despite 3–5 balloon dilation attempts [43, 46].

Balloon Dilators

As described earlier, balloon dilation can be performed under endoscopic or fluoroscopic guidance [44]. TTS dilation has the advantage of assessing the stricture visually. The procedure is as described earlier. Briefly, the stricture is visualized by gastroscopy, 6–18 mm balloon catheter is inserted through a side channel and through the stricture [44, 49]. Fluoroscopy then confirms that the balloon is traversing the waist of the stricture and the balloon is inflated until the waist disappears on fluoroscopy [44]. After 30–60 s, the balloon is deflated, withdrawn and the endoscopy is advanced through the dilated anastomosis [44]. The goal of the dilation is to achieve a diameter at least 2.5 times the original strictured diameter or at least 12-mm, with repeated dilations as necessary with progressively large balloon sizes and repeated sessions for reserved for recurrences [3, 43].

Other Endoscopic Procedures

Endoluminal Stents

The role of endoluminal stents in the treatment of refractory strictures is controversial [46]. Small case series have shown varying success with management of refractory strictures causing continued feeding intolerances, with success rates ranging from 0 to 80 % [46, 47, 50]. Eubanks et al. reported significant abdominal pain associated with all patients in their anastomotic stricture subgroup, requiring most stents to be removed after only 1 week [50]. Stent migration from the gastrojejunostomy is the most common complication, reported in almost 50 % of patients, likely from small bowel peristalsis and the unique stricture formation of these particular strictures [46, 50].

Savary-Gilliard Dilators

Bougie dilators have been reported to be successful in treating gastric anastomotic strictures [43, 51]. The procedure is the same as described previously and often involves fluoroscopy [3]. While rigid dilators have been reported to be successful, TTS balloon dilation is the preferred method due to the long distance from the mouth to the anastomosis and the presence of a potentially difficult curvature of the Roux limb [3, 43].

Colorectal Anastomotic Strictures

Definition

Colorectal strictures can be defined clinically as a significant intestinal obstruction causing either defecation difficulties, pain with passing flatus or stool and abdominal distention in a patient with a history of a colorectal surgery [52]. Endoscopically, it is the inability to pass a 12-mm [53] endoscope through the anastomotic stricture [52, 53]. This is an extremely heterogeneous group of stricturing disease from a number of different colorectal surgeries, including low anterior resections, sigmoidectomies, and ileal-anal pouch creations [52].

Pathophysiology

Similar to previously aforementioned esophageal and gastric anastomotic strictures, colorectal anastomotic strictures are not fully understood but important factors include continued inflammation with ischemia, leakage and, in some cases, radiotherapy [53]. For unclear reasons, it s reported that the rectum is the most commonly site for stricturing disease [52]. Other possible proposed factors include discrepancies in size between the two ends of the anastomosis and an abnormal collagen synthetic reaction [54].

Incidence and Risk Factors

The incidence of benign colorectal anastomotic strictures ranges between 3 and 30 %, yet only 5 % of patients become symptomatic [27, 52, 53, 55]. Risk factors can be separated into four categories: patient factors, surgical technique (stapled anastomosis [53], smaller stapler diameter [53], temporary diverting loop ileostomy [53]), and complications (anastomotic ischemia and leak [52], pelvic sepsis [3, 52]) and adjuvant therapy (radiation [3, 52]).

Treatment

The mainstay of therapy remains endoscopic balloon dilation. Dilation is favored over bougienage for the simple fact that it causes less traumatic injury [56]. While dilation is generally successful, frequently repeated dilation sessions are usually required. Stents, steroids, and incisional therapy with electrocautery, laser, or argon are reserved for combination treatment adjuncts or for dilation failures.

Balloon Dilators

The TTS balloon dilation is as described previously. For extremely stenotic strictures or angulated intestines a technique called Over the Wire (OTW) dilation is preferred over TTS, which uses an endoscopically placed guidewire to allow for more successful proximal placement of the balloon [26, 53]. OTW uses a Seldinger method for balloon insertion and generally has larger diameter balloons than the TTS type. Balloon dilation, including both TTS and OTW, has been shown to be efficacious with medium-term success rates reported between 33 and 86 %, however recurrence rates after initial dilation are reported to be

quite high at 30–88 % [52, 53, 56]. The large disparity in success rates speaks to the high heterogeneity amongst the results of the studies; this is likely in keeping with difference in technique, especially in the diameter of the balloon used for dilation.

Di et al. reported improved results for the use of second, simultaneous balloon dilation for colorectal strictures [27]. In double balloon dilation, two guidewires are employed, each passed separately through the endoscope. The first balloon, usually a 20-mm, is used for initial stricture dilation under fluoroscopic surveillance for 1–3 min [56]. Then a second guidewire is passed alongside with a smaller balloon, usually 10–15-mm, and then the two balloons are inflated simultaneously [27]. At the end of the procedure, water-soluble contrast medium is injected into the rectum to rule out perforation [56]. 71–100 % of patients reported long-term success in the management of symptomatic colorectal anastomotic strictures post-double balloon dilation [56]. This reported improvement with double balloon dilation could be explained by the fact that balloon size appears to be the most important factor regarding dilation efficacy for colorectal anastomotic stricturing disease [3]. Therefore, the additional benefit in diameter from the second balloon accounts for its success [56]. The largest balloon diameter reported in the literature for this population is 40-mm. Increased balloon diameter appears not to be correlated with an increased complications rate [56]. Balloon dilation procedure is relatively safe with minimal morbidity and complications [3, 53].

Other Endoscopic Procedures

Rigid Dilators

The Savary-Gilliard bougies have been shown to have similar success rates, approximately 80 %, to balloon dilators with the added advantage of being cheaper as the bougies are reusable [57].

Stents

Stents for colorectal strictures are reserved for patient with recurrent symptoms after failed initial dilation treatment. Success rates range between 70 and 80 % [54, 58].

SEMSs' role in malignant colonic unresectable strictures is well established but in benign disease its role is yet to be defined [54]. SEMS,

once again, can be covered or uncovered, with the uncovered stents promoting tissue hyperplasia and embedding and therefore are harder to remove. This characteristic can lead to possible re-occlusion but have lower migration rates as a result, with uncovered stents being the opposite [54, 55].

Biodegradable stents have gained popularity of late as a management option for colorectal anastomotic strictures. Building upon the limitations of SEMS and SEPS, avoiding a second endoscopic removal procedure and its gradual expansion and dilatory effect gives these stents inherit advantages over both [55, 58]. Repici et al. reported suboptimal efficacy of these stents with stricture resolution in only 45 % of patients and surprisingly high stent migration rates of 36 %. The authors attributed these poor results to the fact that colorectal specific biodegradable stents are not yet available, therefore the stents, originally meant for esophageal strictures, were too small in diameter to be adequate for colonic strictures [55]. At this time clinical availability of biodegradable stents is dependent on varying regulatory approval throughout the world.

Electrocautery

Electrocautery and other less commonly described incisional procedures like laser stricturotomy, microwave coagulation therapy, and argon plasma coagulation can be performed independent or in conjunction with balloon dilation [53]. Radial incisions at multiple locations occur just prior to the planned dilation. These incisional procedures have shown synergistic results when combined with balloon dilation, especially for high-grade stenosis (<7-mm luminal diameter) [59].

Endoscopic Transanal Resection of Strictures (ETAR)

ETAR involved actually resecting out the anastomotic stricture. The procedure involves the insertion of a urologic rectoscope into the rectum and using a loop-cutting electrode to resect the lesion superficial to the muscular wall [60]. The incision by the loop-cutting electrode is in the posterior part of the stricture, where the peri-rectal fat and fibrosis limit the morbidity of colonic wall perforation [59]. The incision into the posterior wall opens up the stricture, allowing a channel to be created by the incision [59]. The site is then sealed using a Foley balloon catheter, which is removed the following day. The limited, small case series on its

use in anastomotic strictures report success rates ranging from 84 to 100 % [59–61]. This procedure is reserved for distal, low-lying strictures, up to 15 cm, that are accessible to the rectoscope [59].

References

1. Zieren HU, Muller JM, Pichlmaier H. Prospective randomized study of one- or two-layer anastomosis following oesophageal resection and cervical oesophagogastrostomy. Br J Surg. 1993;80(5):608–11.
2. Briel JW, Tamhankar AP, Hagen JA, DeMeester SR, Johansson J, Choustoulakis E, et al. Prevalence and risk factors for ischemia, leak, and stricture of esophageal anastomosis: gastric pull-up versus colon interposition. J Am Coll Surg. 2004;198(4):536–41. discussion 41–2.
3. Stangl JR, Gould J, Pfau PR. Endoscopic treatment of luminal anastomotic strictures. Tech Gastrointest Endosc. 2006;8(2):72–80.
4. Serhal L, Gottrand F, Sfeir R, Guimber D, Devos P, Bonnevalle M, et al. Anastomotic stricture after surgical repair of esophageal atresia: frequency, risk factors, and efficacy of esophageal bougie dilatations. J Pediatr Surg. 2010;45(7):1459–62.
5. Ruigomez A, Garcia Rodriguez LA, Wallander MA, Johansson S, Eklund S. Esophageal stricture: incidence, treatment patterns, and recurrence rate. Am J Gastroenterol. 2006;101(12):2685–92.
6. Holm AN, de la Mora Levy JG, Gostout CJ, Topazian MD, Baron TH. Self-expanding plastic stents in treatment of benign esophageal conditions. Gastrointest Endosc. 2008;67(1):20–5.
7. Chung WC, Paik CN, Lee KM, Jung SH, Chang UI, Yang JM. The findings influencing restenosis in esophageal anastomotic stricture after endoscopic balloon dilation: restenosis in esophageal anastomotic stricture. Surg Laparosc Endosc Percutan Tech. 2009;19(4):293–7.
8. Kochhar R, Poornachandra KS. Intralesional steroid injection therapy in the management of resistant gastrointestinal strictures. World J Gastrointest Endosc. 2010;2(2):61–8.
9. Luechakiettisak P, Kasetsunthorn S. Comparison of hand-sewn and stapled in esophagogastric anastomosis after esophageal cancer resection: a prospective randomized study. J Med Assoc Thai. 2008;91(5):681–5.
10. Muehrcke DD, Kaplan DK, Donnelly RJ. Anastomotic narrowing after esophagogastrectomy with the EEA stapling device. J Thorac Cardiovasc Surg. 1989;97(3):434–8.
11. Honkoop P, Siersema PD, Tilanus HW, Stassen LP, Hop WC, van Blankenstein M. Benign anastomotic strictures after transhiatal esophagectomy and cervical esophagogastrostomy: risk factors and management. J Thorac Cardiovasc Surg. 1996;111(6):1141–6. discussion 7–8.

12. Johansson J, Oberg S, Wenner J, Zilling T, Johnsson F, von Holstein CS, et al. Impact of proton pump inhibitors on benign anastomotic stricture formations after esophagectomy and gastric tube reconstruction: results from a randomized clinical trial. Ann Surg. 2009;250(5):667–73.
13. Park JY, Song HY, Kim JH, Park JH, Na HK, Kim YH, et al. Benign anastomotic strictures after esophagectomy: long-term effectiveness of balloon dilation and factors affecting recurrence in 155 patients. AJR Am J Roentgenol. 2012;198(5):1208–13.
14. Law S, Fok M, Chu KM, Wong J. Comparison of hand-sewn and stapled esophagogastric anastomosis after esophageal resection for cancer: a prospective randomized controlled trial. Ann Surg. 1997;226(2):169–73.
15. Rindani R, Martin CJ, Cox MR. Transhiatal versus Ivor-Lewis oesophagectomy: is there a difference? Aust N Z J Surg. 1999;69(3):187–94.
16. Lee TH, Lee SH, Park JY, Lee CK, Chung IK, Kim HS, et al. Primary incisional therapy with a modified method for patients with benign anastomotic esophageal stricture. Gastrointest Endosc. 2009;69(6):1029–33.
17. Fennerty MB. The continuum of GERD complications. Cleve Clin J Med. 2003;70 Suppl 5:S33–50.
18. El-Serag HB. Temporal trends in new and recurrent esophageal strictures in Department of Veterans Affairs. Am J Gastroenterol. 2006;101(8):1727–33.
19. Committee AT, Siddiqui UD, Banerjee S, Barth B, Chauhan SS, Gottlieb KT, et al. Tools for endoscopic stricture dilation. Gastrointest Endosc. 2013;78(3):391–404.
20. Scolapio JS, Pasha TM, Gostout CJ, Mahoney DW, Zinsmeister AR, Ott BJ, et al. A randomized prospective study comparing rigid to balloon dilators for benign esophageal strictures and rings. Gastrointest Endosc. 1999;50(1):13–7.
21. Saeed ZA, Winchester CB, Ferro PS, Michaletz PA, Schwartz JT, Graham DY. Prospective randomized comparison of polyvinyl bougies and through-the-scope balloons for dilation of peptic strictures of the esophagus. Gastrointest Endosc. 1995; 41(3):189–95.
22. Abele JE. The physics of esophageal dilatation. Hepatogastroenterology. 1992;39(6): 486–9.
23. Kim JH, Shin JH, Song HY. Fluoroscopically guided balloon dilation for benign anastomotic stricture in the upper gastrointestinal tract. Korean J Radiol. 2008;9(4): 364–70.
24. Hordijk ML, van Hooft JE, Hansen BE, Fockens P, Kuipers EJ. A randomized comparison of electrocautery incision with Savary bougienage for relief of anastomotic gastroesophageal strictures. Gastrointest Endosc. 2009;70(5):849–55.
25. London RL, Trotman BW, DiMarino Jr AJ, Oleaga JA, Freiman DB, Ring EJ, et al. Dilatation of severe esophageal strictures by an inflatable balloon catheter. Gastroenterology. 1981;80(1):173–5.
26. Lin S-C, Sy E, Lin B-W, Lee J-C. Management of colorectal anastomotic strictures using multidiameter balloon dilation. J Soc Colon Rectal Surgeon. 2009;20:62–9.
27. Di ZH, Shin JH, Kim JH, Song HY. Colorectal anastomotic strictures: treatment by fluoroscopic double balloon dilation. J Vasc Interv Radiol. 2005;16(1):75–80.

28. Ikeya T, Ohwada S, Ogawa T, Tanahashi Y, Takeyoshi I, Koyama T, et al. Endoscopic balloon dilation for benign esophageal anastomotic stricture: factors influencing its effectiveness. Hepatogastroenterology. 1999;46(26):959–66.
29. Martin RC, Woodall C, Duvall R, Scoggins CR. The use of self-expanding silicone stents in esophagectomy strictures: less cost and more efficiency. Ann Thorac Surg. 2008;86(2):436–40.
30. Repici A, Conio M, De Angelis C, Battaglia E, Musso A, Pellicano R, et al. Temporary placement of an expandable polyester silicone-covered stent for treatment of refractory benign esophageal strictures. Gastrointest Endosc. 2004;60(4):513–9.
31. Cwikiel W, Stridbeck H, Tranberg KG, von Holstein CS, Hambraeus G, Lillo-Gil R, et al. Malignant esophageal strictures: treatment with a self-expanding nitinol stent. Radiology. 1993;187(3):661–5.
32. Wilson JL, Louie BE, Farivar AS, Vallieres E, Aye RW. Fully covered self-expanding metal stents are effective for benign esophagogastric disruptions and strictures. J Gastrointest Surg. 2013;17(12):2045–50.
33. Committee AT, Varadarajulu S, Banerjee S, Barth B, Desilets D, Kaul V, et al. Enteral stents. Gastrointest Endosc. 2011;74(3):455–64.
34. 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(6):1374–81.
35. Buscaglia JM, Jayaraman V, Nagula S. Temporary use of a new fully-covered self-expanding metal stent for the management of post-esophagectomy strictures. Dig Endosc. 2011;23:187–9.
36. Evrard S, Le Moine O, Lazaraki G, Dormann A, El Nakadi I, Deviere J. Self-expanding plastic stents for benign esophageal lesions. Gastrointest Endosc. 2004;60(6):894–900.
37. Pennathur A, Chang AC, McGrath KM, Steiner G, Alvelo-Rivera M, Awais O, et al. Polyflex expandable stents in the treatment of esophageal disease: initial experience. Ann Thorac Surg. 2008;85(6):1968–72. discussion 73.
38. Sanchez Munoz D, Ortiz-Moyano C, Gomez-Rodriguez B. Resolution of a refractory anastomotic stricture with a novel biodegradable esophageal stent. Clin Gastroenterol Hepatol. 2013;11(9):e63.
39. Hindy P, Hong J, Lam-Tsai Y, Gress F. A comprehensive review of esophageal stents. Gastroenterol Hepatol. 2012;8(8):526–34.
40. Kochhar R, Makharia GK. Usefulness of intralesional triamcinolone in treatment of benign esophageal strictures. Gastrointest Endosc. 2002;56(6):829–34.
41. Miyashita M, Onda M, Okawa K, Matsutani T, Yoshiyuki T, Sasajima K, et al. Endoscopic dexamethasone injection following balloon dilatation of anastomotic stricture after esophagogastrostomy. Am J Surg. 1997;174(4):442–4.
42. Brandimarte G, Tursi A. Endoscopic treatment of benign anastomotic esophageal stenosis with electrocautery. Endoscopy. 2002;34(5):399–401.
43. Da Costa M, Mata A, Espinos J, Vila V, Roca JM, Turro J, et al. Endoscopic dilation of gastrojejunal anastomotic strictures after laparoscopic gastric bypass. Predictors of initial failure. Obes Surg. 2011;21(1):36–41.

44. Nguyen NT, Stevens CM, Wolfe BM. Incidence and outcome of anastomotic stricture after laparoscopic gastric bypass. J Gastrointest Surg. 2003;7(8):997–1003. discussion.
45. Carrodeguas L, Szomstein S, Zundel N, Lo Menzo E, Rosenthal R. Gastrojejunal anastomotic strictures following laparoscopic Roux-en-Y gastric bypass surgery: analysis of 1291 patients. Surg Obes Relat Dis. 2006;2(2):92–7.
46. Marcotte E, Comeau E, Meziat-Burdin A, Menard C, Rateb G. Early migration of fully covered double-layered metallic stents for post-gastric bypass anastomotic strictures. Int J Surg Case Rep. 2012;3(7):283–6.
47. Cusati D, Sarr M, Kendrick M, Que F, Swain JM. Refractory strictures after Roux-en-Y gastric bypass: operative management. Surg Obes Relat Dis. 2011;7(2):165–9.
48. Carter JT, Tafreshian S, Campos GM, Tiwari U, Herbella F, Cello JP, et al. Routine upper GI series after gastric bypass does not reliably identify anastomotic leaks or predict stricture formation. Surg Endosc. 2007;21(12):2172–7.
49. Caro L, Sanchez C, Rodriguez P, Bosch J. Endoscopic balloon dilation of anastomotic strictures occurring after laparoscopic gastric bypass for morbid obesity. Dig Dis. 2008;26(4):314–7.
50. Eubanks S, Edwards CA, Fearing NM, Ramaswamy A, de la Torre RA, Thaler KJ, et al. Use of endoscopic stents to treat anastomotic complications after bariatric surgery. J Am Coll Surg. 2008;206(5):935–8. discussion 8–9.
51. Csendes A, Burgos AM, Burdiles P. Incidence of anastomotic strictures after gastric bypass: a prospective consecutive routine endoscopic study 1 month and 17 months after surgery in 441 patients with morbid obesity. Obes Surg. 2009;19(3):269–73.
52. Hiranyakas A, Da Silva G, Denoya P, Shawki S, Wexner SD. Colorectal anastomotic stricture: is it associated with inadequate colonic mobilization? Tech Coloproctol. 2013;17(4):371–5.
53. Suchan KL, Muldner A, Manegold BC. Endoscopic treatment of postoperative colorectal anastomotic strictures. Surg Endosc. 2003;17(7):1110–3.
54. Lamazza A, Fiori E, Sterpetti AV, Schillaci A, Scoglio D, Lezoche E. Self-expandable metal stents in the treatment of benign anastomotic stricture after rectal resection for cancer. Colorectal Dis. 2014;16(4):O150–3.
55. Repici A, Pagano N, Rando G, Carlino A, Vitetta E, Ferrara E, et al. A retrospective analysis of early and late outcome of biodegradable stent placement in the management of refractory anastomotic colorectal strictures. Surg Endosc. 2013;27(7):2487–91.
56. Kim PH, Song HY, Park JH, Kim JH, Na HK, Lee YJ. Safe and effective treatment of colorectal anastomotic stricture using a well-defined balloon dilation protocol. J Vasc Interv Radiol. 2012;23(5):675–80.
57. Werre A, Mulder C, van Heteren C, Bilgen ES. Dilation of benign strictures following low anterior resection using Savary-Gilliard bougies. Endoscopy. 2000;32(5):385–8.
58. Caruso A, Manno M, Manta R, Bertani H, Mirante VG, Conigliaro R. Alternative management of anastomotic colorectal strictures: our experience with fully covered self-expanding metal stents. Surg Endosc. 2013;27(12):4752–3.

59. Forshaw MJ, Maphosa G, Sankararajah D, Parker MC, Stewart M. Endoscopic alternatives in managing anastomotic strictures of the colon and rectum. Tech Coloproctol. 2006;10(1):21–7.
60. Sutton CD, Marshall LJ, White SA, Flint N, Berry DP, Kelly MJ. Ten-year experience of endoscopic transanal resection. Ann Surg. 2002;235(3):355–62.
61. Hunt TM, Kelly MJ. Endoscopic transanal resection (ETAR) of colorectal strictures in stapled anastomoses. Ann R Coll Surg Engl. 1994;76(2):121–2.

8. Endoscopic Stent Placement and Suturing: Management of Gastrointestinal Anastomotic Leaks

Tarek El-Ghazaly, Pornthep Prathanvanich, and Bipan Chand

Introduction

Anastomotic leakage represents one of the most dangerous complications after gastrointestinal (GI) surgery. While the incidence varies according to location within the GI tract, GI leakage can lead to significant morbidity and mortality in patients across all types. The incidence of leak after esophagectomy is approximately 0.6–10.4 % [1], while it ranges between 0 and 7 % for laparoscopic sleeve gastrectomy (LSG) [2], 0–5.6 % (mean of 2.4 %) for laparoscopic Roux-en-Y gastric bypass (LRYGB) [3], and 2.6–5 % for rectal resections [4, 5].

Early Detection of GI Leaks

If the surgeon has a high suspicion of a leak, the steps to approach this are:

- Complete history and physical examination, focusing on type of operation and presenting symptoms.
- Laboratory: Full set of blood work such as CBC, coagulations, liver function, and amylase.
- Drain fluid analysis such as fluid amylase, Gram stain, and culture.

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- Diagnostic imaging such as acute abdominal series, upper gastrointestinal (GI) contrast study, abdominal ultrasound (US), computer tomography (CT) scan of abdomen and pelvis with IV/oral contrast.

After complete history taking and physical examination, if a drain was left in place at the time of surgery, the drain fluid can be sent for an amylase level (for upper GI surgery) and Gram stain and culture for lower GI surgery. An amylase fluid level much higher than normal serum levels (in the 1000s) suggests that saliva is finding its way into the drain. However, and regardless of the drain amylase level, early imaging is warranted if clinical suspicion of a leak exists. A gastrointestinal contrast study is frequently used postoperatively to assess the presence of an anastomotic leak. In general, a water-soluble contrast material (Gastrografin) is used. In case of doubt, or in order to increase sensitivity, abdominal computerized tomography (CT) scan can be performed. CT scan can provide additional information in regards to fluid collections, abscess or the presence of sub-diaphragmatic air.

Abdominal CT scan should be performed with intravenous and oral contrast material. Findings suggestive of anastomotic leakage include: Extravasation of contrast agent through the GI anastomosis or the wall of the gastric sleeve, accumulation of contrast agent adjacent to the leak site, free intra-abdominal liquid, free intra-abdominal gas, or residual contrast agent in the drainage tube.

Management

The management of the leak depends on the patient's clinical condition (Fig. 8.1). The physician or surgeon managing this complication must have a clear treatment strategy or algorithm based on the patient's status, the duration of the leak, and the resources available. Interventional options include surgery (laparoscopy [Fig. 8.2] or laparotomy or thoracoscopy or thoracotomy with adequate washout, wide adequate drainage close to the anastomotic site, and possible enteral access), radiological procedures (percutaneous drainage) and endoscopic procedures (covered self-expandable metal stents (SEMS), endoscopic suturing, clips, biological glue, pigtail drains, and T-tube gastrostomy drain).

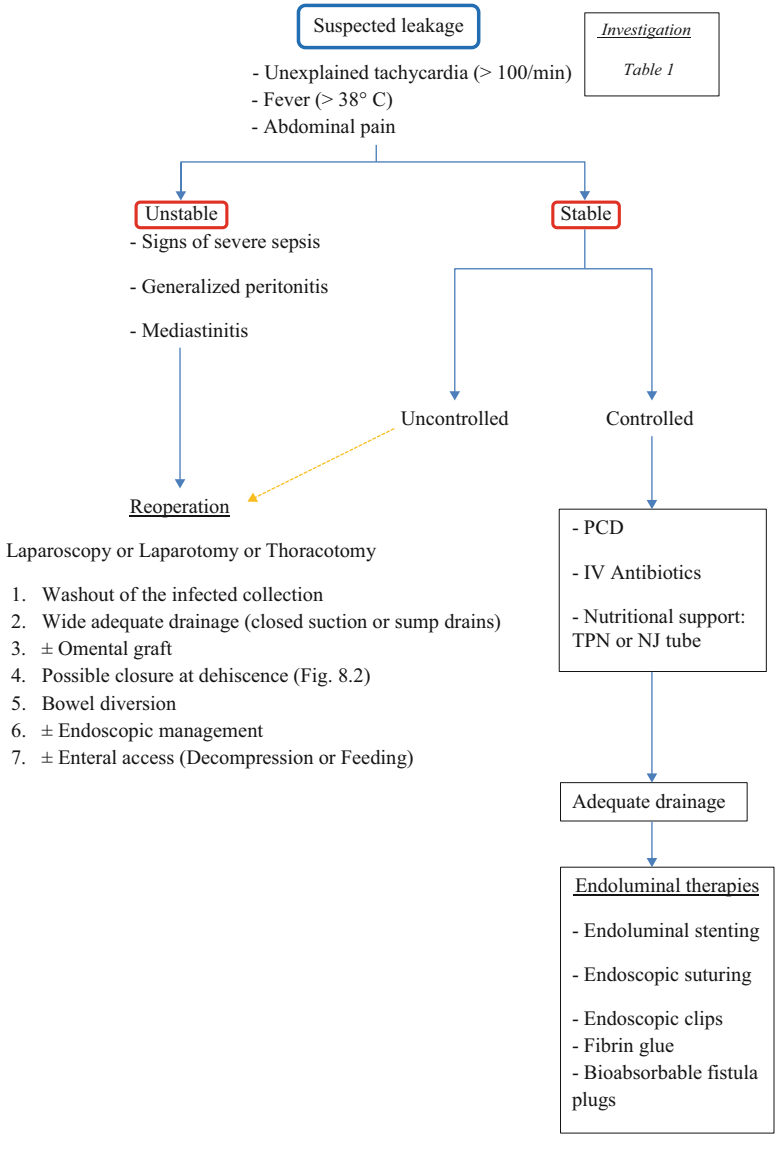

Fig. 8.1. Algorithm for management of anastomotic leak.

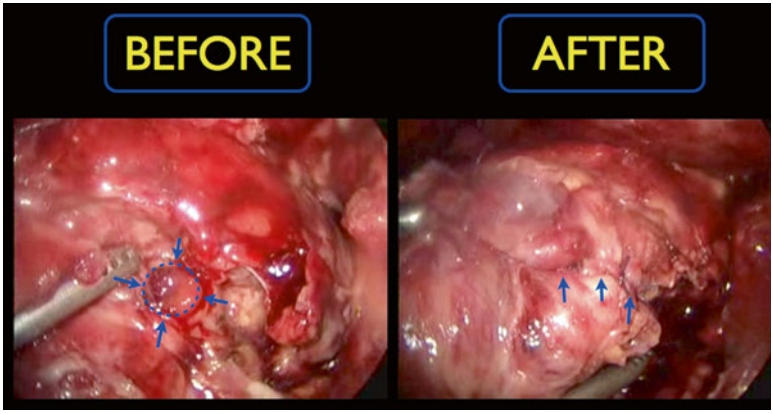

Fig. 8.2. Patients who are manifesting signs of sepsis or are unstable should be managed operatively with laparoscopy or laparotomy. Drainage and washout of the infected collection and wide drainage of the area is the primary goal of the operation. Primary closure of the defect (*circle* sign) can be performed if discovered early. Direct primary closure of the defect with or without sealants should be reserved for cases diagnosed early (within 24–48 h) and have good tissue viability.

Endoscopic Stent and Suturing Management of Anastomotic Leakage after Esophagogastric Surgery

Management of an esophageal anastomotic dehiscence is challenging and is associated with high morbidity and high mortality. Treatment is often selected based on patients' symptoms, site of leak, and extent of leak. The incidence of a leak and its outcome is dependent on the site of anastomosis (cervical or intrathoracic anastomosis). Cervical anastomoses are associated with a higher leakage rate of 10–20 %, but the leak-associated mortality is low [6]. In contrast, intra-thoracic leak rate has been reported at 7.9 %, resulting in a 3-month mortality rate of 18.2 % (OR 3.0) [6]. If treatment is delayed beyond the first 24 h, a mortality rate has been reported at up to 50–60 % [7, 8].

Successful management of an esophageal leak requires early recognition, prompt control of sepsis, and elimination of ongoing contamination of the mediastinum. For large esophageal anastomotic leaks with significant contamination of the pleural cavity, treatment includes a

thoracotomy or thoracoscopic approach, surgical drainage and repair, and gastrointestinal diversion. While small-contained leaks are treated with conservative management including percutaneous drainage alone, the patients should receive nothing by mouth, parenteral nutrition, and intravenous antibiotics. Mortality associated with conservative treatment of esophageal leak ranges from 8.5 % to as high as 46.2 % in selected case series and success rate ranging between 40 and 96.3 % [9–12].

Endoscopic management of GI leaks has gained great importance as it avoids the morbidity and mortality of surgical intervention. Over the past decade, covered self-expanding metal stents (SEPS: Self-Expanding Plastic Stents; FSEMS: Fully covered Self-expanding Metal Stents; PSEMS: Partially covered Self-Expanding Metal Stents) were the mainstay of endoscopic therapy for anastomotic dehiscence after esophagogastric surgery. These stents were initially designed for use in the setting of malignant strictures; however, they have been used successfully in an off-label setting for the treatment of leaks. Inherent to their design, the main limitations of these stent types include stent migration and hyperplasic tissue in- and/or overgrowth, especially with prolonged placement of stents. Treatment success of stent placement would be defined if the intervention resulted in control of the leak, healing of the leak site, and cessation of mediastinal contamination or sepsis. In 2011, van Boeckel et al. [13] demonstrated in a systematic review of the currently available 25 studies of treating benign esophageal ruptures and anastomotic leaks with temporary placement of a stent with different stent designs. They found that clinical success was achieved in 85 % of reported 267 patients and was not significantly different between stent types (SEPS: 66–100 %, FSEMS: 50–100 % and PSEMS 69–100 %, $P=0.97$). In 2012, van Boeckel et al. [14] presented the first cohort study comparing different stent types, i.e., FSEMS, PSEMS, and SEPS, for treatment of benign esophageal ruptures and leaks. Clinical success was achieved in 34/52 (76 %, intention-to-treat: 65 %) patients with no statistically significant differences between partially and fully covered metal and plastic stents (PSEMS: 73 %, FSEMS: 83 % and SEPS: 83 %) after a median of 1 (range 1–5) stent and a median stenting time of 5–6 weeks (range 1–17). In total, 33 complications in 24 (46 %) patients who ocuured tissue in or overgrowth ($n=8$), stent migration ($n=10$), ruptured stent cover (all Ultraflex; $n=6$), food obstruction ($n=3$), severe pain ($n=2$), esophageal rupture ($n=2$), hemorrhage ($n=2$). One (2 %) patient died of a stent-related cause. Although all three stent designs were found to be effective in sealing esophageal anastomotic leak, they all have their advantages and disadvantages.

Historically, endoscopic stent management of esophageal anastomotic leaks was developed using the only self-expandable plastic stent (Polyflex®, Boston Scientific) with diameters ranging from 16 to 21 mm and lengths from 90 to 150 mm. The stent was made from silicone, entirely covered with a polyester film and flared at the proximal end. The polyester film helped decrease the risk of ingrowth into the esophageal mucosa, and facilitated stent removal; however it also enhanced the risk of migration. Van Boeckel et al. [13] also found that stent migration requiring re-intervention occurred in 25 % of patients and most commonly occurred with fully covered stents—both SEPS (26 %) and FSEMS (26 %)—compared to PSEMS (13 %) ($P \leq 0.001$). This evidence demonstrated the previously known reduced anchoring capacity of FSEMS and SEPS compared with PSEMS which contributed to an increased migration rate of FSEMS and SEPS. We note that the majority of these patients had no obstructive lesion keeping the stent in place. While plastic stents are less expensive than their metallic counterparts, drawbacks of plastic stents include their larger diameter and higher rigidity, which led to a higher incidence of complications (e.g., perforation, hemorrhage) as shown in a randomized prospective comparison between SEPS (9 %) vs. PSEMS (3 %) [15].

Currently, self-expanding metal stents (partially covered or completely covered) are used in the treatment of complications of esophagogastric surgery (Fig. 8.3). Even though their cost is clearly higher than the plastic stents, their utilization is easier (more flexible and pre-assembled) and the risk of complications associated with their use—namely perforation, hemorrhage, and migration is less than SEPS. The stents are composed of one or several braided strands of a metal with high shape memory, most commonly made of Nickel Titanium, also known as "Nitinol." They are contained within a tight sheath placed on a carrier tube. The caliber of the assembled system ranges from 18 to 24 Fr, which is not compatible with the passage of the stent through the operating channel of an endoscope (over-the-wire, OTW, system). However, there are novel models with a thinner delivery diameter (10 Fr) that can be passed through a 3.7 mm operating channel referred to as a 'through-the-scope' system, TTS. The self-expandable metal stents vary according to the alloy used, the length (70–170 cm and even longer), the diameter (18–23 mm or greater), the delivery system, as well as the coating material. The proximal, and sometimes the distal ends are flared (approximately 5 mm larger than the shaft), in an attempt to limit the risk of migration. Several options (anti-reflux valve, anti-migration systems, or proximal deployment) are available. The choice of the stent is

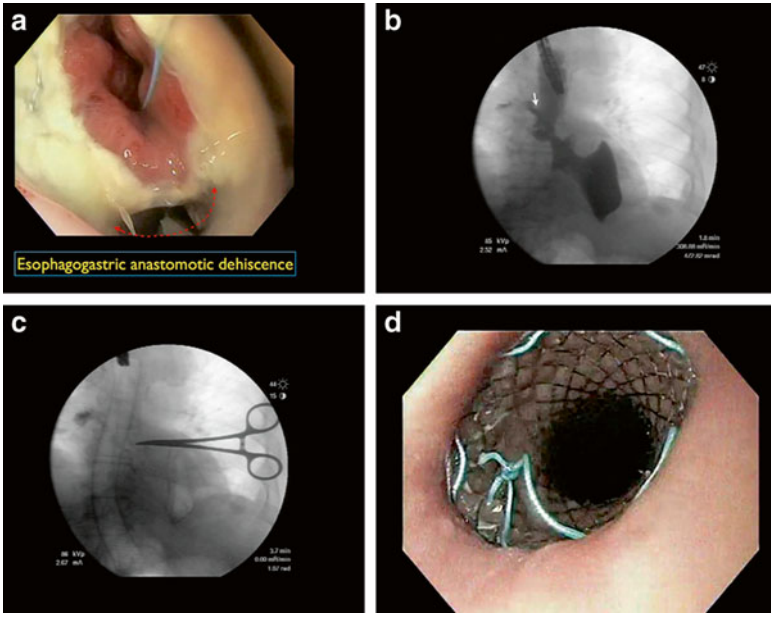

Fig. 8.3. (**a**) Esophagogastric anastomotic dehiscence (*arrow* sign). (**b**) Contrast leak at the Esophagogastric (EG) anastomosis after Ivor-Lewis esophagectomy (*white arrow*). (**c**) Intraoperative fluoroscopy demonstrated PSEMS insertion in order to bypass the leak site with cutaneous landmarking (Hemostat). (**d**) Endoscopic view demonstrating completed PSEMS deployment.

crucial in case of proximal esophageal leaks or fistulas, especially after the Lewis-Santy operation where the low radial force of the Ultraflex® (Boston Scientific) stent is most appropriate. Proximal deployment systems allow adjustment of the position of the stent between the high-riding fistula and upper esophageal sphincter.

Esophageal self-expanding stents are placed under endoscopic and radiologic guidance typically with sedation or general anesthesia. The initial step consists of visualizing and marking the leak site endoscopically and by contrast opacification, as well as estimating the extent of the leak in order to choose a stent of appropriate length. Radiopaque objects (e.g., paper clip or hemostats) are used for cutaneous marking if patient movements can be limited, or more rarely internal markings (submucosal injection of contrast or clip placement) are used. After placement of a guide-wire the endoscope is withdrawn and the stent deployment system placed over the wire under fluoroscopic guidance.

A rigid guide-wire (Savary type) is preferred. An endoscope can be inserted along side the deployment system for visualization. The distal end of the stent is placed in the stomach, duodenum or jejunum, according to the preceding procedure. Small adjustments can be made at the beginning of delivery. Contact between the stent and the endoscope must be avoided immediately after delivery as it can increase the risk of migration. Contrast medium is injected within the stent itself after deployment to check for extravasation and proper sealing. A plain X-ray after the procedure can help evaluate the degree of expansion of the stent and the degree of early migration. Patients can resume oral intake if there is no evidence of ongoing leak on contrast imaging. Recommendations to avoid the risk of food impaction within the stent include: eating while in the seated position, avoiding thick, dense aliments (meat), avoiding stringy aliments (leeks for example), avoiding karaya gum gastric demulcents, and drinking sparkling water at the end of the meal. Stent surveillance protocols should be in place with weekly X-ray to look for migration. There are currently select stents with on-label status outside of the USA for the management of gastrointestinal leak.

Tissue overgrowth involving endolumenal stents mostly occurs at the uncovered part of PSEMS. It is caused by the proliferation of granulation tissue and/or local fibrotic reaction (Fig. 8.4) that can clinically manifest as early as 2 weeks after stent deployment. This can lead to difficult stent removal, which may result in a secondary esophageal perforation [16]. On the other hand, the hyperplasic epithelium growing

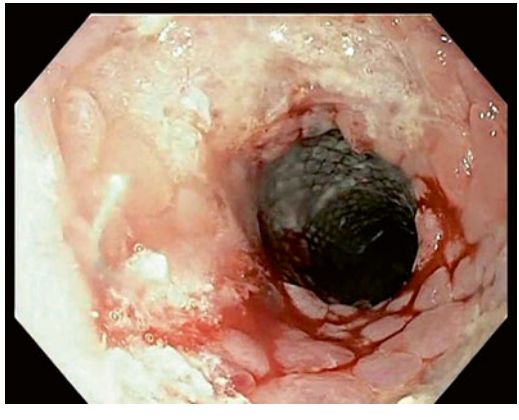

Fig. 8.4. The proliferation of granulation tissue (tissue overgrowth).

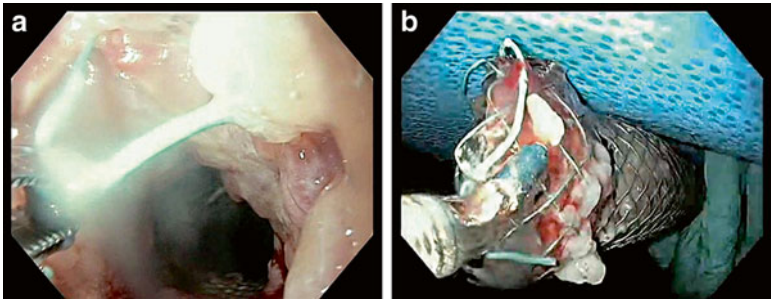

Fig. 8.5. (**a**) Stent extraction with rat toothed forcep. (**b**) PSEMS after removing.

into the stent meshes may reduce the risk of stent migration, providing a better watertight barrier to saliva and fluids, and ultimately favoring fistula healing [17]. The mean healing time varies and has been reported to be 7 weeks (range: 6–8 weeks) in some series. Six to eight weeks have been suggested as the optimal time for stent removal (this may require two separate stent intervals). A shorter interval may lead to incomplete closure of the fistula or the leak site, whilst a longer interval may cause either stent migration or excessive mucosal overgrowth within the stent with subsequent dysphagia or difficulty in stent removal. Stent extraction can be done simply by pulling on the nylon string attached to the proximal end of the stent, either with a toothed forceps or polypectomy snare (Fig. 8.5). In more difficult cases, particularly extraction of partially covered metallic stents with epithelial ingrowths into the mesh, grasping the stent at two points via the two channels of a double-channel endoscope can be helpful. When the proximal extremity of the stent is close to the upper esophageal sphincter area, placing an over-tube can be useful for extraction. A useful technique to remove an embedded PSEMS is to place a fully covered stent of the same diameter inside the first one. This so-called stent-in-stent technique causes necrosis of the hyperplastic epithelium and both stents can be more easily removed after 7–14 days [17, 18].

Esophageal stenting is often performed with simultaneous endoscopic or percutaneous drainage of mediastinal fluid collections. The success rate for control of anastomotic leak with covered stenting appears to be similar or better than that of conservative treatments, ranging between 77.3 and 100 % [19–23]. A major advantage of endoscopic stenting in the treatment of anastomotic leak is that a surgical intervention can often be avoided. When conventional approaches are used to

manage anastomotic leaks, surgical reoperation is often required in 23–74 % [9–12] of these cases, compared to the use of esophageal cover stents where the rate of reoperation is 0–22.2 % [19–23]. Martin et al. [9] reported that the mortality associated with an intra-thoracic leak following esophagectomy had decreased in the modern era; the leak-associated mortality between 1970 and 1986 was 43 %, which decreased to 3.3 % in 1987–2004. Presently, a leak-associated mortality is closer to 0 % with a variety of multidisciplinary approaches available. Endoscopic treatments (SEMS, endoscopic suturing, clips and biological glue), percutaneous drainage, broad-spectrum intravenous antibiotic, and nutritional support are all employed in leak management [14, 24]. Compared to the conservative treatment group, patients who were treated with endoscopic stents had earlier oral intake, a less extensive intensive care course, and shorter hospital stay. Given these findings, it is very likely that esophageal covered stents would be associated with significant cost savings over conventional treatments.

Literature describing endoscopic suturing of esophageal leaks is limited to a few case reports. A 77-year-old man with a Boerhaave's disease, who had undergone emergent surgical repair and later esophageal diversion procedure along with jejunal feeding, developed an esophagopleural fistula. The fistula was closed by using a combination of fistula tract coagulation and endoscopic suturing (Endocinch, CR Bard Interventional, Murray Hill, New Jersey) [25]. Bonin et al. [26] reported a case involving endoscopic suturing to close a chronic esophagopleural fistula in a 66-year-old woman. A 10-mm fistula (for which thoracostomy was unsuccessful) was successfully closed after two sessions of endoscopic suturing. In another study, Kurian et al. [27] described closure of an inadvertent full-thickness esophagostomy while performing mucosotomy during peroral endoscopic myotomy. With use of the OverStitch suturing device (Apollo Endosurgery, Austin, TX), the defect was successfully closed and laparoscopy was prevented. In this particular case, the esophagus was dilated from achalasia disease, which precluded adequate apposition, making an esophageal cover stent a less than ideal option. The patient had an uneventful postoperative course. At 9-month follow-up, the patient had excellent palliation of dysphagia without reflux.

Most recently, endoscopic vacuum-assisted closure (E-VAC) has been described to treat anastomotic leaks after rectal and esophageal resections. Similar to the idea behind the established usage of vacuum-assisted closure for extensive cutaneous infected wounds, accessible upper gastrointestinal leakages have been treated by endoscopically placing sponges that have been connected with a drainage tube in the

necrotic cavities. The favorable outcomes of this treatment may be a result of the reduction in the intraluminal pressure and the induction of marked growth of granulation tissue.

E-VAC therapy is applied by endoscopic insertion of the Endo-SPONGE system (B. Braun Melsungen AG, Melsungen, Germany) through the esophageal defect, and into the cavity. The Endo-SPONGE is composed of an open-pored polyurethane sponge cut to fit into the paraesophageal cavity. The sponge is positioned via an overtube in the vicinity of the leak, and then inserted with the grasper forceps into the paraesophageal cavity (intracavitary vacuum therapy). In case of a small orifice, the polyurethane sponge can be placed at the level of the esophageal wall defect (intraluminal vacuum therapy). The sponge is then connected with a nasogastric tube, and suction is applied via a portable pump. Secretions are continuously evacuated using a negative pressure of 100 mmHg. After 2–3 days of continuous suction, the pump is inactivated, and the sponge is removed by pulling at the nasogastric tube, or using an endoscopic forceps if the sponge is adherent to adjacent tissues. Persisting leakage can be adequately managed using a self-expanding metal stent placed for a period of 4–6 weeks. This hybrid therapy combining two endoscopic treatment strategies for esophageal wall defects has been described by Bludau et al. [28] in a series of 14 patients. Complete restoration of the esophageal defect was achieved in 12 patients (86 %), while 2 patients died due to severe mediastinitis and ensuing sepsis before E-VAC therapy could be successfully completed.

Brangewitz et al. [29] compared the outcomes of 39 patients who were treated with SEMS or SEPS to those of 32 patients who were treated with EVAC for intrathoracic esophageal leaks. They found the overall closure rate to be significantly higher in the EVAC group at 84.4 %, compared with the SEMS/SEPS group at 53.8 %. No difference was found for either hospitalization or hospital mortality. They reported significantly more strictures occurring in the stent group at 28.2 % versus 9.4 % with EVAC.

Endoscopic Stent and Suturing Management of Gastrointestinal Leak after Gastric Bypass and Sleeve Gastrectomy

Most existing data on post-bariatric surgery leaks are related to the management of the two most common bariatric procedures: laparoscopic Roux-en-Y Gastric Bypass (RYGB) and laparoscopic sleeve

gastrectomy (LSG). Endoscopic treatment strategies may attempt to bypass a leak (stenting) or occlude it (clips, plugs, glues, or suture). Control of abdominal contamination, use of systemic antimicrobials, and nutritional support are all required as well. Gastrointestinal leak after bariatric surgery have also been described in terms of:

- Time to diagnosis
  - Lalor et al. [30] classified gastric leaks as either *early-onset* (postoperative day 1–7) or *delayed-onset* (after postoperative day 8)
- Site of leakage: Identification of the gastric leak site based on:
  - LSG: anatomic thirds (upper, middle, or distal third of the remaining stomach)
  - RYGB: there are seven potential sites for a leak [3], described from proximal to distal:
  - Type 1 Gastric pouch
  - Type 2 Gastrojejunal (GJ) anastomosis
  - Type 3 Jejunal stump
  - Type 4 Jejuno-jejunal (JJ) anastomosis
  - Type 5 Excluded stomach
  - Type 6 Duodenal stump (in resectional bypass)
  - Type 7 Blind end biliary jejunal limb

The most frequent location of leaks is the GJ anastomosis (49–53 %). The highest mortality was associated to the JJ anastomosis.

Early Gastrointestinal Leak After Gastric Bypass

Patients manifesting signs of sepsis or instability are most commonly found to have type 2 (GJ anastomosis) leaks, and rarely, type 4 (JJ anastomosis) leaks. Early onset leaks in this setting should be managed operatively with laparoscopy or laparotomy with washout of the infected collection and wide drainage of the area. Direct primary closure of the defect with or without sealants should be reserved for cases diagnosed early (within 24–48 h) and with good tissue viability. Closed suction or sump drains should be placed in close vicinity and omentum sewn over the defect to help contain contamination. If the patient is stable during the case, a feeding jejunostomy should be placed for long-term enteral access (Fig. 8.1).

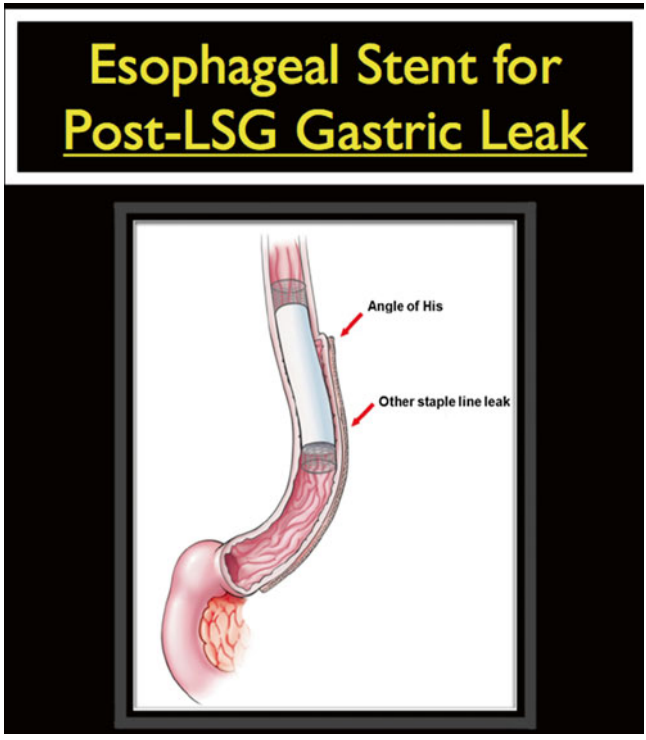

Fig. 8.6. Schematic illustration of gastric anatomy after sleeve gastrectomy (LSG) with stent in situ.

Endoscopic therapy is an alternative in this situation and is associated with acceptable risk (Fig. 8.6). Stent placement in these patients allows them to resume oral intake while the leak heals. Stenting also accelerates and promotes closure when a leak test is positive after primary or omental closure.

In a case series by Yimcharoen et al. [31] 18 patients—of whom 14 were bariatric patients—underwent endoscopic stent placement for anastomotic complications. A total of 31 stents (21 covered metal, 5 salivary, and 5 silicone-coated polyester) were used to treat anastomotic leaks ($n=13$), strictures ($n=3$), and fistulas ($n=2$). Symptomatic improvement occurred in all but 2 patients (89 %), and early oral intake was initiated in 11 (61 %). Stent treatment was successful in definitively managing the anastomotic leak in all 13 patients. Stent migration

occurred in four cases and was amenable to endoscopic management. Two patients died, with both deaths unrelated to stent placement.

A leak may also present as a well-defined abscess several days or weeks after surgery. In such cases, percutaneous image-guided drainage or pigtail drainage, intravenous antibiotics, and nutritional support (intravenously or through an enteral access) is appropriate. If drainage is adequate, endolumenal therapies can be used to facilitate closure of the leak. This process often includes placement of endolumenal stents, endoscopic clips, suturing, fibrin glue, or bioabsorbable fistula plugs across the leak. Before attempting to stent, the extraluminal collection must be adequately addressed in all cases and placement of drains with washout of the infected field is often warranted to promote closure of the leak.

Puli et al. [32] conducted a systematic review and meta-analysis that reviewed safety and efficacy of self-expandable stents (SESs) for the management of post-bariatric surgery leaks. A total of 189 related articles were reviewed of which seven studies (67 patients with leaks) met inclusion criteria. Successful leak closure using SESs was calculated at 87.77 % (95 % CI, 79.39–94.19 %). Successful endoscopic stent removal was 91.57 % (95 % CI, 84.22–96.77 %) and stent migration was noted in 16.94 % (95 % CI, 9.32–26.27 %).

Early Gastrointestinal Leak after Sleeve Gastrectomy (LSG)

Compared to post-RYGBP leaks, LSG leaks are more difficult to manage. Proximal fluid collections often contain saliva and gastric acid while distal leaks may additionally drain bile. In proximal leaks, the use of drains (surgical or percutaneous) plus alimentary support should be initiated. In addition to adequate drainage, the application of endoscopic agents like fibrin sealants in combination with somatostatin and placement of endolumenal stents have yielded promising results. Stenting has been shown to be effective in selected cases, but results can be variable depending on the size and duration of the leak [31]. Although placement of self-expanding covered, or partially covered stents (Polyflex or Wallflex stents, Boston Scientific, Natick, Massachusetts) may be beneficial, the current stent technology is not ideal for this anatomy. The difficulty is in the two different lumen diameters and the curvature of the gastric lumen (Fig. 8.6).

Several principles should be followed when an esophageal stent is considered for management of a gastric leak after sleeve gastrectomy. First, an upper GI endoscopy must be performed to evaluate the site and size of the leak, as well as the viability of the conduit. Gastric leaks at the proximal and mid-aspect of the gastric sleeve are the only leaks amenable to endoscopic stenting. A leak at the distal staple line of the gastric sleeve near the gastric antrum will not be amenable to endoscopic stenting, owing to the stent's smaller diameter, and inability to provide appropriate sealing of the defect. The selection of stent size is based on evaluation of the gastric sleeve diameter and the ability to deploy the stent. Another strategy to minimize stent migration is to use a longer stent or two stents whereby the distal aspect of the stent is rested along the wall of the gastric antrum, preventing luminal migration. Many studies have suggested routine stent removal no later than 6 weeks in order to avoid tissue hyperplasia and difficult extraction. Tolerance to stents is variable, with some patients reporting nausea, vomiting, drooling, and retrosternal discomfort. This tends to improve after the first few days. Covered SEMS also present significant morbidity–mortality, with migration being one of the main concerns. The high migration rate has been explained by the "abnormal" placement of the stent along the last portion of the esophagus and the gastric pouch. The type of stent used may also be lead to higher rates of migration. Fully covered stents will have the greatest degree of migration while less covered stents will have a greater degree of tissue ingrowths. Overall, the success rate for stent treatment ranges between 50 and 100 % with a migration rate between 8 and 58 % (Table 8.1) [31, 33–37].

There are fewer reports on the management of distal leaks; however the same principles as previously described should be applied. Court

Table 8.1. Endoscopic stent for gastric leak after laparoscopic sleeve gastrectomy.

Author	Year	Number of patients	Number of covered SEMS	Success rate (%)	Migration rate (%)
Serra et al. [33]	2007	3	7	66	14
Eubanks et al. [34]	2008	19	34	84	58
Casella et al. [35]	2009	5	11	100	9
Tan et al. [36]	2010	14	8	50	25
Pequignot et al. [37]	2011	25	50	84	8
Yimcharoen et al. [31]	2010	6	6	66	17

et al. [38] presented a case report with distal and proximal disruptions of the staple line. A T-tube gastrostomy with a large proximal and distal limb was placed into the most distal area of disruption. After thorough over sewing and drainage of the proximal site and T-tube (distal), a feeding jejunostomy was placed. Four weeks postoperatively, the T-tube was removed after the patient had a negative Gastrografin study and tolerated oral fluids with a clamped T-tube. Persistent leaks (both proximal and distal) may require conversion to a low-pressure system, unlike sleeve gastrectomy. In this circumstance, the alternative treatment could be to conversion to a RYGB.

Another important factor when treating proximal or distal leaks is to rule out distal obstruction, in particular at the incisura angularis. If present, an upper endoscopy and endoscopic deployment of a covered stent across the leak site and obstruction will both cover the leak but more importantly decrease the pressure in the gastric lumen.

Treatment success is defined as the absence of contrast agent leakage in CT and endoscopic evaluations after placement of covered SEMS, T-tube, or pigtail drains and their subsequent removal. In contrast, "treatment failure" is defined as the need for surgery for persistent GL (total gastrectomy or Roux-en-Y gastroenterostomy at the site of GL).

While endoscopic clips were initially described with promising outcomes for the closure of gastrostomy in porcine models, particularly after NOTES procedures [39, 40], they are less useful for larger defects owing to the restricted opening distance between their jaws, reduced closure force, and the inability to adequately capture deeper tissue.

Haito-Chavez et al. [41] described a large, multicenter experience with the usage of over-the-scope clips (OTSCs) for the management of GI defects. A total of 188 patients who had 108 fistulae, 48 perforations, and 32 leaks were included in the study. Long-term success was achieved in 60.2 % of patients during a median follow-up of 146 days. Rates of successful closure in perforations (90 %) and leaks (73.3 %) were significantly higher than those of fistulae (42.9 %). Long-term success was significantly higher when OTSCs were applied as primary therapy (69.1 %) in comparison to rescue therapy (46.9 %). Moreover, patients who had OTSC placement for perforations and leaks had significantly higher long-term success compared with those who had fistulae [41].

Alternatively, a number of endoscopic tissue approximation suturing devices have emerged with early studies showing superior withstanding of high endolumenal pneumatic bursting pressure than endoclips [42]. Only a few have been used in human subjects, including the OverStitch

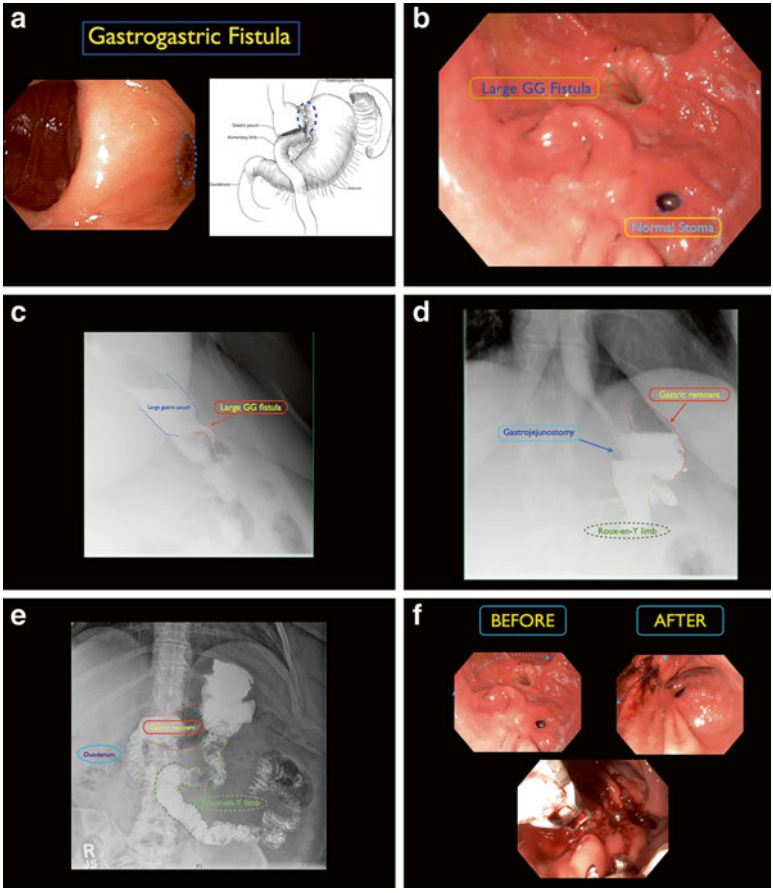

Fig. 8.7. (**a**) Endoscopic view and schematic illustration of gastrogastric (GG) fistula after LRYGB. (**b**) Endoscopic view of a GG fistula and normal gastrojejunostomy (GJ) stoma. (**c**) Lateral view of upper gastrointestinal contrast radiograph shows large GG fistula. (**d**) Anterior–posterior view of upper gastrointestinal contrast radiograph shows abnormal contrast pass to the gastric remnant from gastrojejunostomy. (**e**) Contrast medium in both gastric remnant and Roux-en-Y limb. (**f**) Endoscopic suturing technique for closuring GG fistula and pouch reduction.

Endoscopic Suturing System (Apollo, Austin, TX) (Fig. 8.7), the G-Prox (USGI Medical, San Capistrano, CA), and the NDO Surgical Plicator (Mansfield, MA), which is no longer commercially available.

The aforementioned deficiencies of endoscopic clips make endoscopic suturing more appropriate in the setting of the inflamed, indurated, and fibrotic tissue. This was readily demonstrated in case reports that described endoscopic suturing techniques involving the repair of late fistulas with good success by incorporating healthy, less-inflamed tissue adjacent to the site of leak [43, 44]. Trials of innovative new endoscopic suturing devices have included the Double-arm-bar Suturing System: DBSS [45], the master and slave transluminal endoscopic robot: MASTER and closure by Apollo OverStitch device [46], and Eagle Claw VIII [42]. These have been used in live and ex vivo porcine experimental studies and are undergoing studies to compare conventional endoscopic closure devices (such as endoclips) in efficacy and safety.

Liu et al. compared the safety and feasibility of closure of a 2-cm linear gastrotomy in 51 ex-vivo porcine stomach models using endoclips, an Eagle Claw VIII suturing device, and surgical suturing [42]. Median pneumatic bursting pressures varied with endoclips being at 19 mmHg, compared to the Eagle Claw VIII (56 mmHg) and surgical suturing (78 mmHg). While median scores for technical difficulties were not significantly different between endoclips and the Eagle Claw, closure time of the latter was significantly the longest of the three. The Apollo OverStitch, with its ability to create full-thickness plications, achieved durable gastrogastric fistula closure in three of seven cases in series presented by Watson and Thompson with no procedural complications reported [47]. As endoscopic suturing technology improves, this procedure may find greater application.

Endoscopic Stent and Suturing Management of Anastomotic Leaks after Colonic Surgery

Anastomotic leak after colonic surgery is one of the most serious postoperative complications following colon surgery. Colonic anastomosis leak rates have been reported between 3 and 9 % [48, 49], with mortality rates of 10.1 % [48]. A postoperative leak should be suspected when fever, abdominal pain, sepsis, peritonitis, or fecal discharge from the drain or wound is present. A C-reactive protein greater than 14 g/dL is a sensitive and specific marker for anastomotic leak [50]. Diagnosis is often delayed, with a clinical diagnosis made at a median of 7 days and radiologic diagnosis made at a median of 16 days; 42 % are diagnosed after hospital discharge [51]. The therapeutic principles described for the

endoscopic management of upper GI complications are sometimes applicable to complications after colonic surgery. Stent placement has been reported for the treatment of anastomotic obstruction with leak presenting after colectomy with ileo-rectal anastomosis [52]. In this case report, a dehiscence of approximately 40 % was noted, along with an associated abscess cavity. Using endoscopic and fluoroscopic guidance, a Polyflex stent (Boston Scientific, Natick, MA) was placed. Despite the use of clips to anchor the stent, the stent migrated and repeat stent placement was performed. Repeat endoscopy showed a healed anastomosis without stricture after 3 months. While covered stents in the setting of anastomotic leak are considered for off-label use, the successful outcomes described have resulted in an increase in their use for this purpose.

To date, endoscopic suturing devices have been predominantly used in foregut applications [53–56], however there are some reports in lower GI conditions. In a porcine model study, a suturing device was used to close an immediate colon perforation [57]. Pauli et al. [58] evaluated the safety and effectiveness of an OverStitch endoscopic suturing device (Apollo Endosurgery, Austin, TX) to place and secure sutures within normal, in vivo human colonic tissue prior to surgical resection. The endoscopic suturing device was used to place sutures in healthy colonic tissue during a 15-min, time-limited period. Following colectomy, the explanted tissue was evaluated to determine the depth of suture penetration and the effectiveness of the suture/cinch element. Four patients were enrolled. Seven sutures were successfully placed, incorporating a total of ten tissue bites in a mean of 13.5 min. On inspection of the explanted tissue, all sutures were found to be subserosal (no full thickness bites were taken). There were no intraoperative or postoperative complications.

Several recent studies have advocated the closure of defects created during endoscopic submucosal dissection (ESD). This can be performed with endoscopic clips or suturing. The rationale is to decrease the number of delayed adverse events such as bleeding and delayed perforation. Kantsevoy et al. [59] evaluated the OverStitch endoscopic suturing device for closure of large mucosal defects after ESD in stomach and colonic lesions. They used endoscopic suturing in 12 patients (4 lesions of the stomach and 8 lesions of the colon; mean lesion size, 42.5 mm). All lesions were removed en bloc. They found the closure of post-ESD defects to be technically feasible with a mean closure time of 10 min per patient. Only one stitch was required for complete closure in eight patients. In the other four patients, the mucosal defect was closed with

2–4 separate stitches (mean number of sutures per patient, 1.6 ± 1.0). There were no immediate or delayed adverse events in any of the study patients.

Voermans et al. [60] compared acute strength of various endoscopic colonic closure techniques by assessing air leak pressures in a porcine colon model. The six examined techniques included surgical suture (gold standard), QuickClips, T-tags, over-the-scope-clip system, and two types of flexible staplers. Perforations managed using hand-sewn sutures resulted in a mean leak pressure of 86.9 mmHg, compared to 85.1 mmHg with QuickClips; 53.9 mmHg with T-tags; 90.3 mmHg with OTSC; 98.5 mmHg with a 15-mm shaft stapler and 96.6 mmHg 8-mm shaft stapler.

Summary

The use of endoscopic therapies continues to play a vital role in the management of surgical complications throughout the gastrointestinal tract. Endoscopy allows for diagnosis of various complications and with newer devices, it allows for therapy. The most common therapies include stents, large clips, and suturing devices. As device technology evolves, the technical skill set of the endoscopist will also need to evolve in order to achieve both initial technical repair as well as durable treatment of the presented complication.

References

1. Beasley WE, Jefferies MT, Gilmour J, Manson JM. A single surgeon's series of transthoracic oesophageal resections. Ann R Coll Surg Engl. 2014;96(2):151–6.
2. Aurora AR, Khaitan L, Saber AA. Sleeve gastrectomy and the risk of leak: a systematic analysis of 4,888 patients. Surg Endosc. 2012;26:1509–15.
3. Csendes A, Burgos AM, Braghetto I. Classification and management of leaks after gastric bypass for patients with morbid obesity: a prospective study of 60 patients. Obes Surg. 2012;22:855–62.
4. Huebner M, Hubner M, Cima RR, Larson DW. Timing of complications and length of stay after rectal cancer surgery. J Am Coll Surg. 2014;218:914–9.
5. Lee WS, Yun SH, Roth YN, et al. Risk factors and clinical outcome for anasto-motic leakage after total mesorectal excision for rectal cancer. World J Surg. 2008;32:1124–9.

6. Rutegard M, Lagergren P, Rouvelas I, et al. Intrathoracic anastomotic leakage and mortality after esophageal cancer resection: a population-based study. Ann Surg Oncol. 2012;19(1):99–103.
7. Alanezi K, Urschel JD. Mortality secondary to esophageal anastomotic leak. Ann Thorac Cardiovasc Surg. 2004;10:71–5.
8. Raju GS. Endoscopic management of gastrointestinal leaks. Gastrointest Endosc Clin N Am. 2007;17:487–503.
9. Martin LW, Swisher SG, Hofstetter W, et al. Intrathoracic leaks following esophagectomy are no longer associated with increased mortality. Ann Surg. 2005;242:392–9.
10. Junemann-Ramirez M, Awan MY, Khan ZM, Rahamim JS. Anastomotic leakage post-esophagogastrectomy for esophageal carcinoma: retrospective analysis of predictive factors, management and influence on longterm survival in a high volume centre. Eur J Cardiothorac Surg. 2005;27:3–7.
11. Crestanello JA, Deschamps C, Cassivi SD, et al. Selective management of intrathoracic anastomotic leak after esophagectomy. J Thorac Cardiovasc Surg. 2005;129: 254–60.
12. Turkyilmaz A, Eroglu A, Aydin Y, et al. The management of esophagogastric anastomotic leak after esophagectomy for esophageal carcinoma. Dis Esophagus. 2009;22:119–26.
13. van Boeckel PGA, Sijbring A, Vleggaar FP, Siersema PD. Systematic review: temporary stent placement for benign rupture or anastomotic leak of the oesophagus. Aliment Pharmacol Ther. 2011;33:1292–301.
14. van Boeckel PGA, Dua KS, Weusten BL, et al. 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.
15. Conio M, Repici A, Battaglia G, 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(12): 2667–77.
16. Hirdes MMC, Vleggaar FP, van der Linde K, Willems M, Totte E, Siersema PD. Esophageal perforation due to removal of partially covered self-expanding metal stents placed for benign perforation or leak. Endoscopy. 2011;43:156–9.
17. Swinnen J, Eisendrath P, Rigaux J, et al. Self-expandable metal stents for the treatment of benign upper GI leaks and perforations. Gastrointest Endosc. 2011;73:890–9.
18. Hirdes MMC, Siersema PD, Houben MHMG, Weusten BLAM, Vleggaar FP. Stent-in-stent technique for removal of embedded esophageal self-expanding stents. Am J Gastroenterol. 2011;106:286–93.
19. Hunerbein M, Stroszczynski C, et al. Treatment of thoracic anastomotic leaks after esophagectomy with self-expanding plastic stents. Ann Surg. 2004;240(5):801–7.
20. Kauer WK, Stein HJ, et al. Stent implantation as a treatment option in patients with thoracic anastomotic leaks after esophagectomy. Surg Endosc. 2008;22(1):50–3.
21. Zisis C, Guillin A, Heyries L, et al. Stent placement in the management of oesophageal leaks. Eur J Cardiothorac Surg. 2008;33:451–6.

22. Tuebergen D, Rijcken E, Mennigen R, et al. Treatment of thoracic esophageal anastomotic leaks and esophageal perforations with endolumenal stents: efficacy and current limitations. J Gastrointest Surg. 2008;12:1168–76.
23. Dai YY, Gretschel S, et al. Treatment of oesophageal anastomotic leaks by temporary stenting with self-expanding plastic stents. Br J Surg. 2009;96(8):887–91.
24. Rajan PS, Bansal S, Balaji NS, et al. Role of endoscopic stents and selective minimal access drainage in oesophageal leaks: feasibility and outcome. Surg Endosc. 2014;28:2368–73.
25. Adler DG, McAfee M, Gostout CJ. Closure of an esophagopleural fistula by using fistula tract coagulation and an endoscopic suturing device. Gastrointest Endosc. 2001;54:652–3.
26. 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:E8–9.
27. Kurian AA, Bhayani NH, Reavis K, Dunst C, Swanstrom L. Endoscopic suture repair of full-thickness esophagotomy during per-oral esophageal myotomy for achalasia. Surg Endosc. 2013;27:3910.
28. Bludau M, Hölscher AH, Herbold T, Leers JM, Gutschow C, Fuchs H, Schröder W. Management of upper intestinal leaks using an endoscopic vacuum-assisted closure system (E-VAC). Surg Endosc. 2014;28(3):896–901. doi:10.1007/s00464-013-3244-5.
29. Brangewitz M, Voigtländer T, Helfritz FA. Endoscopic closure of esophageal intrathoracic leaks: stent versus endoscopic vacuum-assisted closure, a retrospective analysis. Endoscopy. 2013;45(6):433–8. doi:10.1055/s-0032-1326435.
30. Lalor PF, Tucker ON, Szomstein S, et al. Complications after laparoscopic sleeve gastrectomy. Surg Obes Relat Dis. 2008;1:33–8.
31. Yimcharoen P, Heneghan HM, Tariq N, et al. Endoscopic stent management of leaks and anastomotic strictures after foregut surgery. Surg Obes Relat Dis. 2011;7:628–36.
32. Puli SR, Spofford IS, Thompson CC. Use of self-expandable stents in the treatment of bariatric surgery leaks: a systematic review and meta-analysis. Gastrointest Endosc. 2012;75:287–93.
33. Serra C, Baltasar A, Andreo L, et al. Treatment of gastric leaks with coated self-expanding stents after sleeve gastrectomy. Obes Surg. 2007;17:866–72.
34. Eubanks S, Edwards CA, Fearing NM, et al. Use of endoscopic stents to treat anastomotic complications after bariatric surgery. J Am Coll Surg. 2008;206:935–8.
35. Casella G, Soricelli E, Rizello M, et al. Nonsurgical treatment of staple line leaks after laparoscopic sleeve gastrectomy. Obes Surg. 2009;19:821–6.
36. Tan JT, Kariyawasam S, Wijeratne T, et al. Diagnosis and management of gastric leaks after laparoscopic sleeve gastrectomy for morbid obesity. Obes Surg. 2010;20:403–9.
37. Pequignot A, Fuks D, Verhaeghe P, et al. Is there a place for pigtail drains in the management of gastric leaks after laparoscopic sleeve gastrectomy? Obes Surg. 2012;22:712–20.

38. Court I, Wilson A, Benotti P, et al. T-tube gastrostomy as a novel approach for distal staple line disruption after sleeve gastrectomy for morbid obesity: case report and review of the literature. Obes Surg. 2010;20:519–22.
39. Merrifield BF, Wagh MS, Thompson CC. Peroral transgastric organ resection: a feasibility study in pigs. Gastrointest Endosc. 2006;63:693–7.
40. Wagh MS, Merrifield BF, Thompson CC. Survival studies after endoscopic transgastric oophorectomy and tubectomy in a porcine model. Gastrointest Endosc. 2006;63:473–8.
41. Haito-Chavez Y, Law JK, Kratt T, et al. International multicenter experience with an over-the-scope clipping device for endoscopic management of GI defects (with video). Gastrointest Endosc. 2014;80(4):610–22. pii: S0016-5107(14)01334-0.
42. Liu L, Chiu PW, Teoh AY, Lam CC, Ng EK, Lau JY. Endoscopic suturing is superior to endoclips for closure of gastrotomy after natural orifices translumenal endoscopic surgery (NOTES): an ex vivo study. Surg Endosc. 2014;28(4):1342–7.
43. Overcash WT. Natural orifice surgery (NOS) using StomaphyX for repair of gastric leaks after bariatric revisions. Obes Surg. 2008;18:882–5.
44. Schweitzer M, Steele K, Mitchell M, Okolo P. Transoral endoscopic closure of gastric fistula. Surg Obes Relat Dis. 2009;5:283–4.
45. Mori H, Kobara H, Fujihara S, et al. Feasibility of pure EFTR using an innovative new endoscopic suturing device: the Double-arm-bar Suturing System. Surg Endosc. 2014;28:683–90.
46. Chiu PWY, Phee SJ, Wang Z, 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.
47. Watson RR, Thompson CC. Applications of a novel endoscopic suturing device in the GI tract. Gastrointest Endosc. 2011;73:AB105.
48. Francone TD, Saleem A, Read TA, et al. Ultimate fate of the leaking intestinal anastomosis: does leak mean permanent stoma? J Gastrointest Surg. 2010;14(6):987–92.
49. Raval MJ, Schnitzler M, O'Connor BI, Cohen Z, McLeod RS. Improved outcome due to increased experience and individualized management of leaks after ileal pouch-anal anastomosis. Ann Surg. 2007;246(5):763–70.
50. Almeida AB, Faria G, Moreira H, et al. Elevated serum C-reactive protein as a predictive factor for anastomotic leakage in colorectal surgery. Int J Surg. 2012;10(2):87–91.
51. Hyman N, Manchester TL, Osler T, et al. Anastomotic leaks after intestinal anastomosis: it's later than you think. Ann Surg. 2007;245(2):254–8.
52. Abbas MA. Endoscopic management of acute colorectal anastomotic complications with temporary stent. JSLS. 2009;13(3):420–4.
53. Flicker MS, Lautz DB, Thompson CC. Endoscopic management of gastrogastric fistulae does not increase complications at bariatric revision surgery. J Gastrointest Surg. 2011;15:1736–42.
54. Neto MG, Rodriguez L, Zundel N. Endoscopic revision of Roux-en-Y gastric bypass stomal dilation with a suturing device: preliminary results of a first out-of-United-States series. Bariatric Times. 2011;8:32–4.

55. Pauli EM, Marks JM. Diagnostic gastro-duodenoscopy via a gastro-gastric fistula prior to OverStitch closure. Surg Endosc. 2012;26:S224–41.
56. Jirapinyo P, Dayyeh BKA, Slattery J, et al. Endoscopic repair of dilated gastrojejunal anastomoses using a novel endoscopic suturing device. Gastroenterology. 2011;140(5 suppl 1):S118.
57. Pham BV, Raju GS, Ahmed I, et al. Immediate endoscopic closure of colon perforation by using a prototype endoscopic suturing device: feasibility and outcome in a porcine model (with video). Gastrointest Endosc. 2006;64:113–9.
58. Pauli EM, Delaney CP, Chanmagne B, Stein S, Marks JM. Safety and effectiveness of an endoscopic suturing device in a human colonic treat-and-resect model. Surg Innov. 2013;20(6):594–9.
59. Kantsevoy SV, Bitner M, Mitrakov AA, Thuluvath PJ. Endoscopic suturing closure of large mucosal defects after endoscopic submucosal dissection is technically feasible, fast, and eliminates the need for hospitalization (with videos). Gastrointest Endosc. 2014;79(3):503–7.
60. Voermans RP, Verqonwe F, Breedveld P, Fockens P, van Berge Heneqonwen MI. Comparison of endoscopic closure modalities for standardized colonic perforations in a porcine colon model. Endoscopy. 2011;43(3):217–22.

9. Endoscopic Treatment of Gastrointestinal Fistulas

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Gastrointestinal Fistulas

A fistula is an abnormal connection between two epithelialized surfaces usually involving the gut and another hollow organ. The origin of the term stems from the Latin root "fistula" meaning "pipe." These visceral connections commonly include neighboring regions of the gastrointestinal tract, bladder, urethra, vagina, and the pulmonary tract. They may also develop between the digestive tract and the skin or an abscess cavity. Rarely, fistulas may arise between a vascular structure and the GI tract, resulting in profound GI bleeding, considered a surgical emergency.

Surgical interventions in the digestive tract often require resections, suturing, stapling, and reconnections by means of anastomoses. Despite the significant advances reached by improved technologies in surgical sciences, the complication of dehiscence of a suture or staple line leading to leaks in the gastrointestinal tract still remains. If left untreated, this condition may lead to infection, sepsis, and sometimes to mortality [1]. The resultant process may create an abnormal trajectory connecting the lumen of the GI tract to another cavity or the skin and thus forming a fistula.

In 75–85 % of cases, digestive tract fistulas occur as a complication of abdominal surgery [2]. Spontaneous fistulas represent 10–25 % of cases, usually resulting from intra-abdominal inflammation such as inflammatory bowel disease, infections such as diverticulitis, or visceral vascular insufficiency. Penetrating trauma to the abdominal cavity, such as gunshot or knife wounds can also result in gastrointestinal fistula development.

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Gastrointestinal tract fistulas have a tremendous impact on patient's health, increase overall health care complexity, result in increased hospital length of stay, and delay subsequent return to work.

Despite improved surgical techniques and better postsurgical care including nonoperative management, the frequency of fistula formation has not decreased. The reasons for this may include treatment of more complicated disease processes, performance of increasingly complex surgeries, progressing through the learning curve of more challenging techniques, and a patient population that is increasing in age and comorbid disease. All these factors are presumed to perpetuate the incidence of fistula formation [1].

Overall, fistulas may have a spontaneous closure about 25 % if treated by nonoperative measures [2].

Cancer, abdominal irradiation, malnutrition, distal obstruction, ongoing infection or blood clots near the suture site, and carcinoma are all factors demonstrated to increase a patient's surgery-related risk of a forming fistula.

Classifications

There are various classification systems based on anatomic, physiologic (output volume), and etiologic characteristics; none of which are used exclusively [3]. Using these classifications in a combined manner may provide integrated better understanding of the fistula and assist in formulating a treatment plan optimal for each case.

Fistulas can be classified as internal and external. Internal fistulas connect the GI tract with another internal organ, the peritoneal space, the retroperitoneal space, the thorax, a blood vessel, or other contained structure. External fistulas connect the GI tract to the skin and typically these appear postoperatively.

Types of Fistulas

Intra-intestinal fistula inappropriately connects one part of the intestine to another lumen in the GI tract. An extra-intestinal fistula tract connects the GI tract to other organs, commonly the bladder, lungs, and vascular structures.

Internal fistula is contained entirely within the luminal space within the body, without egress. The symptoms may include any loose

stool/diarrhea, dehydration, rectal bleeding, malnutrition, and weight loss because of poor absorption of nutrients, fever, elevated WBC, infection, hypotension, sepsis. External fistula, also known as enterocutaneous fistula, connects the lumen of the GI tract to the skin. Symptoms of an external fistula include discharge through the skin, abdominal pain, obstruction, fever, and elevated white blood cell count. Enterocutaneous fistula conveys significant risk with reports of mortality rates of 5–20 % and a successful healing rate of 75–85 % with surgery [4].

Complex Fistulas Involve Internal Organs and the Skin

Approximately 85 % of gastric fistulas are the result of iatrogenic injury. Other causes include radiation therapy, malignancy, and secondarily from inflammation or ischemia.

Gastric resections for cancer, peptic ulcer disease, or bariatric surgery may lead to anastomotic leaks with resultant contamination. The initial result is either significant peritoneal contamination and peritonitis or abscess formation, which initially may be localized. Evolution of either of these scenarios may lead to fistula formation.

Gastrogastric fistulas have an incidence of approximately 1.2 % after RYGB. Patients may present with epigastric pain, nausea, vomiting, heartburn, or weight regain. Evaluation at this time by either upper endoscopy or contrast study may identify marginal ulcerations, some of which may be refractory to medical management [5].

In up to 80 % of cases, small bowel fistulas develop from complications of abdominal surgery. These typically occur at the anastomotic suture site secondary to a disruption, devascularization, or tension. Other causes of small bowel fistulas include inadvertent enterotomy, injury of the bowel tissue during closure, and failure of the suture line secondary to intrinsic disease process, such as inflammatory bowel disease.

Colonic fistulas are often the result of inflammatory bowel disease, diverticulitis, malignancy, and appendicitis. Management is somewhat different from small bowel and gastric fistulae in that often abscess may precede fistula requiring percutaneous drainage.

Aortoenteric fistulas are unusual complications that can occur after surgical placement of a graft in the aorta associated with inflammation and infection. The high morbidity and mortality associated with this type of fistula warrants immediate surgical intervention, and aside from diagnosis, an endoscopic therapeutic approach is not typically recommended.

Testing and Diagnosis

Workup should include a thorough medical and surgical history with particular attention to nutritional assessment. Initial blood testing should include serum electrolytes, complete blood count, and acute as well as chronic nutritional parameters including transferrin, albumin, and prealbumin. Additional information may be gleaned from effluent sample to evaluate for culture analysis.

A radiographic fistulogram may be performed by injecting contrast dye into the opening of the tract at the level of the skin. This permits obtaining X-ray images.

Internal fistulas may be evaluated by upper or lower endoscopy, upper or lower intestinal radiography with contrast medium. This typically is via barium swallow for foregut or proximal small bowel defects and by barium enema in cases of suspected colorectal fistula. Ultrasound, or more commonly, computed tomography enterography scan can delineate intestinal fistula as well as extra-intestinal disease including abscess. Fistulogram can be helpful as an adjunct or for primary evaluation if the opening is accessible percutaneously. In cases of fistulas involving the biliary or pancreatic ducts, magnetic resonance cholangiopancreatography or endoscopic retrograde cholangiopancreatography (ERCP) is helpful. The additional advantage of ERCP is therapeutic maneuvers, such as tract dilation, sphincterotomy, or stent placement can be performed simultaneously.

Treatment of Gastrointestinal Fistula

The conventional treatment of digestive track leaks and fistulas is drainage to accomplish source control and measures to decrease fistula output in hopes of allowing the body to seal the fistula and regain normal visceral function. This may be accomplished by decreasing or eliminating oral intake and using parenteral nutrition or enteral nutrition distal to the leak/fistula site [3]. In most cases this approach leads to healing. Nevertheless some variables are associated with a bad prognosis in terms of healing such as high output, distal obstruction, foreign body, suboptimal drainage, and large dehiscence [6].

Variables Associated with a Delay/Impaired Healing

- High output (>500 mL/24 h)
- Distal obstruction
- Foreign body
- Suboptimal drainage
- Large lumen dehiscence (>50 % of lumen diameter)

If otherwise healthy, a patient can often make a full recovery. However, ongoing medical treatment is required to manage symptoms or to prevent serious health complications. To aid in spontaneous fistula closure, active infection needs to be treated and the patient's overall nutritional status needs to be optimized.

If the fistula does not heal spontaneously in 3–6 months surgical intervention may be warranted. In this chapter we discuss less invasive endoscopic options to treat gastrointestinal fistulas, adding an alternative between medical and more invasive surgical strategies.

Initial treatment includes medical optimization through intravenous hydration to replenish fluid and electrolyte loss, correction of electrolyte abnormalities and acid/base imbalances, reducing fistula output, control and avoidance of infection, appropriate nutrition to avoid hypoalbuminemia, and, if there is an external fistula, skin protection and ongoing wound care. The fistula treatment should cater to the specifics of each type of GI fistula, affected organs, external drainage, and output level. The use of endoscopic techniques for fistula treatment is not well documented, but there has been significant progress in the field of advanced therapeutic endoscopy. Therapeutic endoscopy has emerged as a minimally invasive option to treat digestive tract leaks and fistulas by using endoluminal approaches using stents, clips and suturing. Success has been demonstrated in acute and even in chronic cases of fistulas [7].

Endoscopic Abscess Exploration, Cleaning, and Foreign Body Removal

Endoscopy allows direct visualization and exploration of the leak/fistula site, and often foreign bodies such as sutures or staples can be identified. Endoscopy can also identify retained fluid for removal and

Endoscopic Strategy on Digestive Leak/Fistula Treatment

- *Endoscopic abscess exploration and cleaning and foreign body removal*
- Correcting the digestive flow into the lumen
  - Balloon dilation
  - Stricturotomy
  - Septoplasty
  - Self expandable stents
- Direct closure of leak/fistula site
  - Traditional approach
    - Clips
    - Glue
    - Mesh
  - Novel approach
    - Suturing
    - Over-the scope Clips
    - Stents

culture in the abscess cavity and as well as promote drainage into the lumen. Foreign bodies impair the healing process and removal can be accomplished using endoscopic tools including graspers, snares and scissors [7] (Figs. 9.1 and 9.2).

Correcting the Digestive Luminal Flow

Balloon Dilation (Dilation of Distal Obstruction)

As demonstrated above, an obstruction distal to the leak/fistula site is a variable that predicts failure. Distal obstruction increases the luminal pressure, which maintains patency of the fistula and it impairs healing of the tract. This is particularly true in bariatric surgery cases where reduced pouches, narrow anastomoses and sleeves are constructed. In these cases, endoscopic dilations are an important part of the therapeutic strategy. The technique for endoscopic dilation is widely available and commonly practiced. Balloon dilations through-the-scope (TTS) and over-the-scope (OTC) can be used and may be preferred over dilation

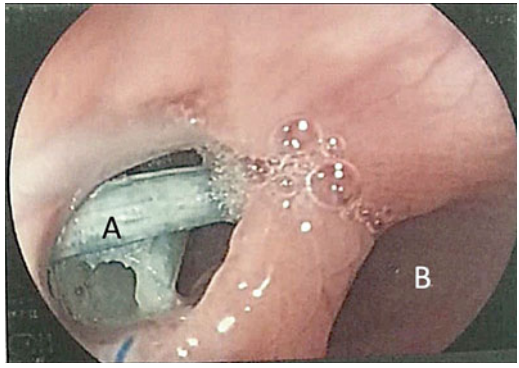

Fig. 9.1. His Angle fistula on Sleeve Gastrectomy. "**a**" identifies to the abscess cavity and "**b**" points to the narrowed lumen.

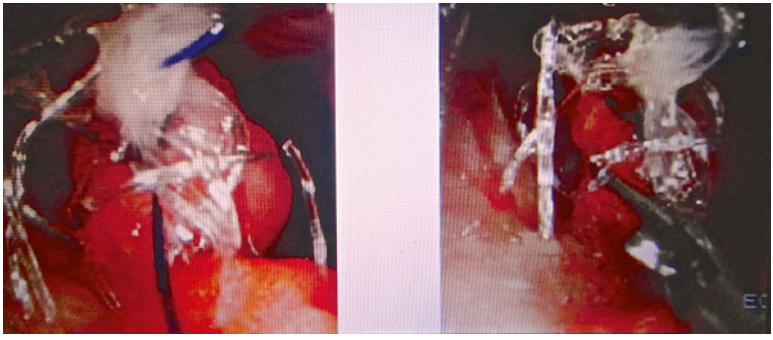

Fig. 9.2. Gastro-cutaneous fistula from a RYGB gastro-jejunostomy presenting with multiple sutures. An endoscopic scissor was used to cut all the sutures and clear the lumen.

with bougie dilators. The balloon can be inflated to a certain fixed diameter with a continuous radial expansion (CRE) technology. These balloons can be pressurized using liquids (hydrostatic) or air (pneumatic). The type of ideal balloon for the dilation will depend on the type of surgical procedure that caused the elevated intraluminal pressure and leak/fistula. Balloon dilations can be repeated successfully until healing is achieved. Individual cases vary widely and the goals of dilation must be tailored to patient needs and endoscopist skill and comfort levels. Typically, TTS dilations are performed with CRE balloons, with and

without fluoroscopic guidance to appropriate diameters based on several factors including type of anastomosis (linear versus stapled versus circular), initial starting diameter prior to dilation, and the general endoscopic appearance of the stricture (soft versus fibrotic, with or without ulcer or foreign material such as suture or staples). In recalcitrant situations, typically under general anesthesia and performed by experienced endoscopists, there are several published protocols that have resulted in successful outcomes when standard TTS balloons and diameters have failed.

- Roux-And-Y Gastric Bypass (RYGB): Dilation with TTS-CRE balloons up to 20 mm for periods of 3 min [8].
- Banded RYGB: If not previously removed, the narrowing caused by the external ring should be dilated with an OTS pneumatic balloon up to 30 mm due to the fact that the CRE balloon is not strong enough to break or "lush" the external ring or mesh. Intubation and radiological guidance is advised [9].
- Sleeve gastrectomy: the narrowing or corkscrew lumen should be dilated with a pneumatic OTS balloon, beginning with 30 mm up to 35 mm. Intubation and radiological guidance is advised [10] (Fig. 9.3).

In addition to endoscopic balloon dilation, other procedures can be used as complementary therapeutic measures to improve luminal flow of the gastrointestinal tract.

Stricturotomy

In RYGB, a stenosis at the level of the gastrojejunal (GJ) anastomosis with a persistent fibrotic stricture can be treated using an endoscopic therapeutic technique called stricturotomy. This is performed using an endoscopic cautery (needle-knife® or similar) in order to stricturotomize the anastomoses on the anterior wall, posterior wall and along the analogue of the greater curvature. The lesser curvature should be avoided because of the risk of bleeding. The stricturotomy is followed by TTS-CRE hydrostatic dilation. In a sleeve gastrectomy if the diameter of the pouch is smaller than the esophagus and there is a stenotic area, a stricturotomy can be added to a pneumatic dilation up to 30 mm [10].

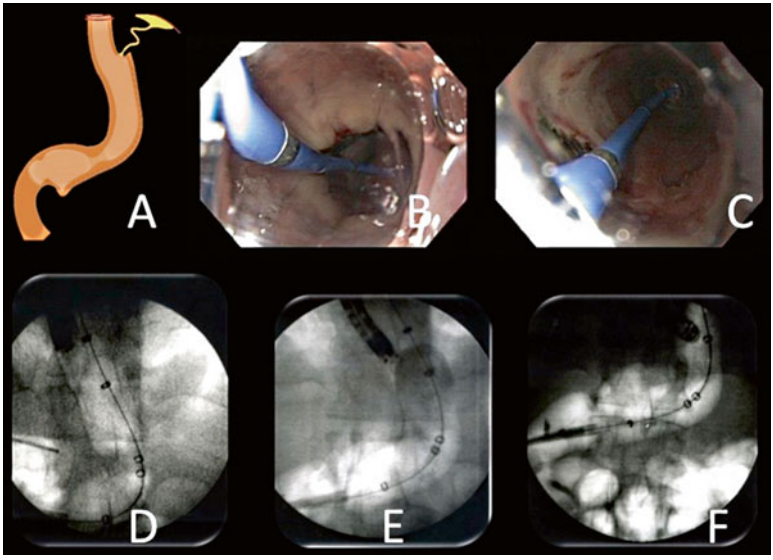

Fig. 9.3. Pneumatic dilation on a Sleeve gastrectomy leak associated with incisura angularis stenosis. "**a**" as a draw points to the stenosis/torsion site reflecting on the leak at his angle. "**b**" and "**c**" are endoscopic images trough the pneumatic balloon were one can see the effects of this aggressive dilation on the lumen. "**d**," "**e**," and "**f**" with radiologic images demonstrated the effect of the balloon on the sleeve gastrectomy axis at different inflation pressures from 10 to 25 psi.

Gastric Septotomy for Internal Drainage of an Abscess

In cases of leak after RYGB and sleeve gastrectomy, the septum near the internal orifice of the fistula at the angle of His facilitates passage of secretions through the tract. This is a contributing factor to maintaining the fistula tract opening, causing an abscess and hindering leak/fistula healing process. A technique where by septum is incised with endoscopic cautery followed by 30-mm balloon dilation has been described. This technique allows for internal drainage of the abscess fluid into the digestive tract, which leads to the closure of the fistula, after the gastric outlet flow has been restored [11] (Fig. 9.4). Though a small series of patients have been treated with acceptable outcomes, this technique is in evolution and should be performed by experts in a comprehensive bariatric surgery center. Potential adverse events including bleeding and formation of a chronic, non-healing cavity exist with this technique.

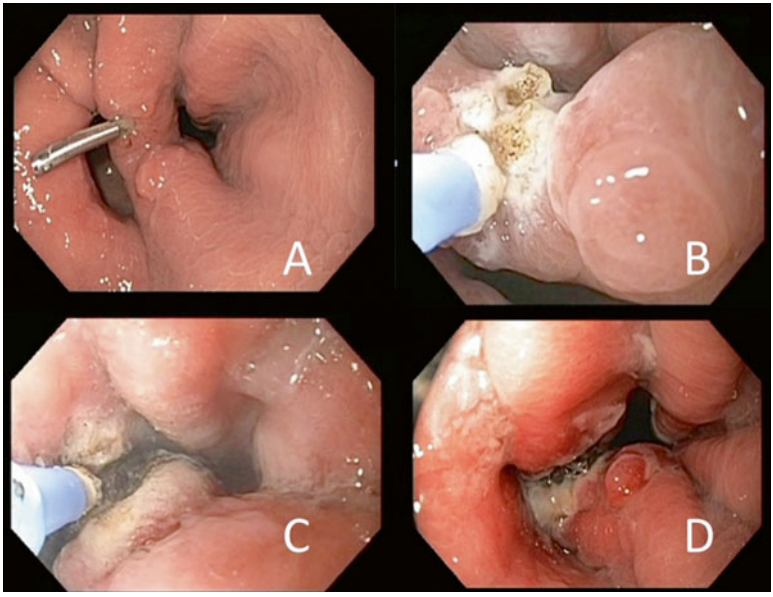

Fig. 9.4. Endoscopic images demonstrating the sequence of a septoplasty. "**a**" point to the fistula and abscess site located on the *left* side with the septum in-between the cavity and the lumen. "**b**" and "**c**" show the septoplasty with APC (Argon Plasma Coag) and "**d**" shows the final result after three sessions showing the healing and a wider lumen.

Further peer-reviewed studies will determine the long-term success rates and generalizability of this technique.

Direct Closure of Leak/Fistula Site with Conventional Endoscopic Tools (Clips, Fibrin Glue and Mesh)

Use of standard through-the-scope endoscopic clips may be successful when distal obstruction is absent. Few cases have been referenced in available literature. These endoscopic clips were originally designed for therapeutic bleeding control, and as such, they are intended to release from the mucosa after a certain time. Such a characteristic may limit their applicability in cases with inflamed or fibrotic tissue. Acute

perforations of healthy tissue can successfully managed with these endoscopy clips.

Other treatment modalities may be used as stand-alone techniques or in combination therapies, including adhesives and scaffolding products. In a series out of Germany, 39 cases with anastomotic leaks or fistulas post GI surgery for malignancy were treated endoscopically. Twenty-four patients underwent therapy with fibrin glue alone and 15 received a combined therapeutic approach of Vicryl plug and fibrin glue. Thirteen patients in the combined therapy group showed complete healing of the leak or fistula after 1–4 treatment sessions [12].

In another series, anastomotic leaks or fistulas after upper digestive disease tract surgery for malignancy were treated by filling the entrance of the communication with Vicryl mesh and sealed that off with fibrin glue. Seven of the nine patients had complete healing after 1–2 endoscopic treatments [9]. In a case series from Korea, three cases of a GI fistula with no response to conservative management in surgically high risk patients were treated successfully with endoscopic injection of Histoacryl via a catheter into the internal opening and fistulous tract [13].

Over the Scope Clips

In contrast to conventional through-the-scope clips, over-the-scope clips (OTSC) allow larger tissue purchase. Often, full thickness approximation of gastrointestinal wall is achieved, potentially aiding in closure of gastrointestinal leakages, fistulas, and perforations.

The OTSC clip is fixed on a cap which is placed at the distal tip of the endoscope, fitted with a thread that allows deployment of the clip. The endoclip is made of nitinol, a metal alloy of nickel and titanium, with a “leg-hold trap” memory shape, that allows considerable compression of tissue with a constant force (Fig. 9.5).

In a single series, nine OTSCs were used for upper GI tract leakages; five for colorectal leakages. Seventy-nine percent of leakages were chronic, treated later than postoperative day 14. In nine patients, other therapies preceded OTSC application. Primary technical success was achieved in all the patients. The early recurrences observed were two colonic fistulas and one esophageal anastomotic leakage. The overall long-term success rate was reported as 79 % (11/14) and no adverse events related to the use of the OTSC device were reported [14].

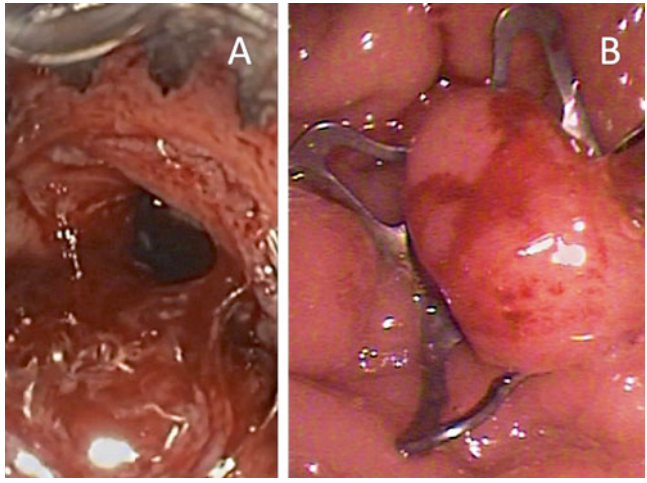

Fig. 9.5. Endoscopic closuring of a sleeve gastrectomy fistula at his angle with an OTSC®. "**a**" shows the fistula luminal orifice with endoscopic cap and the OTCS® armed. "**b**" shows the clip applied and the fistula healed on 30 d follow-up.

Another study of ten patients with GI leaks from perforations, fistulas, and anastomotic dehiscence (two gastric, two duodenal, and six colonic leaks) examined treatment with OTSC. The diameter of leaks ranged between 7 and 20 mm. OTSC devices were used to seal the GI leaks in all cases with fluoroscopic confirmation. Repeat endoscopy was performed at 3 months post-procedure and complete sealing of leaks was achieved by using OTSC alone in eight of ten patients. One patient required surgical repair of the leak. No complications from the OTSC devices were reported [15].

A retrospective review was conducted of all OTSC placements at Mayo Clinic (Rochester, MN) between October 2011 and September 2012. A total of 21 patients underwent chronic fistula treatment during this period and the fistula were located throughout the upper and lower GI track. Initial success was achieved in 20 of 21 patients (95 %). Repeat intervention for fistula recurrence was required in 14 patients (67 %) at a median of 40 days follow-up. In 11 of these patients the OTSC was still in place at follow-up and the fistula was found to be adjacent to the original location in 8 patients. The repeat endoscopic interventions included: OTSC ($N=6$), endoscopic suturing (OverStitch, Apollo

Endosurgery, Austin, TX) ($N=2$), through-the-scope (TTS) clips ($N=2$), and self-expandable metal stent ($N=1$).

While the fistula recurrence rate after initial intervention was 67 %, after the second intervention an overall success rate of 86 % was achieved. The authors concluded that OTSC was found to be a safe technique but required frequent reintervention [16].

The OTSC seems to be a feasible device to close chronic fistulae of the GI tract when the tissue is flexible enough to be properly pulled into the device. In circumstances of severe scarring or fibrosis, complete incorporation of the defect into the applicator cap and successful OTSC application might not be feasible. Given the appropriate circumstances the OTSC can achieve full-thickness closure of transmural defects, leaks, and fistulas in both the upper and lower GI tract.

Endoscopic Suturing

Endoscopic suturing devices utilize needles and suture to approximate tissue in the GI tract. There are several devices that are both in development and commercially available. These devices have been applied to different applications in the GI tract. One such use has been implementation in fistula and in leak management.

One series examining the EndoCinch suturing system versus clips for endoscopic repair in 95 patients. Seventy-five underwent sutured repair and 24 underwent clip repair. An average of 2.2 sutures or 3 clips (range 2–7) was used. Complete initial Gastrogastric Fistula closure was achieved in 90 patients (95 %), with reopening in 65 % an average of 177 ± 202 days. The average follow-up was 395 ± 49 days, with 22 patients lost to follow-up. Two significant complications were reported (bleeding and an esophageal tear). None of the fistulae with an initial size >20 mm remained closed during the follow-up period compared with 32 % fistulas ≤10 mm in diameter remained closed.

Peroral endoscopic repair of postbariatric Gastrogastric Fistulae with EndoCinch is appears technically feasible and safe but with limited durability. The fistula size was predictive of long-term outcomes, and the best results were seen in fistulas ≤10 mm in diameter [17].

In a matched cohort study, the repair of Gastrogastric Fistulae was compared for a suction-based superficial suturing device (EndoCinch) to a full-thickness suturing device (OverStitch; Apollo Endosurgery, Austin, Texas, USA). Eleven consecutive fistula treated with the full-thickness device were matched based on fistula size to 22 patients

treated with the superficial suturing system. Fistula closure was evaluated after the initial treatment with imaging or endoscopy.

Gastrogastric Fistula closure was achieved in 45 % of full-thickness suturing cases and 22 % of superficial suturing cases ($p = 0.237$). Two complications in two separate patients were noted with the full-thickness device (dysphagia and functional bowel obstruction). One complication was noted with the superficial device (mucosal tear) [18].

Applications of suturing devices have been limited to small series and case reports. In a case a 66-year-old woman with a 3-month history of chronic esophagopleural fistula secondary to Boerhaave syndrome, who failed prior endoscopic clipping and stent placements, was treated with an endoscopic suturing device. A contrast esophagogram revealed extravasation through a persistent esophagopleural fistula opening 2 cm above the gastroesophageal junction, with a diameter measured at 10 mm. Using the OverStitch device, placement of a three stitch running 3.0 polypropylene suture was successful at closing the fistula and initial contrast demonstrated no leak (Fig. 9.6). Additionally, a partially covered metal stent was placed to cover the mucosa defect. Four weeks later

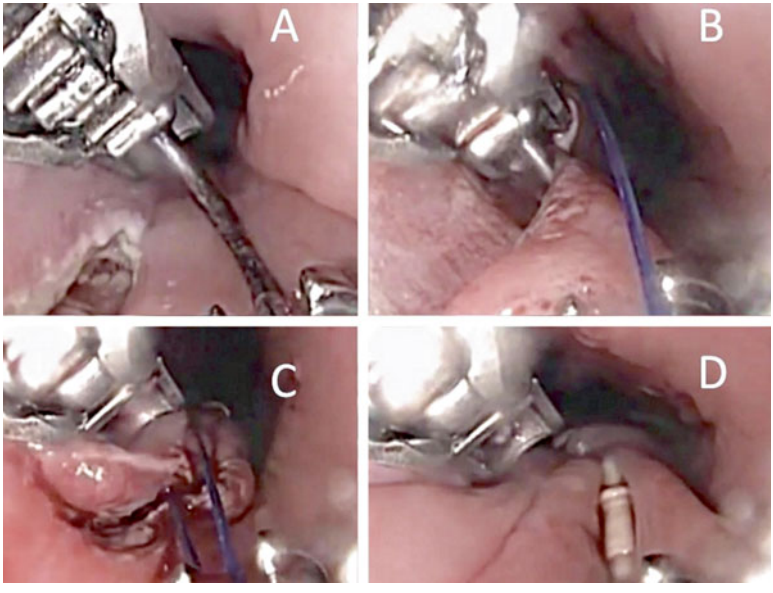

Fig. 9.6. Sequence of images demonstrating a successful closure of a His angle fistula on a Sleeve Gastrectomy with endoscopic suture by means of OverStitch® from "**a**" to "**d**".

after the stent removal a follow-up esophagogram contrast leak was detected although the fistula had narrowed to 5 mm in diameter. A second suturing procedure was performed. The orifice was first treated with argon plasma coagulation, followed by 10 mL human fibrin glue injection and sutured with three interrupted stitches. Follow-up studies and contrast examination showed complete fistula closure [19]. In an abstract at DDW 2014 the OverStitch device was used to close fistulas in six patients, all had chronic enteric fistulas. One esophago-mediastinal fistula was aided with stent fixation, three gastrocutaneous fistulas post bariatric surgery were all closed successfully with a combination of interrupted and running sutures in two separate layers, and one required a second suturing procedure. The two patients with bronchial esophageal fistulas required repeat suturing sessions prior to final closure of the fistulous tract. No complications were documented [20]. In a US nationwide endoscopic suturing registry, 27 fistula closures included gastrogastric, rectovaginal, gastrocutaneous, and enterocutaneous, rectovesical, ileal pouch fistula, and Hartman's pouch fistula. Fistula closure was performed with a mean 1.8 ± 0.4 sutures. In this registry the full thickness endoscopic suturing device was used to close luminal defects such as perforations, leaks and fistulas. Other procedures performed were procedural incision closure after endoscopic mucosal resection, endoscopic submucosal dissection and per oral endoscopic myotomy, as well as ulcer oversewing, stent fixation, gastrointestinal bleeding treatment, transoral outlet reduction following gastric bypass for weight regain and endoscopic sleeve gastroplasty [21].

References

1. Fernandez Jr AZ, DeMaria EJ, Tichansky DS, et al. Experience with over 3,000 open and laparoscopic bariatric procedures: multivariate analysis of factors related to leak and resultant mortality. Surg Endosc. 2004;18(2):193–7.
2. Stawicki SP, Braslow BM. ABSITE Corner, gastrointestinal fistulae. OPUS 12 Scientist. 2008;2(1):13–6.
3. Yurcisin BM, DeMaria EJ. Management of leak in the bariatric gastric bypass patient: reoperate, drain and feed distally. J Gastrointest Surg. 2009;13(9):1564–6.
4. Draus J, et al. Enterocutaneous fistula: are treatments improving? Annual Meeting of the Central Surgical Association, Kentucky, March 9–11, 2006. Surgery. 2006;140(4):570–8.
5. Carrodeguas L, et al. Management of gastrogastric fistulas after divided Roux-en-Y gastric bypass surgery for morbid obesity: analysis of 1292 consecutive patients and

review of literature. 2005 ASMBS presentation 2005. Surg Obes Relat Dis. 2005; 1(5):467–74.
6. Hiyama DT, Zinner MJ. Complicações cirúrgicas. In: Schwartz S, Shires GT, Spencer FC, editors. Princípios de Cirurgia. 6ath ed. Madrid: Interamericana McGraw-Hill; 1996. p. 410–37.
7. Campos JM, Evangelista LFL, Galvao Neto MP et al. Endoscopia em cirurgia bariátrica—Diretriz SOBED. Sociedade Brasileira de Endoscopia Digestiva. 2008. (http://www.sobed.org.br/web/arquivos_antigos/pdf/diretrizes/Endoscopia_e_cirurgia_bariatrica.pdf).
8. Galvao Neto M, Moura EGH, Campos JM, et al. Gastrojejunostomy stenosis: endoscopic dilatation with TTS balloons in 107 patients. Obes Surg. 2005;15(Suppl):942.
9. Campos JM, Evangelista LF, Ferraz AA, et al. Treatment of ring slippage after gastric bypass: long-term results after endoscopic dilation with an achalasia balloon (with videos). Gastrointest Endosc. 2010;72(1):44–9.
10. Zundel N, Hernandez JD, Galvao Neto M, Campos J. Strictures after laparoscopic sleeve gastrectomy. Surg Laparosc Endosc Percutan Tech. 2010;20(3):154–8.
11. Campos JM, Pereira EF, Evangelista LF, Siqueira L, Neto MG, et al. Gastrobronchial fistula after sleeve gastrectomy and gastric bypass: endoscopic management and prevention. Obes Surg. 2011;21:1520–9.
12. Böhm 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(7):599–602.
13. Lee YC, et al. Three cases of fistulae arising from gastrointestinal tract treated with endoscopic injection of Histoacryl. Endoscopy. 2001;33(2):184–6.
14. Mennigen R, et al. Endoscopic closure of postoperative gastrointestinal leakages and fistulas with the Over-the-Scope Clip (OTSC). J Gastrointest Surg. 2013;17(6): 1058–65.
15. Parodi A, et al. Endoscopic management of GI perforations with a new over-the-scope clip device (with videos). Gastrointest Endosc. 2010;72(4):881–6.
16. Law R, Irani S, Wong Kee Song LM, Baron TH. Sa1480 delayed outcomes following fistula closure using the over-the-scope clip (OTSC). Gastrointest Endosc. 2013; 77(5):AB221.
17. Fernandez-Esparrach G, et al. Endoscopic repair of gastrogastric fistula after Roux-en-Y gastric bypass: a less-invasive approach. Surg Obes Relat Dis. 2010; 6(3):282–8.
18. Tuyama AC, Kumar N, Aihara H, Ryan MB, Thompson CC. Endoscopic repair of gastrogastric fistula after Roux-en-Y gastric bypass: a matched cohort study evaluating two methods of fistula closure. Gastroenterology. 2013;144(5):S-220.
19. Bonin EA, et al. Closure of a persistent esophagopleural fistula, assisted by a novel endoscopic suturing system. Endoscopy. 2012;44:E8–9.
20. Catalano MF, Sorser SA, Henderson JB, Ali S, Enteric AA. 810 successful closure of enteric fistulas using the Apollo OverStitch suturing system. Gastroenterology. 2014;146(5):S142–3.
21. Kumar N, et al. Presentation: nationwide endoscopic suturing registry: interim activity report. Gastrointest Endosc. 2014;79(5):AB146.

Part III
Endoscopic Operations

10. Enteral Access: Percutaneous Endoscopic Gastrostomy, Gastrostomy–Jejunostomy, and Jejunostomy

Shawn Tsuda

Abbreviations

PEG	Percutaneous endoscopic gastrostomy
PEG-J	Percutaneous endoscopic gastrostomy–jejunostomy
PEJ	Percutaneous endoscopic jejunostomy

Introduction

Enteral access is artificial access to the gastrointestinal tract to provide a means of nutritional support and/or gastrointestinal decompression. Enteral nutrition allows patients with a functional gastrointestinal tract and who have difficulty with oral intake of food to maintain nutritional status. Enteral feeding allows for natural digestion and preserves gastrointestinal integrity and local defense. Enteral feeding is increasingly recognized as therapeutic for critically ill patients, attenuating severity and reducing complications of their underlying conditions.

Access for enteral feeding is established by placement of tubes through natural orifices or directly by percutaneous or surgical approaches. For short-term use (<4 weeks), enteral tubes are temporarily placed through the nasal or oral passage. However, prolonged use of oral or nasal enteral tubes is poorly tolerated; thus direct access to the stomach or small intestine is recommended for use of enteral tubes longer than 4 weeks. The percutaneous approach is a popular alternative to

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surgically created stomas, albeit each has its own advantages and disadvantages.

Percutaneous endoscopic gastrostomy (PEG) was introduced in 1980 by Michael Gauderer, MD and Jeffrey Ponsky, MD [1]. The procedure was performed on a 4-month old infant with the intent to create a sutureless opposition of stomach to peritoneum and abdominal wall without laparotomy [2]. Although originally intended for children, PEG is widely performed in all age groups currently. In the USA, more than 200,000 PEG procedures are performed annually by surgeons and gastroenterologists. The advantages of PEG include convenience and the use of moderate, conscious sedation compared to general anesthesia. Compared to the standard open Stamm gastrostomy, PEG is associated with reduced operative time, expense, incidence of complications, and less recovery time [3]. The PEG procedure has also undergone several modifications and has led to the other modalities of enteral access such as, percutaneous endoscopic gastrojejunostomy (PEG-J) and percutaneous endoscopic jejunostomy (PEJ) [2].

Patient Selection

The suitability for enteral access should be assessed and confirmed by a multidisciplinary team, including the endoscopist and nutrition support team. Patients should be evaluated by history, physical examination, and risk factors prior to performing the operation. Proper patient selection is a key for achieving successful outcomes.

Gastric Feeding and Decompression

Gastrostomy is the most common route of prolonged enteral feeding (>4 weeks). Patients must have normal gastrointestinal motility and adequate stomach anatomy for gastric access. Patients selected for PEG have impaired swallowing, contraindications to oral intake, metastatic disease, or neurologic impairment.

Patients with upper GI malignancy are candidates for PEG due to obstruction and side effects of tumor radiation impeding swallowing abilities. Up to 64 % of patients with head and neck cancer have dysphagia and associated malnutrition. Malignancies in the upper gastrointestinal tract can cause gastric outlet or intestinal obstruction. PEG is performed in these patients for decompression of abdominal pressure, to

alleviate nausea and vomiting, and to provide supplemental nutrition. However, PEG should not be performed if the patient has esophageal cancer and may require gastric conduit reconstruction.

Inability to swallow or difficulty swallowing due to neurologic disorders, such as stroke and ALS, are indications for enteral feeding [5]. Predictors of prolonged dysphagia may include aspiration, pneumonia, and lesions of frontal and insular cortex of the brain [8]. Because undernutrition is associated with poor prognosis, stroke patients should be initiated for enteral feeding early in their convalescence, as most require prolonged nutrition support [6]. However, one study did show that placement within 7 days of stroke may increase the risk of death [7]. Compared to NG tube feeding, PEG-tube feeding for neurologic disorders is associated with fewer treatment failures and GI bleeding, and had higher feed delivery and albumin concentration. However, placement of PEG in patients with advanced dementia or Alzheimer's disease may not be useful [13]. Although these patients have poor nutritional intake, PEG-tube feeding does not appear to prolong survival according to seven observational studies [10, 11].

Patients with severe cerebral injury or trauma may also require implementation of enteral nutrition. Although recovery time and the expected duration of nutrition support is unclear, some studies suggest that PEG placement can be placed in 14 days to restore digestive physiological function [14].

PEG also allows patients with chronic partial intestinal disorders, such as Crohn's disease and cystic fibrosis, to meet their nutritional needs. Crohn's disease was initially believed to be a contraindication due to disease occurrence within the gastrostomy tract. However, PEG placement is now commonly performed to improve weight and growth in children with Crohn's disease. Similarly, patients with cystic fibrosis experience a greater improvement in nutritional status and pulmonary function with early intervention from PEG [15].

Jejunal Feeding

Jejunal feeding is achieved through percutaneous endoscopic gastrostomy–jejunostomy (PEG-J) or percutaneous endoscopic jejunostomy (PEJ). Although there is no difference in mortality between gastric feeding and jejunal feeding, jejunal feeding is considered in situations when placement of a conventional PEG tube is unsuitable. Several meta-analyses show that there is no difference in mortality between jejunal

feeding and gastric feeding. Both procedures are acceptable; however jejunal feeding may be more feasible due to anatomical factors and intolerance to PEG. Insufficient amount of stomach due to gastrectomy and gastrojejunostomy allows easy access to the jejunum by the endoscope. Common scenarios for this are patients with a Roux-en-Y gastrojejunostomy, where the endoscope can access the roux limb. Thus, PEJ is preferable compared to PEG-J or PEG in patients with previous upper gastrointestinal surgeries for nutrition support.

Jejunal feeding is also recommended in patients with recurrent aspiration or who had gastric feeding intolerance. Delivery of nutrient to the small bowel can attenuate problems with aspiration, vomiting, or reflux, due to gastroparesis, GERD, or recurrent aspiration. If a PEG is already present, PEG can be converted to PEG-J. A PEG-J is also beneficial for simultaneous jejunal feeding and gastric decompression in the presence of gastric outlet obstruction.

Jejunal feeding may be physiologically beneficial for patients with severe chronic pancreatitis. Nutritional management for pancreatitis should include minimal stimulation of exocrine pancreas, while providing optimal nutrition. Oral or gastric feeding stimulates cephalic, gastric, and intestinal phases of pancreatic secretion, and thus leads to significant pancreatic secretions. Conversely, jejunal feeding has less disturbance or impact on normal gut hormone and exocrine pancreas secretions. Few case reports have reported successful outcomes from PEJ therapy in these patients [16].

Special Considerations

Obesity: With the emergence of the obesity epidemic over the last few decades, increasing number of obese patients are requiring enteral nutrition support. Obese patients can present a challenge due to increased difficulty of trans-illumination or digital palpation with a thicker abdomen and additional adipose tissue. However, recent studies report a 89.6–97 % success rate and 0 % mortality rate for PEG in overweight and obese patients [17–19].

Pregnancy: Special precautions must be taken when performing PEG in pregnant women. PEG insertion may impose injury to uterus and fetus. However, PEG has been performed successfully in pregnant women without any major complications.

Absolute Contraindications

Patients' prognosis and ability to recover are important considerations. Although increasing studies suggest earlier initiation is acceptable, the consensus remains that enteral feeding is reserved for long term feeding (>4 weeks). PEG, PEG-J, or PEJ tubes should not be offered if life expectancy is <4 weeks or cannot improve the patient's quality of life. Other contraindications are severe ascites, discontinuous esophagus, hemodynamic instability, septic shock, and coagulopathy (INR > 1.4).

Preoperative Considerations

Antibiotic Prophylaxis

Wound infection is the most common complication associated with trans-abdominal enteral access. In addition, many patients who require enteral nutrition are inherently at high-risk for infection, such as old age, malnutrition, and immunosuppression, further emphasizing the need for prophylactic antibiotics. The risk for infection indicates the need for prophylactic antibiotics with broad-spectrum coverage, such as cefazolin. According to a meta-analysis of ten randomized clinical trial, cephalosporin and penicillin based antibiotics have a similar relative risk reduction (64 and 62 %) and absolute risk reduction (10 % vs. 13 %, respectively) [21]. Systemic antibiotics should be administered as prophylaxis 30 min prior to the procedure, unless the patient is already receiving broad-spectrum antibiotics. Decolonization of equipment prior to procedure may also decrease risk for MRSA-infection.

Sedation

Moderate or conscious sedation is frequently used for endoscopic procedures. However, comorbid conditions, such as obesity, seizure disorders, or neurologic impaired consciousness, indicate the need for anesthesia-assisted sedation. Accordingly, sedation is associated with risk for cardiopulmonary complications. Patients should be carefully assessed for these risks preoperatively and interventional equipment should be present during the procedure.

Anticoagulation and Antiplatelet

Anticoagulation and antiplatelet therapy both increase risk for hemorrhage during the procedure. In a prospective study of patients undergoing upper endoscopy, cessation of antiplatelet therapy 10–14 days prior to procedure was associated with less procedural bleeding. While the use of aspirin can be continued, discontinuation of warfarin and clopidogrel is recommended. The use for heparin would be contingent on the risk for thromboembolism. Cardiac consultation is recommended for patients with severe cardiac conditions or at high risk for cardiac occurrences.

Consent

Consent should be obtained from the patient, or family members or representative if the patient is unable. The concept of tube feeding, including nutritional benefits and the burden of tube placement and feeding, must be acceptable to the patient and family or caregivers. Although the goal of enteral nutrition is to prolong survival, tube feeding may have major implications on quality of life.

Techniques

Percutaneous Endoscopic Gastrostomy

In principle, PEG can be placed by: pull, push, or introducer techniques. The original method, referred to as the "pull" technique, was first described in 1980 by Ponsky and Gauderer and is the most frequently used method today. Prior to the procedure, feeding is suspended for 8 h and systemic antibiotic prophylaxis is administered. Patients undergo conscious sedation, with topical sprays for the posterior oropharyngeal anesthesia. The procedure begins with an upper endoscopy. The gastroscope is introduced transorally and advanced through the esophagus and into the stomach, and into the proximal duodenum. The stomach anatomy is evaluated and its contents are aspirated. Insufflation is performed to ensure that the stomach is in close apposition to the abdominal wall.

Next, an access site in the mid-epigastrium region, where the stomach and abdominal wall are in closest apposition, is chosen for PEG

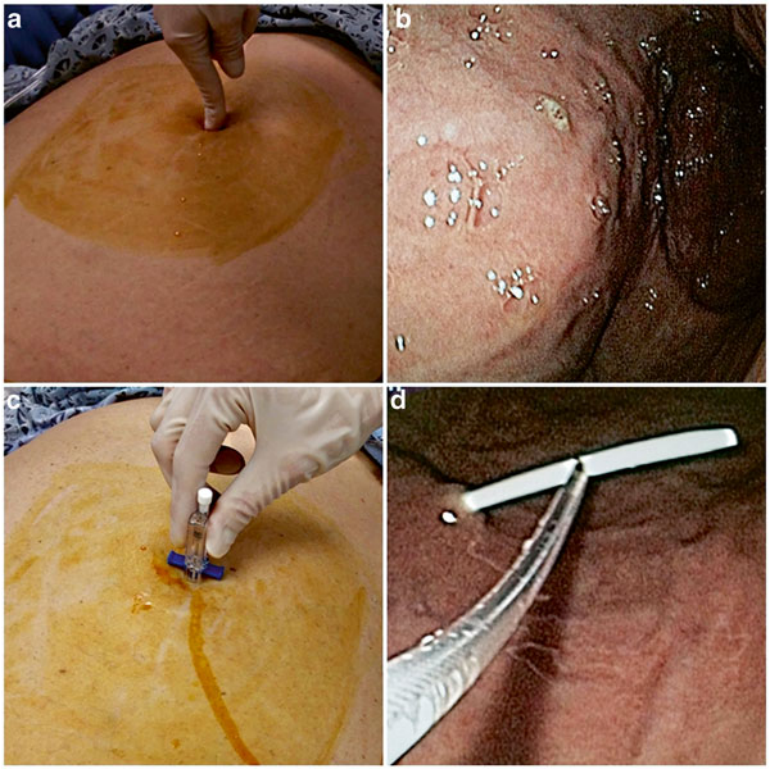

Fig. 10.1. (**a**) Once transillumination is performed, insertion site is identified and confirmed with a finger palpation. (**b**) Visualization of finger pressure. (**c**, **d**) Insertion of needle from external and internal view.

placement. This is marked by the area with maximal trans-illumination in the mid-epigastrium region and is ascertained with indentation of the anterior gastric wall by external digital pressure (Fig. 10.1).

At the site of gastric indentation, a small incision, approximately 0.5 cm in length is made. Under endoscopic visualization, the trocar and/or guidewire are inserted via puncture needle through the abdomen and grasped by the endoscope snare. As a unit, endoscope and snared guide wire are withdrawn through the mouth. The gastrostomy tube is connected to the guidewire from the mouth end and "pulled" back into the stomach via the guidewire from the abdominal end. An internal bumper is placed for fixation against the gastric wall, as well as an

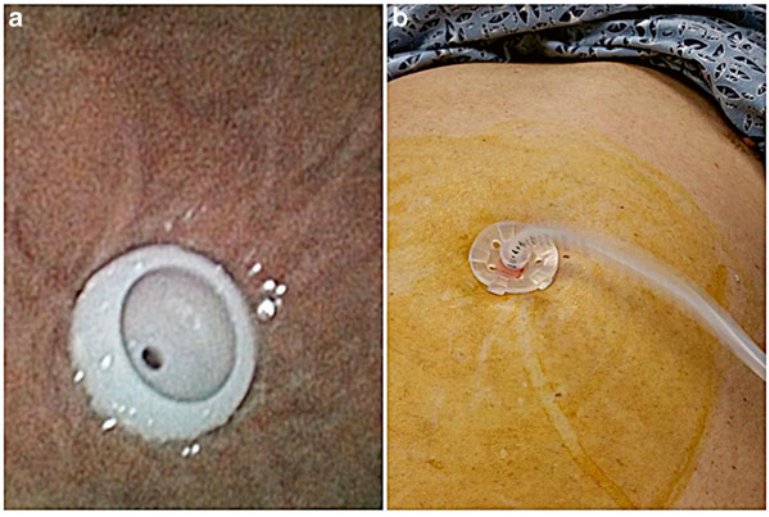

Fig. 10.2. (**a**) An internal bumper is loosely positioned against the gastric wall. (**b**) An external bumper is placed to affix the catheter.

external bumper to secure the PEG tube in place (Fig. 10.2). An upper endoscopy is repeated to confirm positioning of the inner opening and bumper placement.

Push and Introducer Techniques

Modifications to the procedure or equipment have led to the development of other techniques for PEG. The Sack-Vine "push" method is similar to the "pull" technique, except that the tube "pushed" through oral cavity and stomach, until it emerges from the abdominal wall. Both "push" and "pull" technique have comparable success and complication rates [22, 23].

The Russell "introducer" method uses principles from insertion of central venous catheters and pacemaker wires. Using an introducer, the balloon-tube is inserted directly from the abdomen into the gastric lumen. With the catheter remaining, the introducer is removed and the balloon is inflated to affix against the stomach wall [21]. Proper placement of the catheter is confirmed endoscopically (Fig. 10.3).

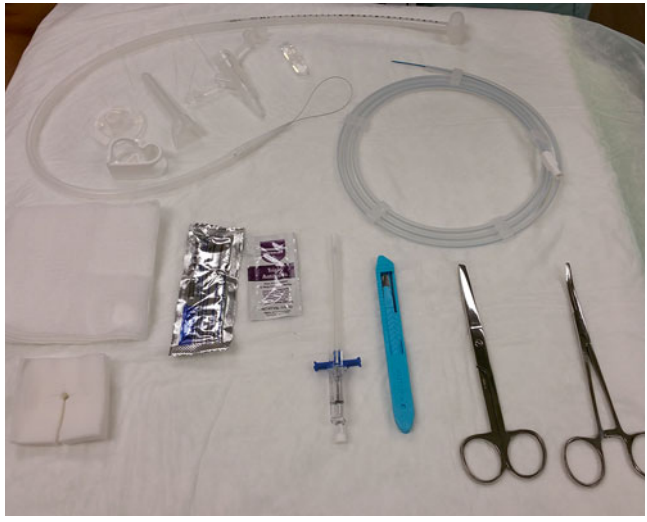

Fig. 10.3. Kits containing the necessary instruments and supplies are available for different techniques.

Safe-Tract Technique

The safety of the site can be tested by performing the safe tract technique as described by Foutch et al. Using an aspirating, lidocaine-filled syringe, the needle is inserted into the stomach. If air bubbles are simultaneously aspirated into the needle, then access to the stomach is successful and a safe tract is achieved. If air or viscous fluid appears prior to entry to the stomach, then the small bowel or colon was punctured, in which case the tube insertion site should be reselected. Some experts suggest that this step may be more favorable than trans-illumination. The effectiveness of trans-illumination has been challenged. Conversely, according to Foutch, no procedural failure occurred when a successful safety tract was achieved [24] (Fig. 10.4).

Percutaneous Endoscopic Gastrojejunostomy

In a PEG-J procedure, a jejunal extension tube is placed through a PEG tube. Like PEG, PEG-J uses a gastrostomy site. In the past, jejunal tubes were inserted through the gastrostomy site but this often resulted in tube migration when the endoscope was withdrawn. Recent techniques

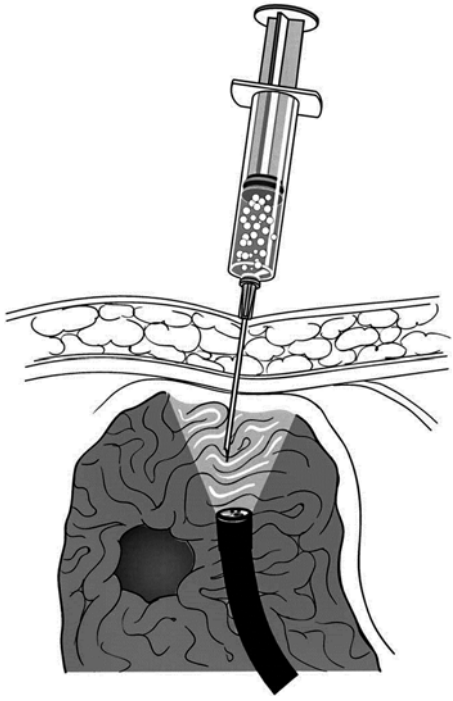

Fig. 10.4. The safe tract technique is an additional method to ensure proper insertion of needle into the stomach. Appearance of air bubbles or contents in the syringe prior to entry through the gastric wall suggests puncture of bowel between the abdomen and stomach. From Ponsky JL. Percutaneous endoscopic gastrostomy. Journal of Gastrointestinal Surgery 2004;8(7). Reprinted with permission from Springer.

and kits use an over-the-wire guide to insert a thinner jejunostomy. The procedure begins similarly to PEG with placement of a PEG tube. From the PEG insertion site, a guidewire is inserted through the PEG tube and advanced into the small bowel with endoscopic assistance. Tube placement distal to the ligament of Treitz is recommended for jejunal feeding to prevent retrograde migration. The tube is also secured by endoscopically placed clips. Then the endoscope is then withdrawn. With the guidewire remaining, the jejunal tube is then positioned over the guidewire through the PEG tube and into the jejunum.

Percutaneous Endoscopic Jejunostomy

Jejunal feeding tubes can also be placed directly into the jejunum via PEJ. The PEJ procedure evolved as a modification of the PEG procedure. Patients are prepared similarly, with conscious sedation and prophylactic antibiotics. Beginning with upper endoscopy, a long endoscope is passed into the intestine, distal to the ligament of Treitz. In the jejunum, an insertion site is identified with maximal trans-illumination and intrajejunal finger indentation.

Following standard skin preparation, the insertion needle is inserted percutaneously into the jejunum. The puncture should be performed quickly as peristalsis may interfere with trans-illumination and cause the intestine to slide. The needle is grasped with endoscope forceps to stabilizes the jejunal segment and facilitate subsequent insertion of trocar and thread. The remainder of the procedure proceeds similar to the pull-PEG technique. The thread is snared endoscopically and withdrawn from the mouth. The jejunal tube is attached to the guidewire from the oral end and pulled into the jejunum from the insertion site. PEJ tube is secured with bumper and position is confirmed by repeat endoscopy.

Complications

The evolution of procedural techniques and equipment have improved outcomes of PEG, with an overall success rate of 95–100 % [25–27]. Failure is often attributed to improper placement of the tube due to insufficient trans-illumination. Procedural and 30 day mortality associated with PEG placement are low (0–2 % and 1.5–2.1 %, respectively) [28–30]. Up to 40 % of patients develop minor complications, and 3–4 % experience major complications that require hospitalization and/or surgical intervention. However, much of the complications that develop are usually attributed to underlying comorbidities and poor patient selection, rather than the procedure itself [22, 31–33]. PEG tubes can last as long as 1–2 years before requiring replacement due to tube degradation [22].

The success rate of PEG-J is approximately 93 %. PEG-J tubes have a mean functional duration of 55 days in adults and 39 days in children. Re-intervention is common due to tube malfunction, such as clogging and migration. Conversely, PEJ uses a larger tube that is anchored directly to the intestine. The functional duration of PEJ tubes is longer,

113 days. PEJ is technically more difficult but success rates remain acceptable at 72–88 % [34].

To ensure successful outcomes, four safety tenets have been postulated. Although intended for PEG, these may also apply to PEG-J and PEJ. These steps include: (1) endoscopic gastric distention via insufflation, (2) endoscopically visible finger-pressure indentation, (3) transillumination, and (4) safe-tract technique. Adherence to these steps enables successful tube placement and decreases procedural complications. The safety tenets ensure close apposition of stomach to the abdominal wall, with no other organs interposed, and puncture of proper organ.

Injury to Internal Organs

Injury to internal organs can occur from improper placement of enteral tube. Over distention of the stomach and small bowel can cause displacement of transverse colon and increase risk of injury. Injury to the small bowel is less likely due to protection by the greater omentum. However, patients who had prior abdominal surgery may have adhesion of the small bowel into the upper abdomen. Injury to the liver is also rare but has been reported in a few patients.

Depending on the organ or severity of injury, conservative management with careful observation may be sufficient. Hemodynamically stable patients without signs of sepsis can be managed nonoperatively. Conversely, colonic injury with peritonitis or liver laceration with intraperitoneal bleeding may require surgery. To avoid injury to internal organs, the safety tenets should be employed for successful insertion of enteral tube. Abdominal imaging, such as ultrasound or CT, may also facilitate insertion and ensure proper placement of tube [19].

Fistula

Fistulas may occur as a result of penetration or misplacement of PEG tube into adjacent small or more commonly, large bowel. Fistulas are rare but can be a potentially serious complication. Many patients remain asymptomatic for months, and thus its diagnosis is often delayed [35, 36]. Factors that could lead to fistula include insufficient gastric insufflation and excessive adhesions, from previous laparotomies. Up to 45 % of colocutaneous fistulae are observed in patients with prior abdominal

history [35]. If there is no leakage, fistulas can be managed conservatively with removal of PEG tube to allow spontaneous closure. In presence of peritonitis, abscess, or leakage, operative intervention, including exploration and colonic repair or resection, may be required [37].

Tube misplacement may be prevented with adequate insufflation and choosing proper PEG tube insertion site carefully. Transillumination, identification of digital pressure, and the safe tract technique endoscopically ensure close apposition of stomach to abdominal wall without interposition of bowels.

Volvulus

Gastric and small bowel volvuli are rare complications of PEG and PEJ. Gastric volvulus is more commonly observed in children, where one case was reported from incorrect insertion of PEG tube into the posterior gastric wall [38]. Small bowel volvulus after PEJ likely occurs more frequently and it has been reported and attributed to internal hernias, adhesions, or bowel motility disorders. Detorsion of volvulus is performed surgically. Volvulus can be prevented by careful placement of the enterostomy tube on the anterior gastric wall and addressing predisposing factors [39, 40].

Metastasis at PEG Site

Abdominal wall metastasis is a devastating complication occurring in <1 % of patients. Cases of tumor were reported with the "pull" method and had a poor prognosis. In patients with oropharyngeal or esophageal malignancies, the "introducer" technique, which does not involve contact of catheter or guidewire with the mouth or esophagus, may be a safer technique of choice [41]. Alternatively, PEG may be withheld until surgical removal of cancer, or a trans-abdominal surgical approach may be used.

Aspiration and Pneumonia

Aspiration is a common concern associated with enteral feeding. Its incidence ranges from 0.3 to 18 % after PEG or PEJ [9, 26, 42, 43]. Aspiration often is minor but can lead to pneumonia, if unresolved.

Aspiration typically presents weeks after the procedure, but few reports showed occurrence during the procedure. Aspiration is common in patients with neurologic impairments, such as stroke or brain injury, or gastrointestinal motility disorder, such as gastroparesis. Jejunal feeding via PEJ is recommended for patients at high risk for aspiration. Patients should be assessed preoperatively in order to perform the correct method for enteral nutrition. Patients with PEG who have recurrent aspiration can be converted to PEG-J.

Necrotizing Fasciitis

Necrotizing fasciitis is a rare but potentially fatal complication of PEG [44]. Necrotizing fasciitis occurred in patients who had tube displacement and/or leakage [45]. Excessive traction and pressure on PEG tubes leading to ulceration or infection can also increase likelihood for progression to necrotizing fasciitis. Other risk factors include diabetes, wound infections, malnutrition, and impaired immunity. Allowing loose contact, often around 3 cm space between PEG bolster and abdomen, may decrease risk for wound infection, peristomal drainage, and necrotizing fasciitis, as observed in one study [19, 46].

Buried Bumper Syndrome

Buried bumper syndrome is a rare complication, in which the bumper migrates and lodges in the gastric wall or gastric lumen. Its incidence is 1.9 % and presents after at least 4 months of PEG procedure. Buried bumper syndrome is mainly caused by excessive traction between the internal and external bumper, but can also occur due to malnutrition, poor wound healing, or a stiff internal bumper. Buried bumper syndrome is diagnosed by inability to infuse feed through tube, leakage, bleeding, and abdominal pain, and is confirmed with endoscopy. Once diagnosed, the buried bumper must be removed in order to prevent further complications and death.

To prevent buried bumper syndrome, additional space (approximately 1.5 cm) should be allowed between external bumper and skin. Mobilizing and loosening PEG tube daily could reduce mucosal overgrowth of the inner bumper. Patients with balloon assisted PEG introducer devices have been found to have a lower incidence of buried bumper syndrome compared to those with traditional bumpered-PEG devices.

Peristomal Infection

Peristomal wound infections are the most common complication of PEG, with an incidence ranging from 4 to 30 % [47]. Wound infections are minor and most resolve with conservative treatment, such as antibiotics. Prophylactic antibiotics should be administered, unless the patient is already taking broad-spectrum antibiotics prior to the procedure. In a pooled analysis of 13 randomized trials, preoperative administration of systemic antibiotics reduced the incidence of peristomal infection (OR = 0.36) [20]. Cephalosporin or penicillin-based antibiotics were similarly effective, but one study demonstrated that co-amoxiclav was associated with less MRSA infections [48]. Nonetheless, the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections indicates decontamination of oral and nasally delivered preparations and equipment. Postoperatively, regular skin and stomal care are also important in preventing local infections.

Gastrointestinal Bleeding and Ulceration

The incidence of acute bleeding after PEG tube placement is 1–2.5 %. Acute bleeding usually results from direct injury to gastroepiploic arteries. Tightening internal and external bolsters may stop bleeding, however compression should be released within 48 h to prevent necrosis or ulceration. Alternatively, delayed bleeding can occur due to esophagitis, gastric pressure ulcer, or the buried bumper syndrome. Esophagitis is the most common cause of gastrointestinal bleeding, occurring in up to 39 % of patients undergoing PEG placement. Studies demonstrate that PPIs may prevent and treat bleeding associated with esophagitis. Additionally, warfarin or clopidogrel use should be temporarily discontinued [49].

Pressure necrosis of the gastric mucosa by the internal bolster can cause ulceration of the anterior gastric wall. Pressure ulcers can be prevented by avoidance of excessive traction or tension by the internal bolster. Ulceration in the posterior gastric wall is more commonly attributed to mechanical injury from long protruding gastrostomy tubes or tall internal bumpers [50]. Ulceration from PEG tubes is treated by replacement of PEG tube at a different location or using a small internal bumper. Histamine$_2$ receptor antagonists may not provide protection from development of ulcers.

Leakage

Peristomal leakage is common but multifactorial. Its occurrence has been reported from excessive cleansing with hydrogen peroxide, lack of tube stabilization, infection, and gastric hypersecretion. Patients with comorbidities associated with poor wound healing are also at increased risk for peristomal leakage. Peristomal leakage is prevented and treated by management of contributing factors and examining securement of the tube and bolsters. Application of zinc-containing barrier creams may be beneficial. If leakage persists, tube may be removed and replaced after 4–6 days. Larger PEG tubes should not be inserted to avoid dilation of the existing tract and further injury.

Dislodgement and Inadvertent Removal

The incidence of accidental PEG removal is 1.6–4.4 % [26, 51], and can be serious if peritonitis develops. The maturation period of a PEG tract is 7–10 days but may be delayed to 3–4 weeks in patients with compromised healing. Immediate detection of removal allows for replacement of PEG tube at or near the original site. However, if detection is delayed in an immature site, the PEG procedure may need to be repeated with administration of broad-spectrum antibiotics. After the maturation of the stoma, the tube can be replaced at bedside without endoscopy. Once a PEG tube is removed, spontaneous closure of PEG tract occurs rapidly. Temporary placement of PEG tract dilators or Foley tube may prevent tract closure.

Circumstances leading to inadvertent removal should be corrected to prevent recurrence. In general, internal bumpers anchor the tube and prevent dislodgement. Optimal placement of bumpers should secure the tube while allowing enough distance to prevent necrosis or ulceration. Steri-strips or abdominal binder may also be beneficial. Use of a shorter tube (<18 cm) or 6–8 in. to prevent getting caught on other objects.

Gastrointestinal Obstruction

In rare cases, dislocation of internal bolster or migration of the PEG tube into the pylorus or duodenum can cause obstruction. This complication has been observed in both children and adults, and has a higher occurrence with Foley-type peg tubes. Patients with gastric outlet

obstruction experience abdominal cramping and vomiting and confirmed by an upper gastrointestinal study. Treatment involves withdrawal of dislocated tube or retrieval of bumpers. Gastric outlet obstruction can be avoided by securement of PEG tubes with an external bolster, placed 1–2 cm space from the skin. In PEJ, internal bumpers <2 cm should be utilized to prevent luminal obstruction.

Clogged PEG Tube

Clogging of enteral tubes is a common minor complication of PEG, due to thick feeds or undissolved medications. Clogging of PEG-J tubes may also be mechanical due to kinking. To prevent this tube malfunction, the use of bulking agents should be minimized and medications should be dissolved. Clogged tubes can be prevented and cleared by frequent water irrigation. Some studies suggest beneficial effects of pancreatic enzymes.

Pneumoperitoneum

Pneumoperitoneum is reported in up to 18–50 % of cases [52, 53]. Pneumoperitoneum related to air insufflation or needle puncture is usually benign and self-resolving. Intervention is not warranted unless there is clinical concern, including worsening of intra-abdominal air, or presence of peritonitis, portal and/or mesenteric venous gas, systemic inflammatory response, and/or sepsis [54]. Symptoms persisting for >72 h may suggest presence of a more serious complication, such as bowel injury.

Conclusion

The percutaneous endoscopic approach has become a widely accepted modality for enteral access. PEG, PEG-J, and PEJ have numerous applications and have been demonstrated to improve nutritional and disease status of select chronically ill patients. Success rates for all three procedures are high and procedural mortality is low. The evolution of techniques and equipment has continued to improve patient outcomes since the first introduction of PEG. Nonetheless, the procedures are not without complications but can be reduced by careful patient selection and precise execution of the procedure.

References

1. Ponsky JL, Gauderer MWL. Percutaneous endoscopic gastrostomy: a nonoperative technique for feeding gastrostomy. Gastrointest Endosc. 1981;27:9–11.
2. El-Matary W. Percutaneous endoscopic gastrostomy in children. Can J Gastroenterol. 2008;22:993–8.
3. Grant JP. Comparison of percutaneous endoscopic gastrostomy with Stamm gastrostomy. Ann Surg. 1988;207:598–603.
4. Mitchell SL, Teno JM, Kiely DK, Shaffer ML, Jones RN, Prigerson HG, et al. The clinical course of advanced dementia. N Engl J Med. 2009;361:1529–38.
5. FOOD Trial Collaboration. Poor nutritional status on admission predicts poor outcomes after stroke: observational data from the FOOD trial. Stroke. 2003;34:1450–6.
6. Dennis MS, Lewis SC, Warlow C, FOOD Trial Collaboration. Effect of timing and method of enteral tube feeding for dysphagic stroke patients (FOOD): a multicentre randomised controlled trial. Lancet. 2005;365:764–72.
7. Broadley S, Croser D, Cottrell J, Creevy M, Teo E, Yiu D, et al. Predictors of prolonged dysphagia following acute stroke. J Clin Neurosci. 2003;10:300–5.
8. James A, Kapur K, Hawthorne AB. Long-term outcome of percutaneous endoscopic gastrostomy feeding in patients with dysphagic stroke. Age Ageing. 1998;27:671–6.
9. Dharmarajan T. Percutaneous endoscopic gastrostomy and outcome in dementia. Am J Gastroenterol. 2001;96:2556–63.
10. Sampson EL, Candy B, Jones L. Enteral tube feeding for older people with advanced dementia. In: The Cochrane Collaboration, editor. Cochrane Database Syst Rev [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2009 [cited 2014 Sep 17]. http://doi.wiley.com/10.1002/14651858.CD007209.pub2.
11. Sanders DS, Carter MJ, D'Silva J, James G, Bolton RP, Bardhan KD. Survival analysis in percutaneous endoscopic gastrostomy feeding: a worse outcome in patients with dementia. Am J Gastroenterol. 2000;95:1472–5.
12. Akkersdijk WL, Roukema JA, van der Werken C. Percutaneous endoscopic gastrostomy for patients with severe cerebral injury. Injury. 1998;29:11–4.
13. Shepherd RW, Holt TL, Thomas BJ, Kay L, Isles A, Francis PJ, et al. Nutritional rehabilitation in cystic fibrosis: controlled studies of effects on nutritional growth retardation, body protein turnover, and course of pulmonary disease. J Pediatr. 1986;109:788–94.
14. Zhu Y, Shi L, Tang H, Tao G. Current considerations in direct percutaneous endoscopic jejunostomy. Can J Gastroenterol. 2012;26:92–6.
15. Bender JS. Percutaneous endoscopic gastrostomy placement in the morbidly obese. Gastrointest Endosc. 1992;38:97–8.
16. Wiggins TF, Garrow DA, DeLegge MH. Evaluation of percutaneous endoscopic feeding tube placement in obese patients. Nutr Clin Pract. 2009;24:723–7.
17. Schrag SP, Sharma R, Jaik NP, Seamon MJ, Lukaszczyk JJ, Martin ND, et al. Complications related to percutaneous endoscopic gastrostomy (PEG) tubes. A comprehensive clinical review. J Gastrointest Liver Dis. 2007;16:407–18.

18. Lipp A, Lusardi G. Systemic antimicrobial prophylaxis for percutaneous endoscopic gastrostomy. Cochrane Database Syst Rev. 2013;11, CD005571.
19. Jafri NS, Mahid SS, Minor KS, Idstein SR, Hornung CA, Galandiuk S. Meta-analysis: antibiotic prophylaxis to prevent peristomal infection following percutaneous endoscopic gastrostomy. Aliment Pharmacol Ther. 2007;25:647–56.
20. Kozarek RA, Ball TJ, Ryan JA. When push comes to shove: a comparison between two methods of percutaneous endoscopic gastrostomy. Am J Gastroenterol. 1986;81:642–6.
21. Hogan RB, DeMarco DC, Hamilton JK, Walker CO, Polter DE. Percutaneous endoscopic gastrostomy—to push or pull. Gastrointest Endosc. 1986;32:253–8.
22. Foutch PG, Talbert GA, Waring JP, Sanowski RA. Percutaneous endoscopic gastrostomy in patients with prior abdominal surgery: virtues of the safe tract. Am J Gastroenterol. 1988;83:147–50.
23. Kwon RS, Banerjee S, Desilets D, Diehl DL, Farraye FA, Kaul V, et al. Enteral nutrition access devices. Gastrointest Endosc. 2010;72:236–48.
24. Larson DE, Burton DD, Schroeder KW, Dimagno EP. Percutaneous endoscopic gastrostomy: indications, success, complications, and mortality in 314 consecutive patients. Gastroenterology. 1987;93:48–52.
25. Taylor CA, Larson DE, Ballard DJ, Bergstrom LR, Silverstein MD, Zinsmeister AR, et al. Predictors of outcome after percutaneous endoscopic gastrostomy: a community-based study. Mayo Clin Proc. 1992;67:1042–9.
26. Loser C, Wolters S, Folsch UR. Enteral long-term nutrition via percutaneous endoscopic gastrostomy (PEG) in 210 patients a four-year prospective study. Dig Dis Sci. 1998;43:2549–57.
27. Kohli H, Bloch R. Percutaneous endoscopic gastrostomy: a community hospital experience. Am Surg. 1995;61:191–4.
28. Davis Jr JB, Bowden Jr TA, Rives DA. Percutaneous endoscopic gastrostomy. Do surgeons and gastroenterologists get the same results? Am Surg. 1990;56:47–51.
29. Blumenstein I, Shastri YM, Stein J. Gastroenteric tube feeding: techniques, problems and solutions. World J Gastroenterol. 2014;20:8505–24.
30. Longcroft-Wheaton G, Marden P, Colleypriest B, Gavin D, Taylor G, Farrant M. Understanding why patients die after gastrostomy tube insertion: a retrospective analysis of mortality. J Parenter Enteral Nutr. 2009;33:375–9.
31. DiSario JA, Baskin WN, Brown RD, DeLegge MH, Fang JC, Ginsberg GG, et al. Endoscopic approaches to enteral nutritional support. Gastrointest Endosc. 2002;55:901–8.
32. Rumalla A, Baron TH. Results of direct percutaneous endoscopic jejunostomy, an alternative method for providing jejunal feeding. Mayo Clin Proc. 2000;75:807–10.
33. Yamazaki T, Sakai Y, Hatakeyama K, Hoshiyama Y. Colocutaneous fistula after percutaneous endoscopic gastrostomy in a remnant stomach. Surg Endosc. 1999;13:280–2.
34. Patwardhan N, McHugh K, Drake D, Spitz L. Gastroenteric fistula complicating percutaneous endoscopic gastrostomy. J Pediatr Surg. 2004;39:561–4.
35. Kim HS, Lee DK, Baik SK, Kwon SO. Endoscopic management of colocutaneous fistula after percutaneous endoscopic gastrostomy. Endoscopy. 2002;34:430.

36. Sookpotarom P, Vejchapipat P, Chongsrisawat V, Mahayosnond A. Gastric volvulus caused by percutaneous endoscopic gastrostomy: a case report. J Pediatr Surg. 2005;40:e21–3.
37. Freeman C, Delegge MH. Small bowel endoscopic enteral access. Curr Opin Gastroenterol. 2009;25:155–9.
38. Potter MB, Bowers SB, Pruitt A. Internal hernia with small bowel volvulus in a patient with altered gut motility: a complication of direct percutaneous endoscopic jejunostomy. Dig Dis Sci. 2007;52:1910–3.
39. Sinclair J, Scolapio J, Stark M, Hinder R. Metastasis of head and neck carcinoma to the site of percutaneous endoscopic gastrostomy: case report and literature review. J Parenter Enteral Nutr. 2001;25:282–5.
40. Grant JP. Percutaneous endoscopic gastrostomy. Initial placement by single endoscopic technique and long-term follow-up. Ann Surg. 1993;217:168–74.
41. Kadakia SC, Sullivan HO, Starnes E. Percutaneous endoscopic gastrostomy or jejunostomy and the incidence of aspiration in 79 patients. Am J Surg. 1992;164:114–8.
42. Greif JM, Ragland JJ, Gage Ochsner M, Riding R. Fatal necrotizing fasciitis complicating percutaneous endoscopic gastrostomy. Gastrointest Endosc. 1986;32:292–4.
43. Cave DR, Robinson WR, Brotschi EA. Necrotizing fasciitis following percutaneous endoscopic gastrostomy. Gastrointest Endosc. 1986;32:294–6.
44. Chung RS, Schertzer M. Pathogenesis of complications of percutaneous endoscopic gastrostomy. A lesson in surgical principles. Am Surg. 1990;56:134–7.
45. Safadi BY, Marks JM, Ponsky JL. Percutaneous endoscopic gastrostomy. Gastrointest Endosc Clin N Am. 1998;8:551–68.
46. Gurusamy KS, Koti R, Wilson P, Davidson BR. Antibiotic prophylaxis for the prevention of methicillin-resistant Staphylococcus aureus (MRSA) related complications in surgical patients. In: The Cochrane Collaboration, editor. Cochrane Database Syst. Rev. [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2013 [cited 2014 Sep 17]. http://doi.wiley.com/10.1002/14651858.CD010268.pub2.
47. 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;70:1060–70.
48. Kanie J, Akatsu H, Suzuki Y, Shimokata H, Iguchi A. Mechanism of the development of gastric ulcer after percutaneous endoscopic gastrostomy. Endoscopy. 2002;34:480–3.
49. Dwyer KM, Watts DD, Thurber JS, Benoit RS, Fakhry SM. Percutaneous endoscopic gastrostomy: the preferred method of elective feeding tube placement in trauma patients. J Trauma. 2002;52:26–32.
50. Wiesen AJ, Sideridis K, Fernandes A, Hines J, Indaram A, Weinstein L, et al. True incidence and clinical significance of pneumoperitoneum after PEG placement: a prospective study. Gastrointest Endosc. 2006;64:886–9.
51. 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;78:591–4.
52. Wojtowycz M, Arata J, Micklos T, Miller F. CT findings after uncomplicated percutaneous gastrostomy. Am J Roentgenol. 1988;151:307–9.

11. Endolumenal GERD Therapies

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Introduction

Gastroesophageal reflux disease (GERD) is an increasingly common illness, with 20 % of the US population reporting GERD symptoms at least weekly [1]. The financial burden of GERD to employers has been estimated at over $3300 per year in health-care costs and lost productivity [2]. GERD is the major risk factor for esophageal adenocarcinoma, which has the fastest rising incidence of any cancer in developed countries [3].

Current treatment of GERD consists of lifestyle modification, acid-suppressive medication, endoscopic procedures, and surgical interventions.

The efficacy of lifestyle modification has been limited. Weight loss has been shown to decrease GERD, but is difficult to achieve. Postural changes during recumbency and avoiding meals just before lying down are effective in decreasing nocturnal reflux; again many patients are unable or unwilling to comply with this regimen. Neither changes in diet (global elimination of certain foods, alcohol) nor cessation of tobacco have not been shown efficacious in treating GERD [4].

Symptom relief with medication, though frequently thought excellent, has increasingly been recognized as ineffective in 20–40 % of patients [5]. Many of these patients have persistent symptoms due to volume regurgitation, non-acid reflux, or other mechanisms that have not been fully elucidated. Concern about long-term side effects of proton-pump inhibitor (PPI) therapy, justified or not, has led some practitioners and patients to seek alternative treatment even when symptom control is excellent with PPI therapy. Prokinetic agents (metoclopramide and motilium) have shown some efficacy in GERD patients, but long-term use has recently been brought into question [6, 7].

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Patients dissatisfied with symptom control by medical therapy frequently look for alternative treatment modalities. Laparoscopic fundoplication is the most commonly recognized alternative invasive treatment modality. High rates of success at controlling typical and atypical GERD symptoms have been reported with laparoscopic fundoplication performed in specialized centers [8]. However the side-effect profile including inability to vomit (>50 %), increased flatulence (30 %), excess bloating (5–10 %), diarrhea (3 %), among others has limited the acceptance of this procedure. AGA guidelines on surgical treatment of GERD summarize the approach of the medical community: "The potential benefits of antireflux surgery must be weighed against the potential deleterious effects (dysphagia, flatulence, an inability to belch, and post-surgery bowel symptoms" [9]. Especially the decreased ability to vent gastric contents has dissuaded many patients, and gastroenterologists, from recommending laparoscopic fundoplication to their patients.

Endolumenal therapies for GERD have been advocated for various reasons. The ability to perform some of these procedures under intravenous sedation, lower perioperative risk, decreased pain and recovery time, and absence of incisions are some of the short-term potential benefits of endoluminal therapies. Probably more significantly, endolumenal treatment of GERD has been fueled by hope that these procedures will have a low incidence of side effects compared to traditional surgical therapy. By and large this hope has been confirmed. However efficacy, durability, and in some cases safety of the procedures have been called into question.

Physiology of GERD and Interventional Treatment

The antireflux barrier is a complex, relatively low-pressure system that relaxes during swallowing, belching, and vomiting, and then closes off during gastric contraction and breathing. Both lower esophageal sphincter (LES) pressure and LES length are important in maintaining an antireflux barrier. Mechanisms of reflux include laxity or shortening of the LES incompetency of the crural diaphragm, and transient lower esophageal sphincter relaxations (TLESRs), and tightening of the sling fibers [10].

Surgical fundoplication, whether laparoscopic or open, creates a nipple-valve that restores the manometric characteristics of a defective valve to normal parameters. Antegrade bolus movement is generally minimally impaired. However the resultant nipple-valve becomes a

one-way, high-pressure system preventing retrograde movement of air or fluid, resulting in problems with belching, venting air, and vomiting. To this extent it is a supra-physiologic valve [11].

By and large endolumenal therapies have tried to bulk up the region of the lower esophageal sphincter. The resultant decreased distensibility results in decreased LES shortening during gastric distention, maintaining a degree of competency beyond an innate increase in LES pressure [12–14].

The role of a hiatal hernia in exacerbating reflux has been clearly demonstrated [15]. As no current endolumenal therapy has attempted to repair a hiatal hernia (i.e., reapproximate an enlarged hiatus), an accepted limitation has been a hiatal hernia of ≤2 cm in axial height.

Endpoints for Assessing Endolumenal Therapy

Adequate control of GERD symptoms has been the primary endpoint of most studies involving antireflux procedures. Studies comparing laparoscopic fundoplication to medical therapy have involved patients with excellent control of symptoms on medical therapy (typically PPIs), and have used symptom control measured by resumption of PPI therapy as indicative of failure of surgical therapy. From a research study design perspective this is an appropriate method to compare relative efficacy of two treatment modalities. However, this type of study design does not address the far more common real-world scenario, in which patients seek an antireflux procedure primarily because symptoms are inadequately controlled by medical therapy. This has important implications for endolumenal therapy. If a patient has troublesome symptoms despite medical therapy, and an intervention results in control of symptoms, the extent to which PPI therapy continues is of far less significance. Most studies of endolumenal GERD therapy have measured improvement in quality of life as a primary endpoint and have included both complete elimination of PPI use *and reduction of PPI use* as secondary endpoints.

A second endpoint that has been used in studies of variations of laparoscopic fundoplication (e.g., partial fundoplication) as well as endolumenal therapy has been control of esophageal acid exposure assessed by ambulatory pH monitoring. Endpoints have been both *normalization* of and *reduction* of esophageal acid exposure as endpoints.

Specific Endolumenal Therapies

Endolumenal therapies have been device dependent in terms of delivery of the therapeutic modality and will be referred to by the manufacturer's device name.

As of 2014, three FDA-cleared GERD-specific treatment devices are available in the USA. These are Stretta (Mederi Therapeutics, Norwalk, CT), EsophyX (Endogastric Solutions, Redmond, WA), and the MUSE System (formerly SRS, Medigus, Omer, Israel).

The EndoCinch, EnteryX, and NDO plicator are currently not available commercially and will not be reviewed here.

Stretta Radiofrequency Treatment of the Gastroesophageal Junction

Overview

Radiofrequency (RF) treatment of the GE junction can be performed with an endolumenal catheter with an inflatable and flexible balloon-basket with four needle electrode sheaths (Fig. 11.1). The electrodes are introduced into the esophageal wall in the region of the LES, and RF

Fig. 11.1. The Stretta device illustrating the handle, catheter with balloon, and extruded radiofrequency needle (courtesy of Mederi Therapeutics).

Fig. 11.2. The Stretta device, illustrating the balloon in place, subsequent areas of ablation (*circles*), and proposed thickening of lower esophageal sphincter tissues (courtesy of Mederi Therapeutics).

energy at 465 kHz is delivered to the electrodes. Cellular heating results in tissue remodeling. A thermocouple on the electrode enables control of energy delivered to reach but not exceed 50 °C. Irrigation of the overlying mucosa minimizes heat injury to the esophageal lining (Fig. 11.2) [16].

Mechanism of Action

Radiofrequency energy produced by the Stretta device induces collagen contraction in animal and human tissue. Animal models show that Stretta results in thickening of the LES, a decrease in transient LES relaxations (TLESRs), and subsequent decrease in reflux events. Human studies have shown a decrease in gastric distention-induced TLESRs (3.5/h pretreatment vs. 1/h posttreatment) [14]. A double-blind, sham-controlled study showed that sildenafil, a smooth muscle relaxant, normalized GE junction compliance to pre-Stretta levels; the authors believe that this argues against fibrosis being a mechanism of action of Stretta [17]. Esophageal motility studies after Stretta have not shown a consistent change in resting LES pressure, nor LES relaxation, compared to pretreatment parameters.

Animal studies of RF energy applied to the intestine demonstrate an increase in smooth muscle fiber size, with more muscle fibers per muscle bundle that results in the lengthening and thickening of the sphincter [18].

Patient Selection

Clinical studies have excluded patients with a hiatal hernia of >2 cm, severe esophagitis (Grade C or D) despite medical therapy, and Barrett's esophagus. Patients with medically responsive but refractory GERD

have comprised the bulk of study subjects. Patients undergoing the Stretta procedure should undergo the same preoperative objective evaluation as a patient undergoing a laparoscopic fundoplication.

Stretta Technique

Under deep sedation, endoscopy confirms eligibility criteria and measures the position of the squamocolumnar junction. A guide wire is introduced, the endoscope is withdrawn, and the RF delivery catheter is introduced orally over a guide wire. The balloon is inflated to 2.5 psi starting 2 cm proximal to the squamocolumnar junction, and the electrode needles (22 gauge, 5.5 mm length) are deployed into the esophageal wall. RF energy is delivered from a device-specific energy source from 60 to 90 s to reach a target temperature of 50 °C. The needles are pulled back; the balloon is deflated; the catheter is rotated 45°; and the procedure is repeated. This sequence is repeated serially every 0.5 cm to cover an area 2 cm above and 1.5 cm below the squamocolumnar junction. Additional sets are deployed below the cardia. An average of 22 sets of needle deployments with RF energy delivery are performed. During the procedure the mucosa is cooled with water irrigation to prevent injury to the mucosa. The procedure takes 30–40 min to perform. Following the procedure, chest pain is fairly common and patients are treated with analgesics as needed. Stretta has generally been a same-day procedure.

Complications and Safety

Immediate complications have been few, and occurred primarily early in the overall learning curve for the device. Temporary gastroparesis and erosive esophagitis have been the most commonly reported SAEs [19]. Double-dose Stretta was associated with gastroparesis in 2 of 12 patients [20].

Stretta is performed under intravenous sedation, obviating the need for general anesthesia.

Published reports of the Stretta procedure indicate only mild complications, including minor GI bleeding, aspiration pneumonia, fever, leukocytosis, sedation-associated hypotension, or superficial mucosal injury. In these trials, there have been no reports of death, esophageal perforation, or other serious adverse events except for several patients who developed transient gastroparesis or esophagitis. Modifications to the Stretta device employed in the current Mederi device, including

more sensitive temperature regulation and prong redesign, have further increased the safety profile [21].

Clinical Results

There have been numerous studies showing that patients treated with Stretta have a significant improvement in quality of life. In the meta-analysis by Perry, 18 studies containing 1441 patients evaluated the effect of treatment on patient quality of life (QOL). The Velanovich GERD-HRQL scale was measured in 433 patients (9 studies) with an average follow-up interval of 19.8 months. The QOL scores improved from 26.11 ± 27.2 at baseline to 9.25 ± 23.7 after treatment ($p = 0.0001$). QOLRAD scores were collected from four studies comprising 250 patients and improved from 3.3 ± 5.9 to 4.97 ± 4.9 at a mean follow-up interval of 25.2 months ($p = 0.001$). SF-36 was utilized to assess global QOL of the patient population in six studies. The SF-36 physical form evaluated in 299 patients with a mean follow-up period of 9.5 months demonstrated an improvement from 36.45 ± 51.6 at baseline to 46.12 ± 61.9 after procedure ($p = 0.0001$). The SF-36 mental form was included in 5 of the 6 studies, and 264 patients, with an improvement from 46.79 ± 20.5 to 55.16 ± 17.6 at 10-month follow-up ($p = 0.0015$) [19].

Sham-Controlled Studies

Three sham-controlled studies of Stretta have been published [17, 20, 22]. There was a statistically significant improvement in medication use, GERD-HRQL, and satisfaction scores in treatment groups but not sham procedure groups. At crossover, similar improvements occurred in the sham patients. No sham group patient was able to discontinue medical therapy, while 50–56 % of treated patients had discontinued PPI therapy at 1 year in two of the three studies. Objective data was variable.

Durability

A recent report by Dughera et al. reported on 26 patients who had completed 4- and 8-year follow-up after Stretta [23]. GERD-HRQL scores were significantly improved compared to baseline at both 4 and 8 years, as were QOL scores. At 4 years 21 (80.7 %) of patients and at 8 years 20 patients (76.9 %) were completely off PPIs. Interestingly, mean esophageal acid exposure was improved at 4 years, but returned to baseline values at 8 years.

A second report by Noar et al. of 99 patients completing 10-year follow-up (217 patients in initial cohort) found that peak improvement in GERD-HRQL, patient satisfaction, and medication use occurred at 2 years after Stretta, and that significant improvement compared to baseline continued out to 10 years [24]. All patients were on double-dose PPI therapy prior to Stretta, at 10 years 64 % sustained at least a 50 % reduction in PPI use, and 41 % of patients remained off PPIs altogether.

Objective Results

Although few in number, studies evaluating esophageal function by manometry have demonstrated no significant change in LES resting and nadir pressure, and no change in esophageal body peristalsis [14].

The Stretta procedure appears to decrease distal esophageal acid exposure. In the abovementioned meta-analysis by Perry and colleagues [19], 7 studies with 267 patients reported DeMeester scores before Stretta and at a mean of 13.1-month follow-up. The DeMeester score improved from 44.37 ± 93 prior to procedure to 28.53 ± 33.4 post-procedure ($p = 0.0074$). Eleven studies comprising 364 patients demonstrated improvement in percent time esophageal acid exposure from 10.3 ± 17.8 % to 6.5 ± 12.5 % at a mean of 11.9-month follow-up ($p = 0.0003$). The improvement in pH at 1-year follow-up appeared to be better than the improvement reported at 6 months in other studies. The significance of improvement in pH control with time is not clear.

Treatment of Stretta Failures

Some patients have undergone repeat Stretta procedure after initial failure or after recurrence of symptoms, with some marginal benefit. Rates of conversion to laparoscopic fundoplication are lacking in most published reports, but technically the conversion has been straightforward.

Summary

Although the mechanism by which RFA to the lower esophagus and cardia improves GERD symptoms is still not clear, studies indicate that postulated mechanisms such as fibrosis or sensory denervation probably are not the major mechanism. Reduction in TLESRs appears to have

the most support [21]. Heartburn, daily PPI use, and standardized quality of life questionnaires have seen improvement following Stretta in a majority of studies, and 8–10 years' data indicate durable success at symptom control in the range of 40 %. Objective data (esophageal acid exposure and lower esophageal sphincter measurements) have been conflicting, although meta-analysis indicates that esophageal acid exposure does decrease in many patients after the procedure. The safety profile of Stretta in its current configuration and use is excellent.

EsophyX Transoral Fundoplication

Overview

The EsophyX device is designed to create an internal esophagogastric fundoplication. It is introduced over a flexible endoscope with the patient under general endotracheal anesthesia. Using a combination of a tissue mold to appose tissue, a helical retractor to pull the lip of the valve distally, and suction to the shaft of device to reduce the hernia, the gastric fundus is folded against the distal esophagus. Small H-shaped polypropylene fasteners are then delivered across the apposed tissue to fix the plication. These full-thickness fasteners create a serosal fusion of the apposed tissues, probably due to inflammation (Fig. 11.3).

Device

The EsophyX device is composed of (1) a handle, wherein the various controls are located; (2) a chassis of 18 mm diameter through which the endoscope is inserted and control channels run; (3) side holes on the distal end of the chassis to which external suction can be applied (the tissue invaginator); (4) a tissue mold, which when brought into retroflexion pushes tissue against the shaft of the device; (5) a helical screw, which is advanced into tissue to pull tissue caudally between the tissue mold and the shaft; (6) two stylets, which advance from the shaft of the device through the plicated tissue and then through eyelets in the tissue mold; and (7) a cartridge containing polypropylene H-shaped fasteners (or plicators), which are deployed over the stylets so that the trailing leg engages within the esophageal lumen and the leading leg engages within the gastric lumen (Fig. 11.4).

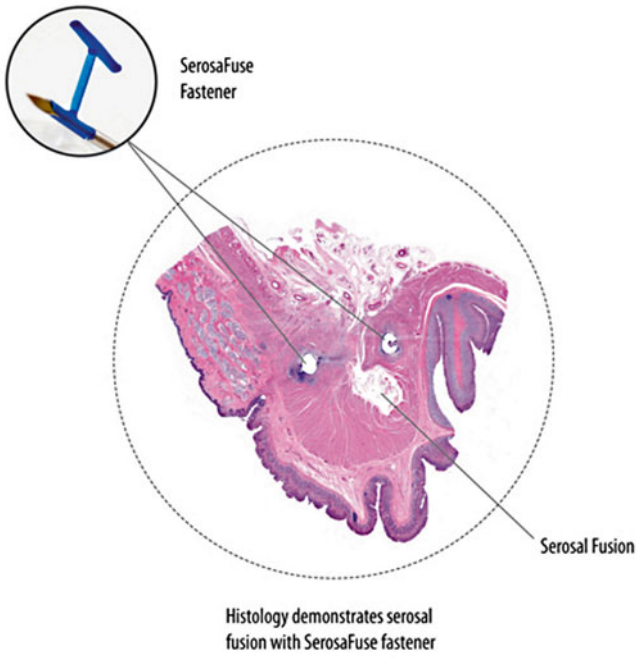

Fig. 11.3. Porcine photomicrograph illustrating fusion of apposed serosa by the EsophyX fastener (courtesy of EndoGastric Solutions).

TIF Technique Development

Initial technique development of the EsophyX™ focused on creating a gastro-gastric plication (EndoLumenal Fundoplication, "ELF," or Transoral Incisionless Fundoplication, "TIF"1). The helical retractor was engaged in the gastric cardia 1–2 cm beyond the *Z*-line, and caudal retraction on the helix elongated the lip of the valve while the tissue mold was closed. Suction was then applied to the tissue invaginator and the device was advanced caudally to reduce the hernia. Then 12 fasteners were deployed at four separate radial positions below the *Z*-line to create an omega-shaped valve of 1–3 cm in length and >220° in circumference.

In a canine model, Jobe and Kraemer subsequently demonstrated the ability of the device to create an esophagogastric fundoplication, deploying fasteners 2 to 4 cm above the *Z*-line rather than below the *Z*-line as in the original technique. Longitudinal distraction by the

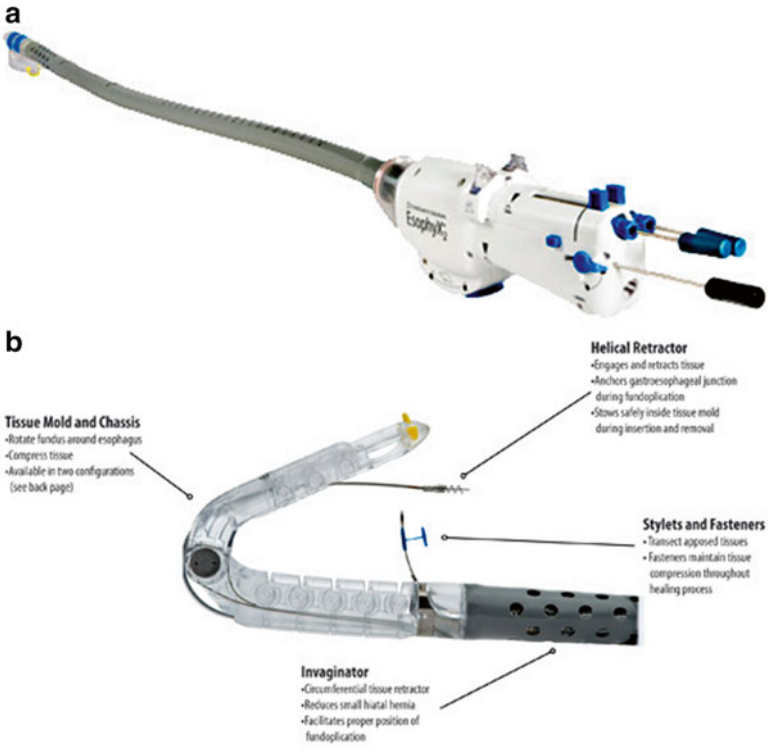

Fig. 11.4. The EsophyX device illustrating the handle and shaft (*top*) and the distal end with tissue mold, helical retractor, tissue invaginator, and stylet with fastener (*bottom*) (courtesy of EndoGastric Solutions).

helical retractor was supplemented by *cranial* movement of the device prior to application of the tissue invaginator, followed by *caudal* movement of the device to ensure fastener delivery below the diaphragm. Multiple fasteners can be deployed in a circumferential fashion to create either a gastrogastric (original technique) or an esophagogastric (current technique) plication (Fig. 11.5). A rotational element was also developed to fold tissue around the esophagus. The techniques have been described in detail by Jobe (25)and Bell [26]. The TIF 2 is the procedure most commonly performed today using the EsophyX™ device. The final construct has an endoscopic appearance similar to a surgical fundoplication (Fig. 11.6).

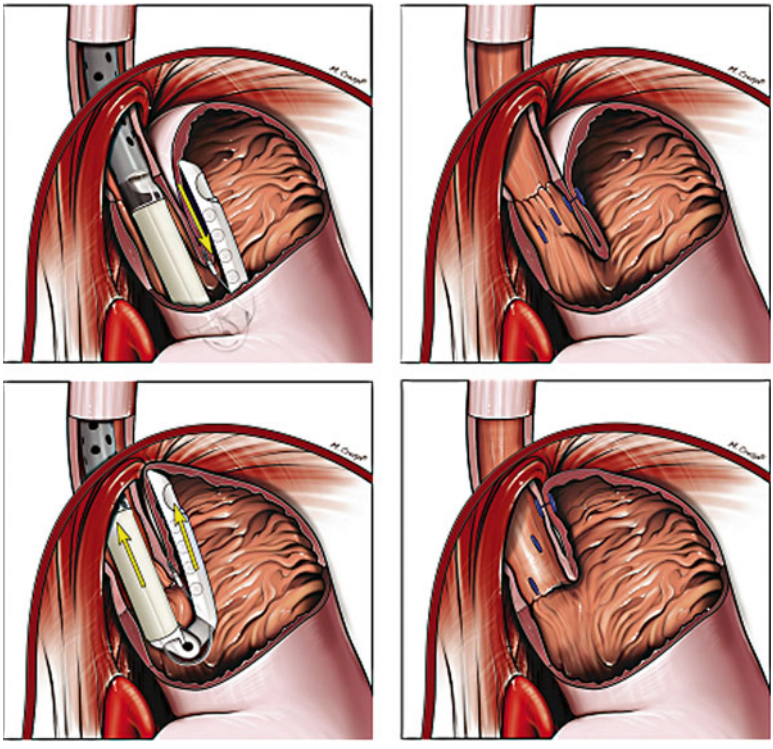

Fig. 11.5. Illustration of use of EsophyX device to create gastro-gastric plication (*top*) or esophagogastric plication (*bottom*) (artist: Massimilano Crespi, info@max-medicalillustrator.com).

Mechanism of Action

Canine studies of a gastrogastric plication created with the EsophyX™ device demonstrated an increase in lower esophageal sphincter length and pressure, primarily due to pressure augmentation at the lower end of the LES. The TIF 2 esophagogastric plication resulted in a valve with sphincter vector–volume characteristics very similar to a Nissen procedure [25]. Human studies using endoluminal functional imaging and impedance have demonstrated a decrease in EG junction distensibility immediately after the procedure, and a decrease in number of liquid and mixed TLESR-related reflux events at 6 months post-TIF (16.8 ± 1.5 vs. 9.2 ± 1.3; $p < 0.01$). TIF also led to a decrease in the number and proximal

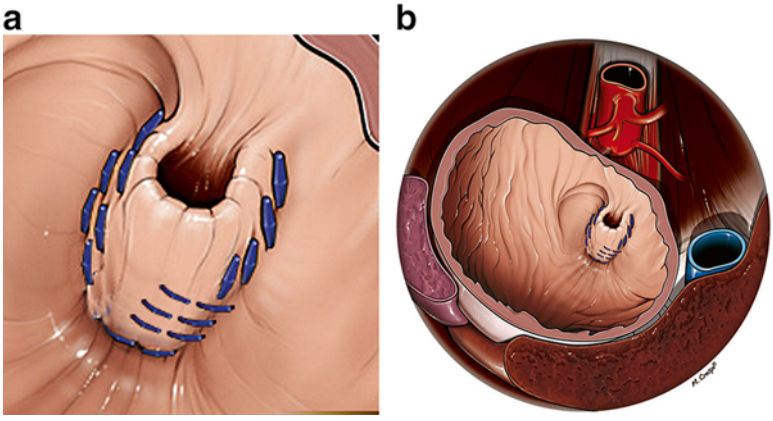

Fig. 11.6. Completed TIF esophagogastric fundoplication with external structures (artist: Massimilano Crespi, info@max-medicalillustrator.com).

extent of reflux episodes and an improvement of acid exposure in the upright position [12].

The mechanism by which the TIF procedure keeps a hiatal hernia reduced has not been thoroughly investigated. Canine studies found that the TIF 2 procedure "captured" a loose phrenoesophageal membrane within the plication. In some cases bulking of the GE valve, or capturing the PE membrane at the edge of the hiatus during fastener delivery, may have a role as well in keeping the hiatal hernia reduced.

Patient Selection and Preoperative Evaluation

Similar criteria to other endoluminal therapies have been used for the TIF procedure: Contraindications have been severe esophagitis, Barrett's, gastroparesis, a hiatal hernia of >2 cm, and BMI >35. Additionally, a transverse hiatal dimension of >3 cm may be a limiting factor as the patient likely will require a crural closure [26].

Patients undergoing the TIF procedure should undergo the same preoperative objective documentation of GERD as a patient undergoing a laparoscopic fundoplication.

TIF Procedure

Anesthetic and Perioperative Management

The TIF procedure is performed under general endotracheal anesthesia. Medication to decrease postoperative nausea, a proton pump inhibitor, and antibiotics are administered preoperatively. Proton pump inhibitors are continued postoperatively for 2 weeks to aid in healing of the gastric portion of the plication.

Procedure

Prior to device introduction, endoscopic evaluation of the hiatus for hernia dimensions and measurement of the distance to the diaphragm are performed.

The endoscope is placed through the EsophyX device and introduced into the esophagus and then both are advanced carefully, especially as the elbow of the device passes through the cricopharyngeus. The device is visualized entering the stomach, and then the endoscope is pulled back and reintroduced so that it is outside the tissue mold. The tissue mold is retroflexed under direct visualization as the spleen lies outside of the stomach on the greater curve.

With both the tissue mold and the endoscope in retroflexed position, the helical retractor is engaged at the gastroesophageal junction (generally the *Z*-line) at the posterior corner of the anticipated fundoplication position. The tissue mold is partially opened and rotated out of this corner. The device is then pulled back (cranially) a predetermined amount, generally 1–3 cm. The tissue mold is then rotated back into the corner while tension is applied to the helical retractor and the stomach is desufflated. With the fundus so rotated, the tissue mold is closed and locked in place, the helix is locked, and the tissue invaginator placed on suction. This set of maneuvers accomplishes the following: withdrawing the device moves the set point for emergence of the stylets cranial to the GE junction, so that an *esophago*-gastric plication will be created; rotation of the tissue mold with the device at this set distance then rotates the fundus around the esophagus; tension on the helical retractor pulls the GE junction slightly caudally and stabilizes the tissue; desufflation of the stomach enables rotation of the gastric fundus.

With the tissue in position, the position of the plication in relation to the diaphragm is assessed so that the stylets and fasteners will not traverse the diaphragm. Understanding of anatomic relations, palpating the diaphragm with the tissue mold prior to tissue positioning, and ensuring

that the device is introduced beyond the depth of the diaphragm (as previously measured to the incisors) are important. Advancing the device caudally with the tissue invaginator on suction enables caudal advancement of gastroesophageal junction below the diaphragm without displacing the device in relation to the esophagogastric junction. Concurrent laparoscopic visualization in humans has confirmed that 2–3 cm of additional separation between the esophagus and diaphragm can be obtained with this maneuver.

The stylet furthest away from the corner is advanced until visible beyond the tissue mold (e.g., the anterior stylet when in the posterior corner). At times, counterrotation of the device is needed to reduce tension on the tissue mold aligning it with the stylet course. With stylet in view, the fastener is advanced gradually, allowing the trailing leg of the fastener to deploy within the esophageal lumen and the leading leg to deploy within the gastric lumen, creating a full-thickness "H" fixation. The fastener closest to the corner is then deployed, leaving two fasteners at the same depth, a "plication set."

The device is reloaded, the tissue mold and helix unlocked, the tissue invaginator taken off suction, and the procedure repeated at a different location.

The precise positions of the plication sets are a matter of surgical judgment. The initial TIF 2 technique involved creating two plication sets 1 cm deep at the anterior and posterior corners (towards the lesser curve), and two plication set 3 cm deep along the greater curve, with a helical deployment at each location and mild degrees of rotation. Evolution of the technique has included increasing the number of plication sets from 6 to 10 or more, decreasing the number of helical deployments, and increasing the rotational component compared with the longitudinal movement.

Once the fundoplication has been created, the tissue mold is straightened under direct vision and the device is withdrawn. Positioning the endoscope at the very end of the chassis during final withdrawal enables careful inspection of the esophageal lumen during withdrawal. A final endoscopy without the device is performed to evaluate for bleeding and to assess final result.

Postoperative Care

Most patients stay in hospital overnight to help with pain and nausea management and are discharged the following day. A soft diet is prescribed as postoperative edema narrows the esophageal lumen.

Complications and Safety

Direct procedure-related complications have been bleeding and infection.

Bleeding during advancement of a stylet will generally stop with fastener deployment. Pneumoperitoneum may be seen after TIF and in and of itself does not indicate a clinically significant complication.

Full-thickness injury to the esophageal or gastric wall has been reported after the TIF procedure, generally developing a few days afterwards. This is likely due to fasteners pulling through the wall of the viscera from excess tension, retching, or vomiting. Abdominal or mediastinal infection can result. Laparoscopy with mediastinal drainage and removal of offending fasteners has been performed successfully. Technique predicated upon understanding external anatomic relations decreases the potential for these complications.

Major procedure-related complications were seen in 2.4 % of 635 patients in reported series including perforation (0.7 %) or bleeding requiring transfusion (1 %). Technique modification to ensure that stylet and fastener deployment occurs below the diaphragm has reduced the perforation rate and recent series have reported no perforations in 160 patients [27–29].

Clinical Outcomes

Multiple single-arm clinical studies have been published with 6 mo-3-year follow-ups. A recent meta-analysis of 15 studies published through 2012 found that GERD-HRQL scores (21.9 vs. 5.9) and Reflux Symptom Index (RSI) scores (24.5 vs. 5.4) were significantly reduced after TIF ($p \leq 0.0001$). PPI discontinuation was 67 % across all studies with mean follow-up of 8.3 months [30].

Regurgitation symptoms respond very well to TIF. In a recent study of 63 patients at 6-month follow-up, troublesome regurgitation was eliminated in 97 % of TIF patients vs. 50 % of PPI patients, relative risk (RR) = 1.9, 95 % confidence interval (CI) = 1.2–3.11 ($p = 0.006$) [31].

A single sham-controlled study of the TIF 2 technique has been reported. Patients were assigned to groups that underwent TIF and then received 6 months of placebo ($n = 87$), or sham surgery (endoscopy and dilation for 45 min under general anesthesia) and 6 months of once- or twice-daily omeprazole (controls, $n = 42$). Patients were blinded to therapy and reassessed at 2, 12, and 26 weeks. At 6 months, patients underwent 48-h esophageal pH monitoring and esophagogastroduodenoscopy.

By intention-to-treat analysis, TF eliminated troublesome regurgitation in a larger proportion of patients (67 %) than PPIs (45 %) ($p=0.023$). Control of esophageal pH improved following TF (mean 9.3 % before and 6.3 % after, $p<0.001$), but not after sham surgery (mean 8.6 % before and 8.9 % after). Subjects from both groups who completed the protocol had similar reductions in GERD symptom scores. Severe complications were rare (3 subjects receiving TF and 1 receiving the sham surgery) [32].

Objective Outcomes

A number of studies of esophageal pH alterations after the TIF 2 technique have demonstrated statistically significant improvement in esophageal acid exposure measured by DeMeester score, % time pH less than 4, and number of reflux episodes [13, 33], though some have not [25]. A recent open-label RCT comparing PPI treatment with TF demonstrated benefit for TF over PPI in control of troublesome GERD symptoms, with 54 % of patients achieving normalization of intra-esophageal pH off PPI following TF [31]. A study of 15 patients prior to and 6 months after having TIF demonstrated a reduced number of postprandial TLESRs (16.8 ± 1.5 vs. 9.2 ± 1.3; $p<0.01$) and the number of postprandial TLESRs associated with reflux (11.1 ± 1.6 vs. 5.6 ± 0.6; $p<0.01$), but the proportion of TLESRs associated with reflux was unaltered (67.6 ± 6.9 vs. 69.9 ± 6.3 %). TIF also led to a decrease in the number and proximal extent of reflux episodes and an improvement of acid exposure in the upright position. TIF had no effect on gas reflux, which may be why TIF has not been associated with an increase in gas-related symptoms [12].

Durability

Only a few studies have reported longer term follow-up. Two-year results of a US Multicenter study found that GERD health-related quality of life and regurgitation scores improved by ≥50 % in 63 of 96 (66 %) and 62 of 88 (70 %) of patients who had elevated preoperative scores. The RSI score normalized in 53 of 82 (65 %) of patients. Daily PPI use decreased from 91 to 30 % [34].

Muls reported 3-year follow-up on 66 of 79 initial patients. GERD-HRQL improved to 4 (0–32) from 25 (13–38) off PPI, 9 (0–22) on PPI prior to TIF. By modified intention to treat, 61 % of patients remained off daily PPIs (unpublished report, in review, by Testoni, 50 patients, 84 % off or halved PPI therapy at 3 and 6 years post-TIF).

Causes of Failure After TIF

Some patients seem to derive no benefit—even immediate—after a TIF procedure. The TIF procedure is technically more demanding than other endolumenal GERD procedures; technique may play a role in these early failures. Edema in the distal esophagus persists for some weeks after the TIF procedure, and some patients have recurrence of their symptoms after this edema resolves. These are probably initial technical failures.

Postoperative retching or coughing has been associated with disruption of the TIF fundoplication.

Unrecognized or developing hiatal hernia may be the leading reason for technical failure of the TIF procedure, and studies have shown that the presence of any hernia is associated with a lower success rate than no hernia [27].

Reoperation After Failed TIF

Two European studies have reported on 26 patients having laparoscopic fundoplication for recurrent reflux after TIF [35, 36] with complications of infection (2 patients). Although objective parameters improved, quality of life did not and dysphagia was noted to be a problem.

Two US studies [34, 37] reported on 33 patients having laparoscopic revision of prior TIF. There were no perforations, and short-term follow-up indicated improved quality of life and no issue with dysphagia. Long-term outcome has not been reported.

TIF After Failed Laparoscopic Fundoplication

Ten to twenty percent of laparoscopic fundoplication failures are due to loosening of the fundoplication alone, without any evidence of hiatal failure. Results of utilizing the TIF procedure in 11 patients with failed laparoscopic fundoplication demonstrated resolution of primary symptom in 8 of 10 patients at a median 14-month follow-up, and reduction in esophageal acid exposure from 8.1 % (21–4.8 %) to 0.6 % (13.4–0.01 %) ($p = 0.008$) [38].

Summary

Transoral incisionless fundoplication creates a valve that resembles a laparoscopic fundoplication endoscopically without restricting the ability to belch and vomit. Gas-bloat has been a very uncommon event.

Clinical success at normalizing GERD quality of life and dependence on daily PPIs has been seen in 65–80 % of patients, and this effectiveness persists up to 3 years and beyond. Most esophageal pH studies have demonstrated improvement in esophageal acid exposure after TIF, with normalization of pH in over 50 % of patients.

The MUSE System

Overview

The MUSE system (formerly called SRS; Medigus, Omer, Israel) is a self-contained transoral endoscopic device, which uses video and ultrasound guidance to place standard surgical staples through esophagus and gastric fundus in order to create an anterior fundoplication. It received FDA 510 k clearance in March 2014 based upon preliminary data from a multicenter pivotal trial [39]. As of the time of this publication there is limited published data on the efficacy of the device.

Mechanism of Action

The MUSE system creates an endoscopic partial anterior fundoplication using full-thickness surgical staples. Mechanism of action is presumed similar to that of the EsophyX transoral fundoplication.

Patient Selection

Current contraindications to the MUSE procedure are a hiatal hernia >3 cm axial height, failure to reduce the hernia during the procedure, BMI >35, and scleroderma. Additionally, patients with a BMI <21 may have tissues that are too thin and outside of the normal operating range of the device.

Device

The MUSE device consists of a light source, control unit, and flexible surgical endostapler with a built-in light source and camera. The device can be operated by a single user including a handle with controls, a long (80 cm) flexible shaft, followed by a 5 cm rigid section holding a cartridge with 5 standard 4.8 mm titanium surgical staples, a ratchet-controlled one-way articulating section, and a distal tip. Within the distal

Fig. 11.7. Photograph showing MUSE device with close-up of articulating anvil (courtesy of Medigus).

tip is an anvil which folds the staples into a B shape, an ultrasonic transducer, the video camera and light source, and two 21-gauge screws. The screws insert into two nuts in the cartridge, enabling tissue compression and a counterforce to bend the staples. Suction/air insufflation and irrigation channels run through the device to the tip (Fig. 11.7). A separate, dedicated control unit interprets signals from the device and displays the resulting data on a video monitor, including the bending angle and force, ultrasound signal level, screw position, and the gap between the distal tip and the cartridge.

Technique

The Medigus SRS procedure is typically performed under general anesthesia with positive end-expiratory pressure applied as needed to keep any hiatal hernia reduced. Inability to reduce the hiatal hernia with reverse Trendelenberg position and PEEP up to 15 mmHg is considered a contraindication to continuing the procedure.

The endoscope is introduced through a 17 mm inner diameter overtube and advanced to the *Z*-line. The measured distance from incisors to the *Z*-line is entered into the system. The endoscope is then advanced into the stomach, retroflexed, and the rigid section of the device is

observed entering the stomach. The radial location for the stapling site is chosen, and the retroflexed tip of the device is opened to between 150° and 180°. The ratchet is locked to prevent further unbending. The device is then pulled cranially so that the staple will be placed 3 cm above the GE junction. This can be determined by the displayed calculated distance from the incisors, by 3 cm from center staple, or 6.5 cm from the 24 cm mark. The tip of the device is then bent (further retroflexed) to 270° to bring fundus into apposition with esophagus. Direct visualization is now lost, and confirmation of appropriate tissue apposition is provided by ultrasound signal strength (indicating device alignment), ultrasound distance measurement of a gap of 1.8–3 mm to anvil, and force feedback measurements.

The motorized alignment pin is then advanced (forward 1 mm, backward 0.5 mm) in cycles until fully deployed. Anvil screws are then advanced from the cartridge until the anvil is fully secured; the alignment pin is then withdrawn. The anvil screws are tightened until the measured gap from cartridge to anvil is 1.4–1.6 mm. The stapler is then fired, deploying five standard 4.8 mm surgical staples. The anvil screws are retrieved; the ratchet is released and gradually straightened.

The device is removed, staples are reloaded, and the procedure is repeated two more times to create a 180° fundoplication, with the staples roughly 3 cm proximal to the *Z*-line (Fig. 11.8).

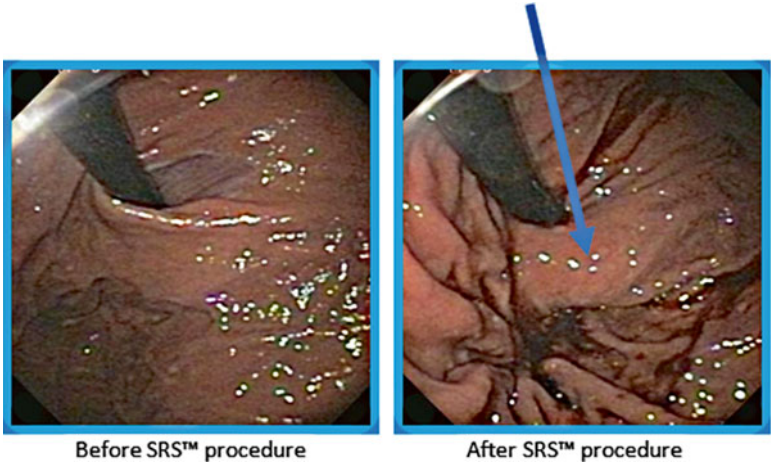

Fig. 11.8. Endoscopic image of gastroesophageal valve before and after the MUSE (formerly called SRS) procedure (courtesy of Medigus).

Whether the staple will incorporate the phrenoesophageal membrane can be suggested by the initial tissue thickness measured by ultrasound.

The device is removed, and endoscopy performed to evaluate the plication and desufflate the stomach.

Clinical Outcomes

A multicenter, prospective, single-arm pivotal study enrolled 69 patients and reported 6-month outcomes of the MUSE procedure [40]. Of 66 patients completing follow-up, GERD-HRQL scores off PPI improved >50 % in 73 % of patients. Daily PPI medication use was stopped in 65 %; and of the 23 patients who continued to take PPIs, 57 % had a ≥50 % reduction in dose.

Three-year follow-up of 22 patients has been presented in abstract form, showing no significant change in GERD-HRQL scores, daily PPI use, or patient satisfaction between 1 and 3 years [41]. Five-year follow-up of 11 patients has been presented in abstract form, and reported elimination or >50 % reduction in 73 % of patients [42].

Objective Outcomes

In the same 6-month follow-up multicenter pivotal study referenced above, mean total % acid exposure per 24 h decreased from 10.9 % (10.7 SD) to 7.3 % (5.1SD) as well as total episodes from 170.8 (181.6 SD) to 100.4 (105.9 SD) with $p<0.001$. Upright esophageal acid exposure decreased from 12 % (11.3) to 8.5 % (6.1) with p-0.013; however supine acid exposure and longest episode did not change. LES pressure, length, and peristaltic amplitude did not change [40].

Safety

In the same multicenter pivotal study, 8 SAEs were recorded in the 69 treated patients, all in the first 24 procedures. One patient developed upper gastrointestinal bleeding on postoperative day 8, requiring hospitalization and blood transfusion. Endoscopy did not disclose source of bleeding and the bleeding resolved spontaneously. There was one case of occult perforation resulting in benign pneumomediastinum. It took 2 weeks to reabsorb, but did not cause any other problem. Following this case, the air pump was disabled before screw insertion. There was 1 case of empyema and pneumothorax treated with chest tube and antibiotics, possibly related to retching.

Subsequent changes to protocol and device, including additional stapling, prophylactic antibiotics and antiemetics, and a device change to decrease air leak during screw insertion, were instituted. With these changes, no further complications occurred in the remainder 45 procedures of the study.

In the same pivotal study, the most common AE were chest pain (22 % of subjects) and sore throat (21 %). There were no reports of dysphagia, bloating, or inability to belch.

At the first week follow-up visit almost all patients were back to normal activity.

Management of Recurrent Reflux After MUSE

There are two case reports of successful laparoscopic Nissen fundoplication for recurrent reflux after the MUSE procedure.

Discordance of Clinical and pH-Metric Results of Minimally Invasive Therapies

A common finding among the endoluminal GERD studies has been discordance between clinical and pH-metric results of these interventions [27]. Although both symptoms and esophageal acid exposure have improved, individual patient improvement has not correlated with individual improvement in esophageal acid exposure. This discordance has been attributed to a placebo effect; however both sham-controlled studies and the consistency of postoperative clinical outcomes in multiple single-arm studies argue strongly against a placebo effect. Similar discord between individual symptom and pH improvement has been noted with laparoscopic fundoplication [43] and PPI therapy [44].

The Future of Endolumenal GERD Therapies

GERD is a chronic and progressive disease manifested primarily by symptoms that affect quality of life. Strategies for treating chronic disease often involve management over cure. In this context, managing a GERD patient's quality of life may involve multimodality therapy, including altering medical therapy or repeating interventions. The need for reintervention with cardiac stents, or repeat arthroscopies, is not so much a failure of technique as it is the nature of a chronic illness. In this light, the ability of the endolumenal procedures to normalize

GERD-HRQL in patients with PPI-refractory symptoms, to do so with minimal side effects, and to achieve >65 % elimination of PPI therapy in the process, is a significant success.

An increasing body of evidence exists that endolumenal therapies are effective in the management of GERD-related symptoms in patients who have incomplete control with medical therapy. Efficacy is in the 65–75 % range and appears durable up to 3 years and beyond, and the option of endolumenal therapy should be provided to patients with symptomatic medically refractory GERD or those wishing to reduce or eliminate dependence on intrusive lifestyle modification or medication. In light of increasing recognition that PPI therapy is effective at symptom control in only 60–80 % of patients, endolumenal therapies have demonstrated similar efficacy and should be considered a maintenance option for patients wishing to decrease or eliminate dependence on PPIs.

References

1. Zhao Y. Gastroesophageal reflux disease (GERD) hospitalizations in 1998 and 2005 – HCUP-US home page. In: HCUP, editor. Online 2012.
2. Goff VV. Managing esophageal reflux disease. National Business Group on health guide for employers using comparative effectiveness research. 2011. https://www.businessgrouphealth.org/pub/f3124c77-2354-d714-5109-a5dddf683531
3. Lagergren J, Bergstrom R, Lindgren A, Nyren O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. N Engl J Med. 1999;340(11):825–31. PubMed eng.
4. Kaltenbach T, Crockett S, Gerson LB. Are lifestyle measures effective in patients with gastroesophageal reflux disease? An evidence-based approach. Arch Intern Med. 2006;166(9):965–71. PubMed.
5. Bytzer P, van Zanten SV, Mattsson H, Wernersson B. Partial symptom-response to proton pump inhibitors in patients with non-erosive reflux disease or reflux oesophagitis – a post hoc analysis of 5796 patients. Aliment Pharmacol Ther. 2012;36(7):635–43. PubMed.
6. Agency MaHpR. Domperidone: risks of cardiac side effects—indication restricted to nausea A1 and vomiting, new contraindications, and reduced dose and duration of use. Drug Safety Update. 2014;7(10).
7. Ehrenpreis ED, Deepak P, Sifuentes H, Devi R, Du H, Leikin JB. The metoclopramide black box warning for tardive dyskinesia: effect on clinical practice, adverse event reporting, and prescription drug lawsuits. Am J Gastroenterol. 2013;108(6):866–72. PubMed.
8. Lundell L, Attwood S, Ell C, Fiocca R, Galmiche JP, Hatlebakk J, et al. Comparing laparoscopic antireflux surgery with esomeprazole in the management of patients with chronic gastro-oesophageal reflux disease: a 3-year interim analysis of the LOTUS trial. Gut. 2008;57(9):1207–13. PubMed eng.

9. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol. 2013;108(3):308–28. quiz 29. PubMed.
10. Kahrilas PJ. GERD pathogenesis, pathophysiology, and clinical manifestations. Cleve Clin J Med. 2003;70 Suppl 5:S4–19. PubMed.
11. Richardson WS, Trus TL, Thompson S, Hunter JG. Nissen and Toupet fundoplications effectively inhibit gastroesophageal reflux irrespective of natural anatomy and function. Surg Endosc. 1997;11(3):261–3. PubMed.
12. Rinsma NF, Smeets FG, Bruls DW, Kessing BF, Bouvy ND, Masclee AA, et al. Effect of transoral incisionless fundoplication on reflux mechanisms. Surg Endosc. 2014; 28(3):941–9. PubMed.
13. Cadiere GB, Buset M, Muls V, Rajan A, Rosch T, Eckardt AJ, et al. Antireflux transoral incisionless fundoplication using EsophyX: 12-month results of a prospective multicenter study. World J Surg. 2008;32(8):1676–88. PubMed eng.
14. DiBaise JK, Brand RE, Quigley EM. Endoluminal delivery of radiofrequency energy to the gastroesophageal junction in uncomplicated GERD: efficacy and potential mechanism of action. Am J Gastroenterol. 2002;97(4):833–42. PubMed.
15. Kahrilas PJ. The role of hiatus hernia in GERD. Yale J Biol Med. 1999;72(2–3): 101–11. PubMed Pubmed Central PMCID: 2579017.
16. Triadafilopoulos G, Utley DS. Temperature-controlled radiofrequency energy delivery for gastroesophageal reflux disease: the Stretta procedure. J Laparoendosc Adv Surg Tech A. 2001;11(6):333–9. PubMed.
17. Arts J, Bisschops R, Blondeau K, Farre R, Vos R, Holvoet L, 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(2):222–30. PubMed.
18. Herman RBM, Murawski M, Nowakowski M, Rys J, Schwarz T, Wojtysiak D, et al. Non-ablative radiofrequency (RF) application to smooth muscle of internal anal sphincter (IAS): a tissue study. Surg Endosc. 2014;28:2323.
19. 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(4):283–8. PubMed.
20. Aziz AM, El-Khayat HR, Sadek A, Mattar SG, McNulty G, Kongkam P, 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(4):818–25. PubMed.
21. Franciosa M, Triadafilopoulos G, Mashimo H. Stretta radiofrequency treatment for GERD: a safe and effective modality. Gastroenterol Res Pract. 2013;2013:783815. PubMed Pubmed Central PMCID: 3775401.
22. Corley DA, Katz P, Wo JM, Stefan A, Patti M, Rothstein R, et al. Improvement of gastroesophageal reflux symptoms after radiofrequency energy: a randomized, sham-controlled trial. Gastroenterology. 2003;125(3):668–76. PubMed.
23. Dughera L, Rotondano G, De Cento M, Cassolino P, Cisarò F, et al. Durability of Stretta radiofrequency treatment for GERD: results of an 8-year follow-up. Gastroenterol Res Pract. 2014;2014:5.

24. Noar M, Squires P, Noar E, Lee M. Long-term maintenance effect of radiofrequency energy delivery for refractory GERD: a decade later. Surg Endosc. 2014;28(8): 2323–33. PubMed.
25. Jobe BA, O'Rourke RW, McMahon BP, Gravesen F, Lorenzo C, Hunter JG, et al. Transoral endoscopic fundoplication in the treatment of gastroesophageal reflux disease: the anatomic and physiologic basis for reconstruction of the esophagogastric junction using a novel device. Ann Surg. 2008;248(1):69–76. PubMed eng.
26. Bell RC, Cadiere GB. Transoral rotational esophagogastric fundoplication: technical, anatomical, and safety considerations. Surg Endosc. 2011;25(7):2387–99. PubMed Pubmed Central PMCID: 3116120.
27. Bell RC, Mavrelis PG, Barnes WE, Dargis D, Carter BJ, Hoddinott KM, et al. A prospective multicenter registry of patients with chronic gastroesophageal reflux disease receiving transoral incisionless fundoplication. J Am Coll Surg. 2012;215(6):794–809. PubMed.
28. Trad KS, Simoni G, Barnes WE, Shughoury AB, Raza M, Heise JA, et al. Efficacy of transoral fundoplication for treatment of chronic gastroesophageal reflux disease incompletely controlled with high-dose proton-pump inhibitors therapy: a randomized, multicenter, open label, crossover study. BMC Gastroenterol. 2014;14:174. PubMed.
29. Trad KS, Turgeon DG, Deljkich E. Long-term outcomes after transoral incisionless fundoplication in patients with GERD and LPR symptoms. Surg Endosc. 2012;26(3):650–60. PubMed Pubmed Central PMCID: 3271216.
30. 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(10):3754–61. PubMed.
31. Trad KS, Barnes WE, Simoni G, Shughoury AB, Mavrelis PG, Raza M, 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. 2014;21. PubMed.
32. Hunter JG, Kahrilas PJ, Bell RCW, Wilson EB, Trad KS, Dolan JP, et al. Efficacy of transoral fundoplication vs omeprazole for treatment of regurgitation in a randomized controlled trial. Gastroenterology. https://www.businessgrouphealth.org/pub/f3124c77-2354-d714-5109-a5dddf683531
33. Bell RC, Freeman KD. Clinical and pH-metric outcomes of transoral esophagogastric fundoplication for the treatment of gastroesophageal reflux disease. Surg Endosc. 2011;25(6):1975–84. PubMed Pubmed Central PMCID: 3098375.
34. Bell RC et al. Transoral incisionless fundoplication: 2 year results from the prospective multicenter U.S. study. Am Surg. 2014;80(11):1093–105.
35. Furnee EJ, Broeders JA, Draaisma WA, Schwartz MP, Hazebroek EJ, Smout AJ, et al. Laparoscopic Nissen fundoplication after failed EsophyX fundoplication. Br J Surg. 2010;97(7):1051–5. PubMed.
36. Witteman BP, Kessing BF, Snijders G, Koek GH, Conchillo JM, Bouvy ND. Revisional laparoscopic antireflux surgery after unsuccessful endoscopic fundoplication. Surg Endosc. 2013;27(6):2231–6. PubMed.

37. Perry KA, Linn JG, Eakin JL, Onders RP, Velanovich V, Melvin WS. Transoral incisionless fundoplication does not significantly increase morbidity of subsequent laparoscopic Nissen fundoplication. J Laparoendosc Adv Surg Tech A. 2013;23(5):456–8. PubMed.
38. Bell RCW, Hufford RJ, Fearon J, Freeman KD. Revision of failed traditional fundoplication using EsophyX transoral fundoplication. Surg Endosc. 2013;27:761–7.
39. Roy-Shapira A, Bapaye A, Kiesslich R, Horgan S, Schoppmann SF, Zacherl J, et al. Mo1488 effective endoscopic treatment of gastroesophageal reflux disease using a new endoscopic stapling system results of a prospective controlled multicenter tria. Gastroenterology. 142(5):S–1076. https://secure.jbs.elsevierhealth.com/action/showCitFormats?pii=S0016-5085%2812%2964180-8&doi=10.1016%2FS0016-5085%2812%2964180-8&code=ygast-site.
40. Zacherl J, Roy-Shapira A, Bonavina L, Bapaye A, Kiesslich R, Schoppmann SF, 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. 2014;19. PubMed.
41. Kessler WRM, Gail, Selzer DJ, Lehman GA. Longer term follow up after endoscopic treatment of GERD with the medigus SRS™ endoscopic stapling device. Abstract, DDW 2014.
42. Bapaye D, Pujari R, Dorwat S, Roy-Shapira A. A pilot study of an endoscopic surgical stapler for the treatment of GERD – five year follow up results. Abstract, UEG week 2013.
43. Markus PM, Horstmann O, Kley C, Neufang T, Becker H. Laparoscopic fundoplication. Surg Endosc. 2002;16(1):48–53. PubMed.
44. Milkes D, Gerson LB, Triadafilopoulos G. Complete elimination of reflux symptoms does not guarantee normalization of intraesophageal and intragastric pH in patients with gastroesophageal reflux disease (GERD). Am J Gastroenterol. 2004;99(6):991–6. PubMed.

12. Barrett's Esophagus: Radiofrequency (RF) and Other Ablation Modalities

Brian J. Dunkin

Introduction

Barrett's esophagus (BE) is a metaplastic change to the lining of the esophagus transforming from normal squamous epithelium to specialized intestinal epithelium. It is also called intestinal metaplasia (IM) and was first described in 1950 by Norman Barrett (1903–1979), an Australian-born British surgeon. Barrett's esophagus is believed to develop as an adaptive response to gastroesophageal reflux, but is associated with a significantly increased risk of developing esophageal adenocarcinoma. The degree of risk is correlated with the presence of dysplasia within the BE.

Over the last decade, there has been a revolution in the treatment of BE with dysplasia. Up until the mid-2000s most patients who developed BE with high-grade dysplasia (HGD) underwent esophagectomy because of a high risk of developing esophageal adenocarcinoma (EAC). By 2009, surgery had been replaced by endoscopic therapies. The change was welcomed, because up to that point in time, ablative therapies for BE were cumbersome with variable results or significant complications. In 2009, Shaheen et al. published their results of endoscopic radiofrequency mucosal ablation for Barrett's with HGD, introducing the world to a well-tolerated, reproducible, and safe technology with excellent results [1]. This ushered in the modern era of endoscopic treatment of dysplastic BE.

This chapter briefly reviews the pathophysiology of BE and its association with EAC, describes how to evaluate it endoscopically, and details modern techniques of esophageal mucosal ablation and their results.

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Pathophysiology of Barrett's Esophagus

Gastroesophageal reflux disease (GERD) is a condition that develops when the stomach contents reflux into the esophagus causing symptoms. In the Western world it has a prevalence of 10–20 % [2]. While there is debate about the indications for performing screening endoscopy for patients with GERD, guidelines from the American Society of Gastrointestinal Endoscopy (ASGE) recommend esophagogastroduodenoscopy (EGD) for patients with alarm symptoms (dysphagia, odynophagia, gastrointestinal bleeding, iron-deficiency anemia, or unexplained weight loss) or patients with over 5 years of symptoms requiring medical therapy, white males greater than 50 years old, or those with a family history of BE or EAC [2]. BE is found in 10–15 % of patients undergoing endoscopy for GERD [3].

Barrett's esophagus is suspected endoscopically by the appearance of salmon-colored mucosa in the distal esophagus (Fig. 12.1) and diagnosed by histologic findings of columnar epithelium with goblet cells in place of the normal squamous epithelium. The columnar epithelium of BE is characterized as "specialized" because, while it contains columnar cells, goblet cells, and villous architecture, the columnar cells lack absorptive capabilities or ultrastructure characteristics of true intestinal cells making them an example of incomplete intestinal metaplasia [4]. There are two other types of histopathological patterns described in

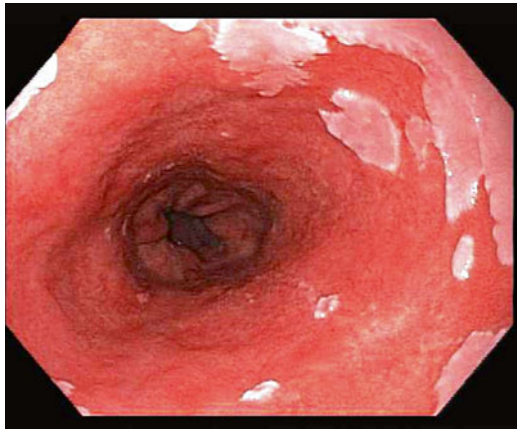

Fig. 12.1. Endoscopic view of Barrett's esophagus.

Barrett's epithelium—cardiac (junctional) and fundic type mucosa. Cardiac mucosa has a predominately foveolar surface containing mucous glands and resembling gastric cardia-type mucosa. Fundic type mucosa contains both parietal and chief cells with atrophic fundic glands [5, 6]. When adenocarcinoma of the esophagus develops in Barrett's mucosa, it virtually always arises in specialized metaplastic columnar epithelium and not from fundic or cardiac type epithelium, indicating that these are precursors in the transformation from squamous epithelium to specialized intestinal metaplasia [6].

BE is associated with an increased risk of developing EAC. The incidence of EAC in the USA has increased more than sevenfold over the last 30 years (Fig. 12.2) and is associated with a 5-year survival rate of less than 20 % [7]. In 2009, 16,470 new cases of esophageal cancer were diagnosed in the USA, of which 60 % were adenocarcinomas. The risk of EAC is 30–40 times higher among patients with Barrett's esophagus (BE) compared to those without this condition. Progression from BE to EAC occurs through accumulated genetic alterations beginning with a metaplastic change from esophageal squamous epithelium to non-dysplastic BE (NDBE) and then progressing to worsening degrees of

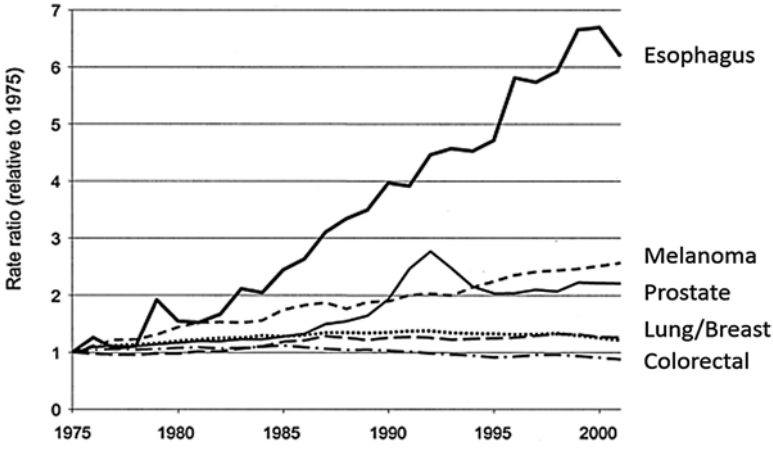

Fig. 12.2. Relative change in incidence of esophageal adenocarcinoma from 1975 to 2001 compared to other malignancies. From Bennett M, Mashimo H. Molecular markers and imaging tools to identify malignant potential in Barrett's esophagus. World Journal of Gastrointestinal Pathophysiology. 2014;5(4):438–49. Copyright ©2014 Baishideng Publishing Group Inc. All rights reserved.

neoplasia starting from low-grade dysplasia (LGD), then high-grade dysplasia (HGD), and finally EAC. Patients with BE and HGD develop EAC at a rate of 6 % per year [8]. The risk of progression from LGD to EAC is less certain in large part because there is poor agreement among pathologists on the diagnosis of LGD and there are contradictory data on its natural history. In a recent US study of 210 patients with LGD, the annual rate of progression to EAC was 0.44 % [9]. The risk of NDBE progressing to EAC is significant as well. Sharma et al. followed 618 patients who had a new diagnosis of BE without dysplasia for 4 years. During that time, 16.1 % developed LGD, 3.6 % HGD, and 2 % EAC [10]. These results suggest that there is a 1.4 % chance per year of BE progressing from NDBE to either HGD or EAC—both states that require surgical or endoscopic intervention. To put this in perspective, a colon polyp carries a 0.58 % incidence per year of progressing to colon cancer. Because of these significant risks and the poor overall survival of patients with invasive EAC, many practitioners have wondered if it would be advantageous to remove or ablate the esophageal epithelium containing BE before it has a chance to progress.

Endoscopic Evaluation of BE

When performing endoscopy in patients found to have BE, it is recommended to use high-definition, white light endoscopy and take time to do a careful inspection. Advanced imaging techniques may be used to better delineate the extent of disease and the presence of dysplasia. The most common imaging adjunct is narrowband imaging (NBI) which refers to a technique of using light with specific blue and green wavelengths to enhance the detail of the mucosal surface. A special filter is electronically activated by a switch on the endoscope leading to the use of ambient light of wavelengths of 440–460 nm (blue) and 540–560 nm (green). Because the peak light absorption of hemoglobin occurs at these wavelengths, blood vessels appear very dark, allowing for improved differentiation between squamous and columnar epithelium and better identification of mucosal abnormalities within the BE segment (Fig. 12.3).

The extent and character of the BE should be described using standardized criteria. The C & M or “Prague” classification is used to describe the extent of disease with “C” indicating the length of circumferential BE and “M” indicating the maximum length (Fig. 12.4). Visible lesions should be described according to the Paris endoscopic classification of superficial neoplastic lesions [11]. This divides lesions into three

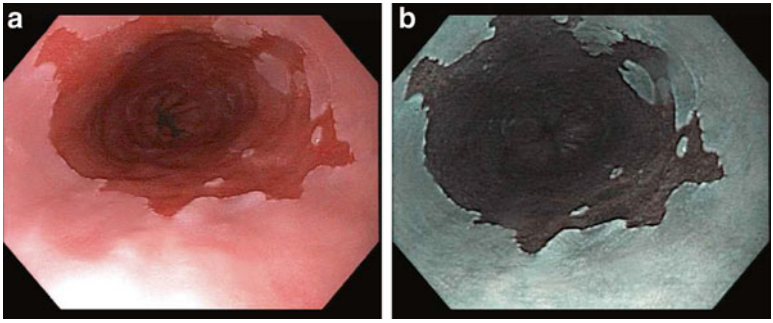

Fig. 12.3. Endoscopic evaluation of Barrett's esophagus using high-definition white light imaging (**a**) versus narrowband imaging (**b**).

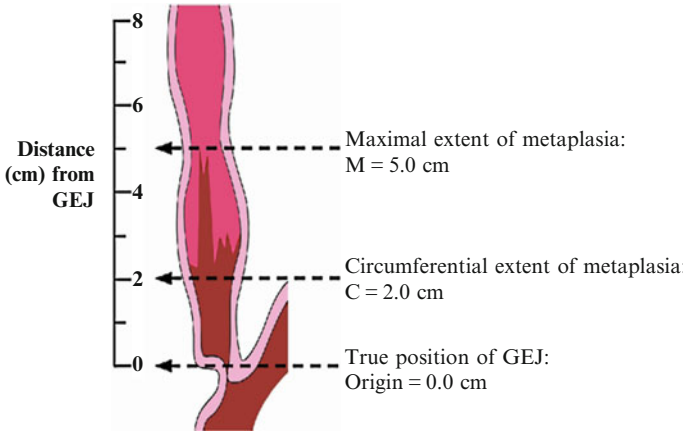

Fig. 12.4. C & M (aka "Prague") classification of Barrett's esophagus. From Sharma P, et al. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. Gastroenterology 2006 Nov;131(5):1392–9. Epub 2006 Aug 16. Reprinted with permission from Elsevier Limited.

groups: protruding (0-I), non-protruding and non-excavated (0-II), and excavated (0-III). Type 0-II lesions may be further subdivided into slightly elevated (0-IIa), flat (0-IIb), or depressed (0-IIc).

After careful evaluation and systematic description, the area of BE should be biopsied using the Seattle protocol. This entails four quadrant biopsies with a large-capacity forceps every 1–2 cm throughout the

entire extent of disease. Nodular areas are often completely excised using endoscopic mucosal resection (see Chapter 13) for better characterization. All specimens should be labeled carefully by level and correlated with the endoscopy report.

Treatment Options for BE

Treatment options for BE are guided by the degree of dysplasia (Table 12.1). NDBE is typically treated with acid suppression and endoscopic surveillance with biopsy at 3-year intervals. LGD is difficult to interpret by pathologists, so a repeat endoscopy and biopsy are recommended in 6 months to confirm the diagnosis. Once confirmed, patients have the option to continue with surveillance biopsies at 1-year intervals, or undergo endoscopic ablation or resection. HGD should be treated with either endoscopic ablation/resection or surgery. Combining radiofrequency (RF) ablation with EMR is also an option, particularly for nodular disease or intramucosal EAC. RF ablation will not remove nodular disease or intramucosal EAC (tumor stage T1a or less). As a result, nodules or suspicious areas within a field of flat BE may be managed with EMR. If the pathology from the resected specimen shows no cancer or only superficial cancer within the mucosa and not extending beyond the muscularis mucosa with deep and lateral margins free of malignancy, then the EMR is considered an adequate resection and the remaining flat BE may be ablated with RF energy.

Principles of Mucosal Ablation

Since BE is confined to the superficial mucosa and does not involve layers deep to the muscularis mucosa, endoscopic ablation has the potential to destroy the Barrett's epithelium without damaging the deeper layers of the esophageal wall (Fig. 12.5). Work by Brandt et al. in 1992 and Berenson et al. in 1993 proved that injuring the metaplastic epithelium followed by healing in an acid-suppressed environment leads to re-epithelialization of the esophagus with a neosquamous lining [12, 13]. Since this discovery, multiple modalities have been employed to ablate BE. These can be classified into two categories: field treatment and focal treatment. Field treatment modalities are capable of expeditiously ablating sizable areas of BE either circumferentially or segmentally. Focal treatments use "point-and-shoot" technology to ablate BE.

Table 12.1 Guidelines for evaluation and management of Barrett's esophagus.

	ACG	ASGE	AGA	BSG
No dysplasia	Two esophageal examination with biopsy within 1 year and follow up with endoscopy every 3 years	Two consecutive esophageal examinations with biopsy within 1 year and follow up with endoscopy every 3 years	Asses within 1 year and if no dysplasia, defer for 5 years or until cancer therapy is not possible or life expectancy is limited	Surveillance every 2 years, if appropriate
Indefinite		Repeat biopsy after 8 weeks of acid suppression, if evidence of acute inflammation due to gastroesophageal acid reflux		Assess with extensive biopsies after course of proton pump inhibitors and return to routine surveillance if no definite dysplasia at 6 months
LGD	Treat based on highest grade of dysplasia seen on two esophageal examinations within 6 months, and follow up with endoscopy every year until dysplasia is absent on two subsequent examinations	Follow up after 6 months with concentrated biopsies in area of dysplasia; follow up every 12 months if dysplasia persists	Assess in 1 year and reexamine every year if dysplasia is confirmed by two pathologists (if there is disagreement about the presence of dysplasia then reexamine in 2 years)	Extensive biopsy after intensive acid suppression for 8-12 weeks; surveillance every 6 months if dysplasia persists; surveillance intervals of 2–3 years if regression occurs on two sequential examinations

(continued)

Table 12.1 (continued)

	ACG	ASGE	AGA	BSG
HGD	Document any mucosal irregularities, repeat esophageal examination with biopsy within 3 months with pathologist's confirmation to eliminate the possibility of cancer; follow up with endoscopic mucosal resection in the case of any mucosal irregularity; then intensive endoscopic surveillance every 3 months or an intervention, such as esophagectomy or ablation, in the case of flat mucosa	Diagnosis should be confirmed by a pathologist; surgical candidates can choose to have a surgery or endoscopic therapy; follow up patients who choose surveillance every 3 months for 1 year with several large biopsies every 1 cm along esophagus; after 1 year without cancer detection, surveillance duration can be lengthened, provided dysplastic changes are absent on two subsequent examinations	Diagnosis should be confirmed by two pathologists; patients should be treated with surgical resection or endoscopic therapy; surveillance can be offered provided follow-up with endoscopy is every 3 months with a minimum of eight biopsies every 2 cm along esophagus	Esophagectomy recommended if changes persist after intensive acid suppression, if confirmed by two pathologists, and if patient considered fit for surgery; if unfit for surgery, use endoscopic ablation or mucosal resection

ACG American College of Gastroenterology, *ASGE* American Society for Gastrointestinal Endoscopy, *AGA* American Gastroenterological Association, *BSG* British Society of Gastroenterology, *LGD* low-grade dysplasia, *HGD* high-grade dysplasia

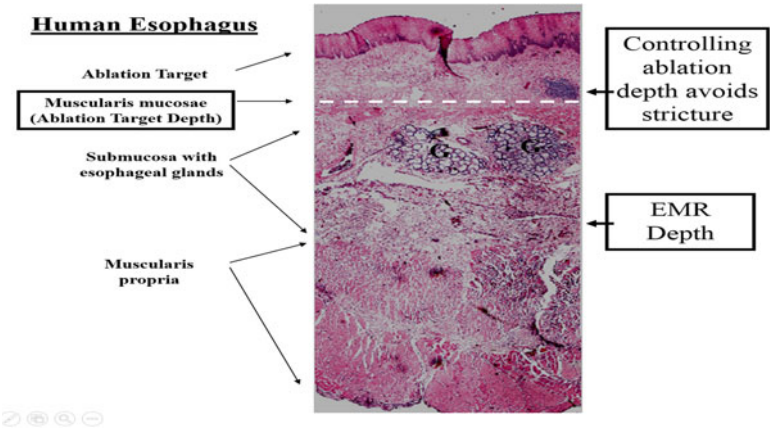

Fig. 12.5. The histology of esophageal ablation and EMR.

Field Treatment Modalities for Mucosal Ablation

Radiofrequency Ablation

The most common field treatment modality used today for BE is radiofrequency ablation (RFA). The only commercially available RFA device for treating BE is the Barrx™ Flex RFA System approved by the Federal Drug Administration in 2005 (Covidien, Mansfield, MA, USA). The system is composed of the Barrx™ Flex RFA Generator, a 360 Soft Sizing Balloon, and an array of treatment catheters (Fig. 12.6). The Barrx™ 360 RFA Balloon Catheter is a balloon-based bipolar electrode array used for treating circumferential segments of BE ≥3 cm. The Barrx™ 90 RFA Focal Catheter (13×20 mm treatment area), 60 RFA Focal Catheter (60 % less treatment area than Barrx™ 90), Ultra-Long RFA Focal Catheter, and Channel RFA Catheter (Fig. 12.7) provide primary or secondary "spot" treatments for smaller areas such as islands and tongues. They can also be used for secondary treatment after circumferential ablation or as an adjunct to other therapeutic techniques.

Barrett's epithelium is approximately 500 μm thick. The Barrx™ Flex RFA Generator and the ablation catheter electrode arrays are designed to apply a uniform, superficial depth of ablation between 500 and 1000 μm. This achieves an ideal ablation depth down to, but not through, the muscularis mucosae, thus decreasing the risk of postproce-

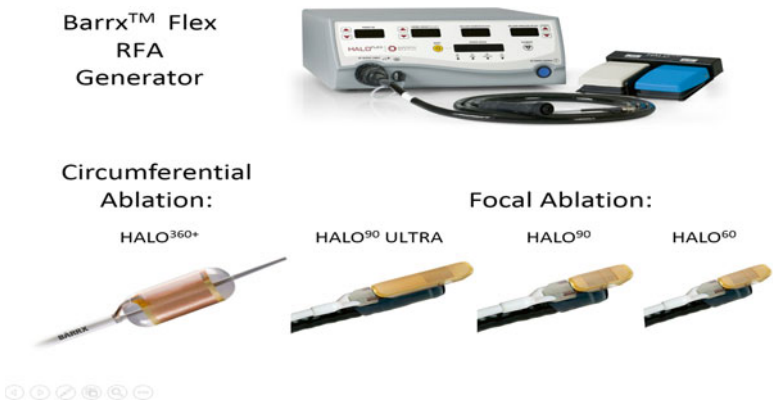

Fig. 12.6. Barrx™ flex RFA system (Covidien, Mansfield, MA, USA).

Fig. 12.7. Barrx™ channel RFA catheter for through-the-scope ablation.

dure stricturing. Contraindications to endoscopic RFA of BE include pregnancy, prior radiation therapy to the esophagus, esophageal varices, prior esophagogastric myotomy, and eosinophilic esophagitis. Common transient post-RFA symptoms are chest pain, mild dysphagia, odynophagia, and fever.

RFA is typically performed every 2 months until all visible Barrett's has been eradicated or a maximum of four treatment sessions performed. Shaheen et al. report that the length of BE predicts the likelihood of complete eradication of intestinal metaplasia (CEIM) and number of required treatment sessions [14]. The mean number of treatment sessions overall to achieve CEIM in their study was 2.6 ± 1.4. However, in patients with longer segments of BE, four or more sessions were required to achieve CEIM. Patients with 2, 5, and 8 cm of BE can be expected to require 2.4, 2.9, and 3.5 treatment sessions, respectively.

Circumferential Ablation Steps

Using standard endoscopic techniques under moderate sedation, the Barrx™ 360 RFA Balloon Catheter facilitates rapid ablation of long and short segments of BE.

Step 1: Sizing. Because the circumferential ablation catheters are non-distensible and come in set diameters only, the esophageal treatment area must be sized in order to choose the correct catheter. The endoscope is introduced to identify the anatomic landmarks and length of the Barrett's epithelium. A guidewire is inserted and the endoscope exchanged off the wire. The Barrx™ 360 Soft Sizing Balloon is introduced over the guidewire and the inner diameter of the esophagus measured. The sizing balloon is then removed, leaving the guidewire in place. Based on the smallest sizing measurement, the appropriate ablation catheter is selected.

Step 2: Ablate. The Barrx™ 360 RFA Balloon Catheter is introduced over the guidewire and the endoscope reinserted alongside. The balloon electrode is positioned under direct visualization so that the proximal edge is slightly above the top of the intestinal metaplasia (Fig. 12.8). The balloon is automatically inflated and energy applied at 300 W and 10 or 12 J/cm^2 (10 J/cm^2 for NDBE; 12 J/cm^2 for LGD and HGD). The electrode is then moved distally by 3 cm, aligning the proximal edge with the distal edge of the ablation zone, and inflation and ablation are repeated (Fig. 12.9). This process continues until the top of the gastric folds is reached.

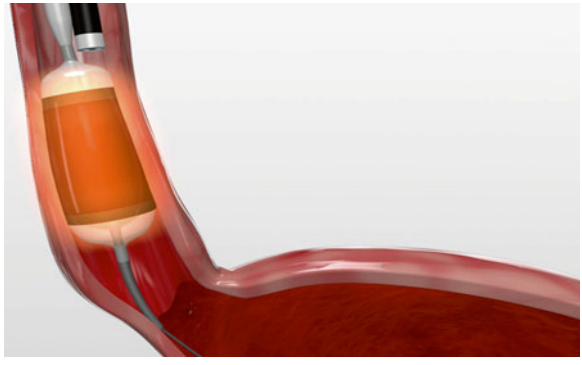

Fig. 12.8. Barrx™ 360 RFA catheter positioned at the proximal extent of Barrett's esophagus with gastroscope positioned alongside.

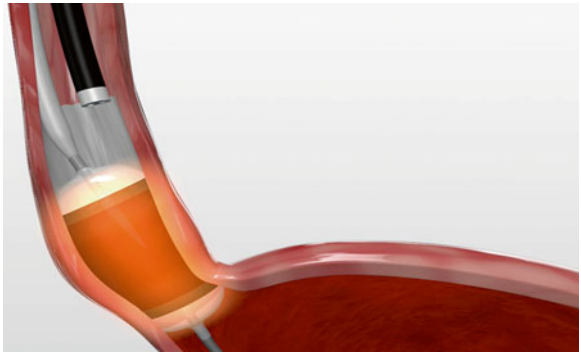

Fig. 12.9. Barrx™ 360 RFA catheter positioned at the distal extent of Barrett's esophagus with gastroscope positioned alongside.

Fig. 12.10. Endoscopic EMR-type cap used to clean sloughed mucosa away between Barrx™ 360 RFA catheter treatments.

Step 3: Clean and Repeat. The treatment catheter is removed and the ablation zone cleaned of coagulum using an EMR cap (Fig. 12.10) to scrape off the sloughed epithelium. The ablation catheter is then cleaned with water and reintroduced over the guidewire. The endoscope is reinserted alongside the ablation catheter, and the ablation steps are repeated for a total of two treatment applications to the entire area of BE.

Focal Ablation Steps

The Barrx™ Focal Ablation Catheters enable primary treatment of short segments of BE, including focal areas such as islands and small tongues, and secondary treatment after ablation with the Barrx™ 360 catheter.

Step 1: Identify. The distal end of the endoscope is inserted into the catheter strap. The endoscope and Barrx™ Focal Ablation Catheter are introduced into the esophagus under direct vision. Anatomic landmarks are identified and measured.

Step 2: Ablate. The endoscope is deflected to bring the electrode into contact with the targeted tissue and 12 J/cm^2 ablation energy delivered. This step is repeated immediately for a total of two treatments to each targeted area.

Step 3: Clean and Repeat. The coagulum is removed from the ablation zones using the edge of the focal catheter. The endoscope and ablation catheter are then removed and the electrode surface cleaned with water. The endoscope and ablation catheter are reintroduced and the ablation steps repeated for a total of four treatment applications to each targeted area.

Results

In 2006 Dunkin et al. proved that the Barrx™ system could be used to ablate normal human esophageal epithelium without energy penetration beyond the muscularis mucosa [15]. Later that same year Smith et al. used the Barrx™ system to successfully ablate BE with HGD in esophagectomy patients, confirming the proper dosimetry for the device and leading to extensive clinical trials [16]. In 2009, Shaheen et al. published their results of a US multicenter, randomized, sham-controlled trial using RFA to treat 127 patients with dysplasia in BE (64 LGD, 63 HGD patients) [1]. Subjects were randomized to receive either RFA or a sham procedure (control group). At 1 year, intention-to-treat analyses revealed complete eradication of dysplasia in 90.5 % of patients with LGD in the RFA group, compared with 22.7 % of those in the control group ($p < 0.001$). Similarly, complete eradication was found in 81.0 % patients with HGD in the RFA group compared with 19.0 % in the control group ($p < 0.001$). Complete eradication of the all Barrett's metaplasia was 77.4 % in the RFA group versus 2.3 % in the control group

($p<0.001$). Post-RFA complications occurred in 6 (7 %) of the 84 patients who received RFA, including one self-limited upper gastrointestinal bleed and five mild esophageal strictures. There were no perforations or deaths. This pivotal study led to widespread use of RFA to treat dysplastic BE, essentially replacing surgery with endoscopic therapy.

The durability of RFA for BE with dysplasia has been established. Shaheen et al. followed a cohort of patients for 3 years after RFA treatment and showed that 98 % had complete eradication of not only dysplastic BE, but also all BE [17]. Recurrence of disease after RFA is low, but not insignificant, at 5.2 % per year with progression of disease occurring at 1.9 % per year [18]. This indicates that even with initial complete eradication of disease, patients must continue with surveillance. Fortunately, recurrent disease often responds to repeat RFA.

One concern about ablative therapies is the possibility of leaving behind buried glands—residual BE under normal-appearing squamous epithelium. This phenomenon may confound surveillance endoscopy leaving the patient at risk for progression of disease. Interestingly, buried glands can be found in over 15 % of BE patients prior to treatment. However, following successful RFA, this phenomenon is eliminated [19].

Photodynamic Therapy

Photodynamic therapy (PDT) is another field treatment modality used for BE with HGD and first described in 1990. PDT uses a combination of laser light and a photosensitizing agent to effect selective tissue destruction. In the USA, intravenous sodium porfimer is given to patients 48–72 h before endoscopy, resulting in photosensitivity for 30–90 days. These patients must avoid exposure to sunlight during this time. The photosensitizer is taken up preferentially by abnormal tissue with higher metabolic activity level, resulting in a degree of selectivity of tissue destruction to the abnormal Barrett's epithelium. Within 48–72 h of administration of the photosensitizing agent, endoscopy is performed to deliver light to the treatment area. Laser light is the only source of photoradiation strong enough to elicit the tissue destruction desired in the gastrointestinal tract. The laser fiber is usually centered with a positioning balloon for even therapy. As much as 200 J/cm^2 is delivered for flat HGD while 300 J/cm^2 is used for nodular disease.

Results

The published results for PDT are variable because much of the data are from single centers using varying techniques. The PORPDT trial, an international, multicenter trial with over 200 patients treated at 30 centers, demonstrated that 52 % of the PDT-treated patients had no residual BE, and 77 % had no more HGD after PDT. This was statistically better than the omeprazole-only group, which had 39 % resolution of HGD. PDT also resulted in a threefold decrease in the development of EAC in these patients [20].

Unfortunately, 95 % of the PDT patients experienced treatment-related adverse side effects with photosensitivity reactions (69 %), esophageal strictures (39 %), and vomiting (32 %) among the top three complaints. The strictures are difficult to treat requiring multiple dilation sessions to resolve. Because of the logistical challenges of administering a photosensitizing agent to patients and the frequent adverse events associated with PDT, its use for BE has been replaced by RFA and it is no longer available in the USA.

Focal Treatment Modalities for Mucosal Ablation

Focal treatment modalities for ablating BE use devices that must be directly aimed at the area of interest and provide a small treatment field. These "point-and-shoot" technologies are used less frequently than RFA because they are technically more challenging to use leading to less reproducible results. Included in this class are cryotherapy, argon plasma coagulation (APC), multipolar electro-coagulation (MPEC), and laser therapy. To date, cryotherapy and APC are used most commonly.

Cryotherapy

Extreme cold can be used to ablate esophageal mucosa. The mechanism of injury differs from RFA or PDT in that it induces transient ischemia causing tissue necrosis coupled with cellular apoptosis and resulting in a stimulatory effect on the immune system. This distinct mechanism may allow cryotherapy to work on segments of BE that have not responded to other modalities. It is also more effective for nodular disease than RFA.

High-pressure nitrous oxide or low-pressure liquid nitrogen can be used for cryotherapy. It is sprayed onto the mucosa using a 7F or 9F probe connected to a delivery device that monitors the cryogen release and warms the catheter. Because the cryogen rapidly expands as it warms, a nasogastric tube must be placed during the procedure to vent the stomach.

Results

There is limited published data on cryotherapy. Ghorbani et al. recently published a multicenter prospective review of a cryospray registry using low-pressure liquid nitrogen cryotherapy in patients with dysplastic BE. Ninety-six subjects underwent 321 treatments with no serious adverse events. One patient developed an esophageal stricture which did not require dilation. Complete eradication of HGD was seen in 81 %, and complete eradication of intestinal metaplasia in 65 %. The mean number of treatments was 3.3, and mean follow-up was 21 months [21]. Two-year follow-up on patients treated with cryotherapy demonstrates that these results are durable with little progression of disease [22].

Argon Plasma Coagulation

Argon plasma coagulation (APC) is high-frequency monopolar electromechanical energy delivered to the target tissue using argon gas as a conductor. It is not much different from the modality of energy used for the "Bovie" pen in the operating room, except that instead of using metal as a conductor, it uses argon gas. The gas, when electromechanically energized, becomes a plasma that conducts the electricity to the target tissue. The advantage of using a gas as a conductor is that the probe can deliver energy without touching the tissue, thus avoiding fouling with coagulum. The broader gas pattern also allows the operator to "paint" larger surfaces more quickly and the depth of thermal energy is fairly well controlled at 1–3 mm. The APC probe is a 7F or 10F catheter that has forward, side, or radially firing tips and is passed down the working channel of the endoscope. Typical energy settings are 30–90 W with argon gas flow rates of 1–2 l per minute. Lower energies cause less penetration into the tissues. The flow of argon gas should be as low as possible to obtain the desired tissue effect as it can easily overinflate the stomach or bowel and must be frequently aspirated throughout the procedure.

Results

One report summarizing data for using APC to treat BE is from Franchimont et al. in which nine studies examining ablation of nondysplastic BE in 333 patients were reviewed [23]. One to eight treatment sessions were required, resulting in complete eradication of BE in 55–100 % of patients. This variability reflects differences in treatment (varying power settings and number of treatment sessions) and acid suppression regimens, the experience of the endoscopist, and length of follow-up. Of additional concern is that one study in the review demonstrated a 44 % incidence of buried glands on follow-up and other studies described five perforations and eight strictures with up to 68 % of patients relapsing back to BE at 12-month follow-up. In the same review, very little data was found for using APC to treat patients with HGD. Of the 11 such patients reported, 9 achieved ablation of their BE, but follow-up was limited.

Milashka et al. followed APC ablated patients for 16 years. Initially 78 % of patients had complete eradication of all disease. At follow-up only 50 % had sustained complete eradication and there was a 24 % incidence of buried glands. Three patients (9 %) went on to develop EAC. They concluded that, in long term, APC did not provide protection against the development of EAC [24].

In summary, APC does not seem to be an effective *de novo* treatment for BE because of variability in efficacy, a relatively high serious complication rate, and the frequent finding of buried glands on follow-up. This "point-and-shoot" technology is mainly used as an adjunct to another treatment modality for cleanup.

Summary

We are living during a time of paradigm shift in managing dysplastic BE. No longer is this a disease that is preferentially treated with surgery. Modern ablative techniques have allowed us to transition from esophagectomy to a well-tolerated outpatient endoscopic procedure for most patients. Combining modalities such as endoscopic mucosal resection and ablation allows for managing even fairly advanced disease endoscopically including nodular BE or intramucosal adenocarcinoma. This is yet another example of endoscopy replacing a surgical procedure and esophageal specialists would be wise to pay attention to this trend and embrace the use of flexible endoscopy in their practice.

References

1. Shaheen NJ, Sharma P, Overholt BE, et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. N Engl J Med. 2009;360(22):2277–88.
2. Lichtenstein DR, Cash BD, Davila R, et al. Role of endoscopy in the management of GERD. Gastrointest Endosc. 2007;66(2):219–24.
3. Wani S, Sharma P. The rationale for screening and surveillance of Barrett's metaplasia. Best Pract Res Clin Gastroenterol. 2006;20:829–42.
4. Spechler SJ, Goyal RK. Medical progress in Barrett's esophagus. N Engl J Med. 1986;315:362–71.
5. Paull A, Trier JS, Dalton MD, Camp RC, Loeb P, Goyal RK. The histologic spectrum of Barrett's esophagus. N Engl J Med. 1976;295:476–80.
6. Thompson JJ, Zinsser KR, Enterline HT. Barrett's metaplasia and adenocarcinoma of the esophagus and gastroesophageal junction. Hum Pathol. 1983;14:42–60.
7. Sharma P. Clinical practice. Barrett's esophagus. N Engl J Med. 2009;361:2548–56.
8. Spechler SJ, Sharma P, Souza RF, et al. American Gastroenterological Association technical review on the management of Barrett's esophagus. Gastroenterology. 2011;140:e18–52.
9. Wani S, Falk G, Post J, et al. Risk factors for progression of low-grade dysplasia in patients with Barrett's esophagus. Gastroenterology. 2011;141(4):1179–86.
10. Sharma P, Falk G, Weston AP, et al. Dysplasia and cancer in a large multicenter cohort of patients with Barrett's esophagus. Clin Gastroenterol Hepatol. 2006;4(5):566–72.
11. Endoscopic Classification Review Group. Update on the Paris classification of superficial neoplastic lesions in the digestive tract. Endoscopy. 2005;37:570–8.
12. Brandt LJ, Kauver DR. Laser-induced transient regression of Barrett's epithelium. Gastrointest Endosc. 1992;38(5):619–22.
13. Berenson MM, Johnson TD, Markowitz NR, et al. Restoration of squamous mucosa after ablation of Barrett's esophageal epithelium. Gastroenterology. 1993;104(6): 1686–91.
14. Shaheen NJ, Bulsiewicz WJ, Rothstein RI, et al. Eradication rates of Barrett's esophagus using radiofrequency ablation (RFA): results from the US RFA registry. Gastroenterology. 2012;142:A1600.
15. Dunkin BJ, Martinez J, Bejarano PA, et al. Thin-layer ablation of human esophageal epithelium using a bipolar radiofrequency balloon device. Surg Endosc. 2006; 20:125–30.
16. 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. 2006;21(4):560–9.
17. Shaeen NJ, Overholt BF, Sampliner RE, et al. Durability of radiofrequency ablation in Barrett's esophagus with dysplasia. Gastroenterology. 2011;141:460–8.
18. Orman ES, Kim HP, Bulsiewicz WJ, et al. Intestinal metaplasia recurs infrequently in patients successfully treated for Barrett's esophagus with radiofrequency ablation. Am J Gastroenterol. 2013;108(2):187–95.

19. Yuan J, Hernandez JC, Ratuapli SK, et al. Prevalence of buried Barrett's metaplasia in patients before and after radiofrequency ablation. Endoscopy. 2012;44(11):993–7.
20. 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(4):488–98.
21. 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 (Epub ahead of print).
22. Gosain S, Mercer K, Twaddell WS, et al. Liquid nitrogen spray cryotherapy in Barrett's esophagus with high-grade dysplasia: long-term results. Gastrointest Endosc. 2013;78(2):260–5.
23. Franchimont D, Van Laethem JL, Deviere J. Argon plasma coagulation in Barrett's esophagus. Gastrointest Endosc Clin N Am. 2003;13(3):457–66.
24. 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(5):367–73.

13. Endoscopic Mucosal Resection: Upper Gastrointestinal Tract

Sara A. Mansfield and Sabrena F. Noria

Abbreviations

BE	Barrett's esophagus
EGC	Early gastric cancers
EMR	Endoscopic mucosal resection
EUS	Endoscopic ultrasound
FAP	Familial adenomatous polyposis
GERD	Gastroesophageal reflux disease
HGD	High-grade dysplasia
IMC	Intramucosal carcinoma
LGD	Low-grade dysplasia
SDA	Sporadic duodenal adenomas

Esophagus

Over the last 20 years, the incidence of adenocarcinoma of the esophagus has substantially increased [1]. This can be attributed to the increased rate of gastroesophageal reflux disease (GERD), which leads to an inflammatory condition of the distal esophagus [2]. Cigarette smoking, obesity, and a diet low in fruits and vegetables also increase the risk of esophageal adenocarcinoma, with a combined population attributable risk of 78.7 % [3].

The pathophysiology underlying esophageal adenocarcinoma is long-standing exposure of the esophagus to gastric acid which can lead to metaplastic changes of normal squamous epithelium to columnar-lined epithelium with goblet cells (intestinal metaplasia) [4]. This

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change is termed Barrett's esophagus (BE) and is considered a premalignant condition that can progress to low-grade dysplasia (LGD), high-grade dysplasia (HGD), intramucosal carcinoma (IMC), and advanced esophageal adenocarcinoma. The risk of progression from BE to cancer has been estimated at 0.6–2.7 % per patient-year [5–7]. Therefore patients with BE should undergo surveillance endoscopy, with multiple biopsies of the diseased tissue, every 2–3 years, in order to detect adenocarcinoma at the earliest possible stage.

Despite the increased use of minimally invasive esophagectomy, the procedure still carries a perioperative mortality rate of 1 % and a morbidity rate of up to 20 %. Although surgery can be lifesaving in the setting of esophageal cancer, functional outcomes related to upper gastrointestinal function remain less than ideal due to esophageal dysmotility. As such, esophageal-sparing procedures have become attractive options for those with HGD or intramucosal (T1) esophageal malignancies. These techniques aim to eliminate dysplastic areas before malignant transformation. One such technique is endoscopic mucosal resection (EMR) through which focal areas of concern can be resected while preserving the esophagus and its function. Thus, EMR may provide a potential cure for early esophageal cancer through endoscopic resection of suspicious lesions otherwise managed through esophagectomy.

Stomach

The incidence of gastric cancer has decreased substantially over the last 50 years, likely due to changes in food preparation and storage. However, it remains the most common cancer diagnosed in most Asian countries [8]. Diet remains the main risk factor for gastric cancer. High intake of salted, smoked, cured, or pickled foods increases risk, while high consumption of fruits and vegetables lowers the risk [9]. Smoking, genetic factors, and blood type A are also implicated [10].

Population-based screening in Japan has led to earlier detection, with nearly 50 % of gastric cancers being diagnosed as early-stage disease [11]. Gastrectomy with lymph node dissection has been the gold standard for all patients with operable gastric cancer, including early T1 lesions. However this approach of radical surgery carries significant risks of morbidity and mortality and can be associated with a long-term reduction in patients' quality of life [12]. As such EMR has become the

cornerstone of treatment in early gastric cancers in Asian countries [13]. Unfortunately, given the lack of formalized screening, late presentation still predominates in Western countries [14].

Duodenum

Duodenal adenomas can occur as part of a familial polyposis syndrome such as familial adenomatous polyposis (FAP) or as sporadic duodenal adenomas (SDAs). Given the rarity of FAP, the majority of duodenal adenomas found at endoscopy are of the sporadic type. Duodenal adenomas have the potential for malignant transformation, although the rate of this is unknown [15, 16]. Traditionally SDAs have been treated with radical surgical excision, most commonly the Whipple procedure. However, the mortality (<5 %) and morbidity (37–41 %) rates remain high for surgical resection [17]. Endoscopic resection of duodenal lesions is technically challenging given the small space, sharp curve, and thin wall of the duodenum [18]. Combined with the fact that duodenal adenomas are a rare entity, there is less data in the literature regarding safety and efficacy [19].

Other lesions, such as carcinoid tumors, may also arise in the duodenum, albeit at lower rates than gastric and rectal carcinoids. In general, carcinoid tumors of the GI tract that are limited to the submucosal layer and small in size (<10 mm) demonstrate a low frequency of lymph node metastasis and are good candidates for endoscopic resection. Although there are no formal recommendations, endoscopic resection appears to be safe and effective for these lesions in early studies [20].

Patient Selection and Preoperative Considerations

As with all invasive procedures, a pre-procedure history and physical exam are required to elucidate cardiac and respiratory risk factors. Conscious sedation or monitored anesthesia care is necessary for complex endoscopic resections. Patients at risk for aspiration should be considered for general endotracheal anesthesia [21].

Work-up for the preceding pathologies requires a systematic approach to defining the depth of invasion, and ruling out metastatic disease

Table 13.1. Esophageal cancer work-up.

H&P
Upper GI endoscopy and biopsy
CT of chest/abdomen
PET-CT if no evidence of M1 disease
EUS if no evidence of M1 disease
EMR considered if:
Lesion <2 cm
Well or moderate differentiation
No invasion beyond muscularis mucosa
No lymphovascular invasion
Clear lateral and deep margins

Summary of NCCN guidelines for esophageal cancer work-up [22]

Table 13.2. Gastric cancer work-up.

H&P
Upper GI endoscopy and biopsy
CT of chest/abdomen/pelvis
PET-CT if no evidence of M1
EUS if no evidence of M1
EMR considered if:
≤2 cm in diameter
Well or moderately differentiated
Limited to superficial submucosa
No lymphovascular invasion
Clear lateral and deep margins

Summary of NCCN guidelines for gastric cancer work-up [23]

(Tables 13.1 and 13.2). The role of EMR in the management of esophageal and gastric cancers includes definitive therapy in cases of superficial lesions, or as part of the preoperative work-up in patients with more invasive lesions. In particular, when combined with endoscopic ultrasound, EMR provides an accurate staging modality. Resected specimens are typically larger than traditional forceps biopsies, allowing more accurate T staging [24, 25]. EMR will often upgrade or downgrade the pre-procedure diagnoses and change patient management.

In terms of esophageal lesions, EMR can be used for premalignant (high-grade dysplasia in BE) and T1N0 intramucosal carcinoma (IMC)

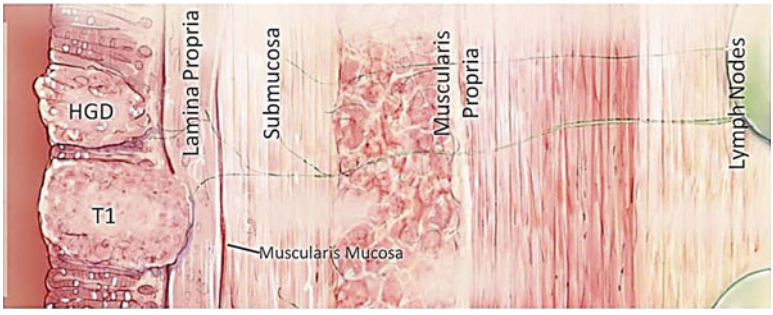

Fig. 13.1. Diagram of the layers of the esophageal wall with depth of lesions amenable to endoscopic resection. Adapted from Spechler SJ. Barrett esophagus and risk of esophageal cancer: a clinical review. *JAMA*. 2013;310(6):627–36 [29].

(Fig. 13.1). The risk of unexpected lymph-node metastases for patients with T1 lesions of the esophagus is in the range of 1–2 % [26]. Therefore EMR can be curative in patients with HGD or T1 lesions with proper work-up to ensure correct staging.

Similar to early esophageal cancers, early gastric cancers (EGC) have demonstrated low risk of metastatic disease if certain features are present. Gotoda et al. reviewed over 3000 patients undergoing gastrectomy with D2 dissection. The absence of lymphovascular involvement in moderately to well-differentiated adenocarcinoma limited to the superficial submucosa carries an acceptably low risk of lymph node metastasis [27]. Therefore these patients are ideal for EMR [28].

Technique

The following EMR techniques are designed to completely remove pathologic mucosa by dissection through the submucosa (Fig. 13.1). Before starting, it may be helpful to superficially mark the margins of the target lesion with cautery. The following techniques are ideally used on lesions 2 cm or smaller due to the size of the cap, ligation devices, and snare. Piecemeal resection of larger lesions is not recommended because it prevents accurate pathologic evaluation. These larger lesions are likely more suitable for endoscopic submucosal dissection (Chap. 15).

Injection-Assisted EMR

This technique starts by injecting saline in the submucosal space under the lesion in order to elevate the mucosa and produce an easier target to snare. This step provides a "safety cushion" by minimizing mechanical or electrocautery damage to the deep layers of the GI tract wall. Resection of the target lesion is performed with a standard snare technique. The method may be modified by using a dual-channel endoscope wherein a grasping forceps is inserted into one channel to lift the lesion and a snare is inserted into the second channel to loop around the base of the lesion. For large gastric lesions, countertraction can be provided via forceps inserted through a separate percutaneous endoscopic gastrostomy tract [30].

Cap-Assisted EMR

This technique utilizes an endoscope fitted with a cap capable of applying suction to the lesion of interest. The lesion is then resected with a standard snare excision technique (Fig. 13.2). The available cap-assisted mucosectomy devices differ primarily in the characteristics of the cap. Caps are composed of clear plastic that may be soft or hard. The caps are cylindrical and available with flat circular (straight) or oblique-shaped tips, both with outer diameters ranging from 12.9 to 18 mm. The oblique caps are usually used for resection of esophageal lesions, to compensate for the parallel position of the endoscope relative to the esophageal wall, whereas the straight caps are most commonly used for gastric EMR [30].

Ligation-Assisted EMR

In ligation-assisted EMR, a variceal band ligation device is positioned over the target lesion with or without prior submucosal injection. Suction is applied to retract the lesion into the banding device, and a band is deployed to capture the lesion (Fig. 13.3). The band has enough contractile force to squeeze the mucosal and submucosal layers, but it is not strong enough to capture the muscularis propria layer. The banding device is then removed and a standard electrocautery snare is used to resect the lesion above or below the band [30].

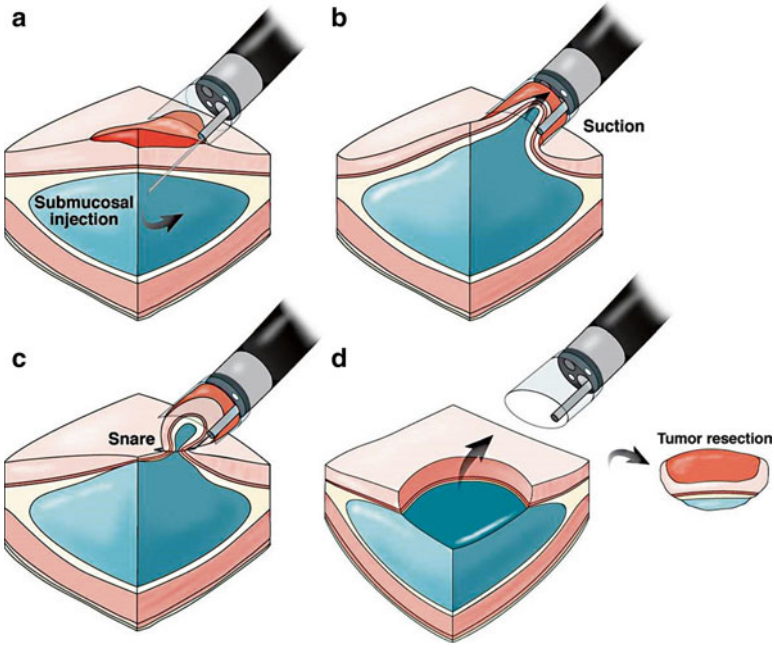

Fig. 13.2. Cap-assisted EMR: Injection of saline to raise target lesion (**a**). Suction used to raise lesion into cap (**b**). Snare is inserted into working channel and deployed around lesion (**c**). Specimen with rim of normal tissue removed (**d**). From Chandrasekhara V, and Ginsberg G. Endoscopic Mucosal Resection: Not Your Father's Polypectomy Anymore. *Gastroenterology* 2011;141:42–49 [31]. Reprinted with permission from Elsevier.

For all techniques, appropriate and adequate depth of resection is a key factor in determining effectiveness, durability, and side effects. The optimal depth of resection should extend down to include the muscularis mucosa (Fig. 13.1), allowing for complete resection of metaplastic cells. Resection deeper into the submucosa results in high rates of stricture and perforation. Handling the resected specimen with care is essential and must be carefully examined for accurate staging [32].

The amount of saline used in each technique is typically in the range of 5–50 ml depending on lesion size. The solution often dissipates within a few minutes, necessitating re-injection. Various other solutions have been tested (hyaluronic acid, hydroxypropyl methylcellulose, glycerol, fibrinogen), but cost, availability, and inflammatory reactions have limited their use. Autologous blood may provide a longer lasting cush-

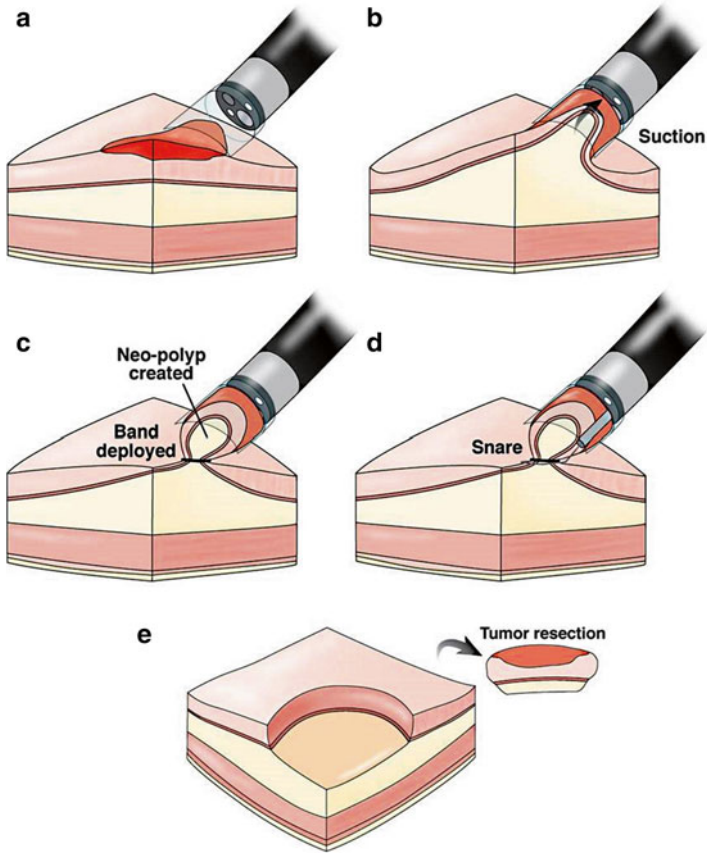

Fig. 13.3. Ligation-assisted EMR: Cap is positioned over lesion (**a**) and suction is used to raise lesion into cap (**b**). Band is deployed around lesion (**c**). The neo-polyp is then resected using electrocautery snare (**d**). Specimen with rim of normal tissue removed (**e**). From Chandrasekhara V, and Ginsberg G. Endoscopic Mucosal Resection: Not Your Father's Polypectomy Anymore. *Gastroenterology* 2011;141:42–49 [31]. Reprinted with permission from Elsevier.

ion without inflammation [33]. If a cushion does not develop during saline injection (i.e., the lesion does not "rise"), EMR should not be attempted (Fig. 13.4). This can be a predictor of deeper invasion, and often the lesion is not amenable to endoscopic removal. Staining dyes, such as indigo carmine or methylene blue, can also be used to mark the deep margin of the specimen.

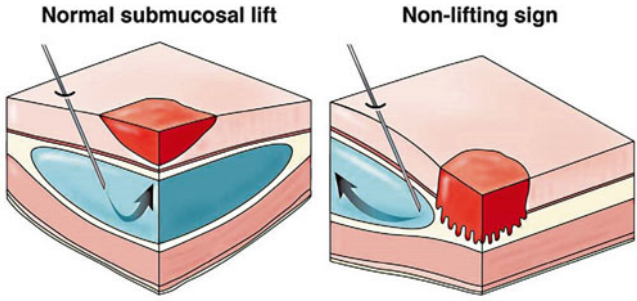

Fig. 13.4. Development of normal cushion during submucosal injection of saline (*left*): Non-lifting of lesion can predict deeper invasion of lesion (*right*). From Chandrasekhara V, and Ginsberg G. Endoscopic Mucosal Resection: Not Your Father's Polypectomy Anymore. *Gastroenterology* 2011;141:42–49 [31]. Reprinted with permission from Elsevier.

Avoiding Complications

Bleeding

Bleeding is categorized as early, occurring during the procedure, and delayed, occurring up to 30 days after the completion of the procedure. Estimated rates of early and late bleeding are on the order of 5 and 3 %, respectively, for esophageal resections [34, 35]. Larger resection size increases the risk for both immediate and delayed bleeding. Early bleeding is usually identified as oozing or a visible bleeding vessel at the end of the procedure. Endoscopic clips, epinephrine injections, endoloops, and cautery can all be used to control bleeding. Using clips or injections when a visible vessel is seen is effective in preventing early bleeding [36].

Duodenal resections are associated with a higher rate of bleeding, particularly delayed bleeding [37]. Lepilliez et al. found that clipping and/or APC of the resection bed in duodenal EMR can significantly reduce the rates of delayed bleeding, which can be as high as 22–33 % [18].

For patients on anticoagulation, temporary cessation of antiplatelet medications, and prompt resumption after EMR, has not been associated with an increased risk of bleeding [38]. However, prolonged cessation

does increase the risk of cardiac ischemic events [36]. Current guidelines from the American Society of Gastrointestinal Endoscopy guidelines recommend stopping anticoagulation 5–7 days prior to the procedure, with resumption on post-procedure day 1 [39].

Stricture

EMR-induced strictures are encountered most commonly in relation to esophageal resections. The rates of stricture are related to the extent of resection, with both large mucosal resections and resection of multiple lesions at the initial procedure, implicated as risk factors [40]. Several techniques to prevent strictures are being investigated. These include injection of anti-scarring agents into the BE resection bed (e.g., steroids, mitomycin) [41], systemic anti-inflammatory agents (e.g., steroids) [42], prophylactic biodegradable stent placement [43], and application of autologous cells [44]. Prophylactic pneumatic dilation, 7 days after circumferential BE resection, has also been tried, but little data is available regarding its efficacy and risks [45]. The current approach to esophageal stenosis post-EMR is treatment with endoscopic dilation. The major risk factor of endoscopic dilation is perforation with reported rates of approximately 1 % [46, 47].

Perforation

Perforations are extremely rare in EMR of the esophagus and stomach [48]. If perforation occurs, it usually manifests as mediastinal emphysema. In an otherwise stable patient, conservative management can be trialed. Rarely is surgery necessary for perforation following esophageal EMR [49, 50]. Duodenal EMR carries a higher risk of perforation (up to 2 %) likely due to the thinner wall of the duodenum and limited space to maneuver the endoscope [51].

Complete Barrett's Eradication vs. Targeted Resection

Although targeted EMR of visible lesions is effective, synchronous lesions and a high rate of recurrence have prompted some endoscopists to employ circumferential EMR, with the goal of complete Barrett's

Table 13.3. Complete Barrett's eradication-EMR.

	Patients, *n*	Follow-up (months)	Outcome	Stricture formation (%)
Seewald et al. [59]	12	9[a]	100 % Complete removal	16
Giovannini et al. [68]	21	18[b]	62 % Complete removal	0
Peters et al. (2006)	37	11[a]	81 % Complete removal	27
Larghi et al. (2007)	24	28[a]	87.5 % Complete removal	12.5

[a]Median
[b]Mean

eradication (CBE). This can be performed using any of the above techniques. The most common approach is to resect ≤50 % of the esophageal circumference in one session, followed by a repeat sessions at 6–8 weeks until the visible Barrett's is completely eradicated. Chennat et al. demonstrated that stricture rates were higher when complete BE eradication was attempted in one session as compared to a multistep approach (i.e., every 2–6 months until complete eradication of all BE) (51 % vs. 26 %, $p<0.01$, respectively). The authors speculate that the presence of larger areas of directly adjacent ulceration might predispose to stricture formation [52]. Generally, most patients are instructed to consume liquids for the first 24 h, followed by soft foods, and then a regular diet by post-procedure day 3 [24].

Circumferential EMR results in a complete response in 62–100 % of patients (Table 13.3), whereas residual disease (synchronous lesions) is detected in 11–45 % of patients undergoing targeted EMR, thereby necessitating frequent surveillance [34, 35, 53–58]. Further studies are needed before formal recommendations can be made on "relaxing" surveillance after CBE.

Conclusions

EMR has evolved into an effective alternative to surgery for early-stage cancers of the upper GI tract. However, as with any technology, there are associated risks and complications. Therefore, when employing EMR a thorough understanding of potential risks, and techniques for avoiding or dealing with these complications, is mandatory (Table 13.4).

Table 13.4. Summary of effectiveness and complications of EMR.

Organ	References	Initial effectiveness (%)	Metachronous/ recurrence (%)	Bleeding (%)	Perforation (%)	Stricture (%)
Esophagus	[34, 35, 48, 60–62]	64–99	11–30	1.2–11	0–0.4	0–7.1
Stomach	[63]	43–59	5	7.09	1.03	–
Duodenum	[18, 64–67]	70–100	22–28	4–13.9	0–2.3	–

EMR can be curative for lesions restricted to the mucosa and may be considered in selected patients with submucosal disease and no lymphovascular invasion. Risk of metastatic cancer is acceptably low in this setting. Therefore success is dependent upon accurate patient selection. Endoscopic surveillance should continue post-procedure to monitor for metachronous lesions.

References

1. Brown LM, Devesa SS, Chow WH. Incidence of adenocarcinoma of the esophagus among white Americans by sex, stage, and age. J Natl Cancer Inst. 2008;100(16): 1184–7.
2. Pohl H, Sirovich B, Welch HG. Esophageal adenocarcinoma incidence: are we reaching the peak? Cancer Epidemiol Biomarkers Prev. 2010;19:1468–70.
3. Engel LS, Chow WH, Vaughan TL, Gammon MD, Risch HA, Stanford JL, et al. Population attributable risks of esophageal and gastric cancers. J Natl Cancer Inst. 2003;95:1404–13.
4. Aichler M, Walch A. In brief: the (molecular) pathogenesis of Barrett's oesophagus. J Pathol. 2014;232(4):383–5.
5. Shaheen NJ, Crosby MA, Bozymski EM, Sandler RS. Is there a publication bias in reporting cancer risk in Barrett's esophagus? Gastroenterology. 2000;119:333–8.
6. van Soest EM, Dieleman JP, Siersema PD, Sturkenboom MC, Kuipers EJ. Increasing incidence of Barrett's esophagus in the general population. Gut. 2005;54:1062–6.
7. Sharma P, Falk GW, Weston AP, Reker D, Johnston M, Sampliner RE. Dysplasia and cancer in a large multicenter cohort of patients with Barrett's esophagus. Clin Gastroenterol Hepatol. 2006;4:566–72.
8. Roder DM. The epidemiology of gastric cancer. Gastric Cancer. 2002;5(1):5–11.
9. Ekstrom AM, Serafini M, Nyren O, Hansson LE, Ye W, Wolk A. Dietary antioxidant intake and risk of cardia cancer and noncardia cancer of the intestinal types: a population-based casecontrol study in Sweden. Int J Cancer. 2000;87:133–40.
10. Nomura A. Stomach cancer. In: Schottenfeld D, Fraumeni JF, editors. Cancer epidemiology and prevention. 2nd ed. New York: Oxford University Press; 1996. p. 707–24.
11. Maruyama K, Kaminishi M, Hayashi K, Isobe Y, Honda I, Katai H, et al. Gastric cancer treated in 1991 in Japan: data analysis of nationwide registry. Gastric Cancer. 2006;9:51–66.
12. Bonenkamp JJ, Songun I, Hermans J, Sasako M, Welvaart K, Plukker JT, et al. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. Lancet. 1995;345:745–8.
13. Gotoda T. Endoscopic resection of early gastric cancer: the Japanese perspective. Curr Opin Gastroenterol. 2006;22(5):561–9.
14. Strong VE, Song KY, Park CH, Jacks LM, Gonen M, Shah M, et al. Comparison of gastric cancer survival following R0 resection in the United States and Korea using an internationally validated nomogram. Ann Surg. 2010;251:640–6.

15. Sellner F. Investigations on the significance of the adenomacarcinoma sequence in the small bowel. Cancer. 1990;66:702–15.
16. Witteman BJ, Janssens AR, Griffioen G, Lamers CB. Villous tumours of the duodenum: an analysis of the literature with emphasis on malignant transformation. Neth J Med. 1993;42:5–11.
17. Cameron JL, Riall TS, Coleman J, Belcher KA. One thousand consecutive pancreaticoduodenectomies. Ann Surg. 2006;244:10–5.
18. Lepilliez V, Chemaly M, Ponchon T, Napoleon B, Saurin JC. Endoscopic resection of sporadic duodenal adenomas: an efficient technique with a substantial risk of delayed bleeding. Endoscopy. 2008;40:806–10.
19. Endo M, Abiko Y, Oana S, Kudara N, Chiba T, Suzuki K, et al. Sefulness of endoscopic treatment for duodenal adenoma. Dig Endosc. 2010;22:360–5.
20. Kim GH, Kim JI, Jeon SW, Moon JS, Chung IK, Jee SR, et al. Endoscopic resection for duodenal carcinoid tumors: a multicenter, retrospective study. J Gastroenterol Hepatol. 2014;29(2):318–24.
21. Agostoni M, Fanti L, Gemma M, Pasculli N, Beretta L, Testoni PA. Adverse events during monitored anesthesia care for GI endoscopy: an 8-year experience. Gastrointest Endosc. 2011;74(2):266–75.
22. Ajani JA, D'Amico TA, Almhanna K, Beer DG, Bentrem DJ, Besh S, et al. Esophageal cancer. JNCCN. 2014;v1.
23. Ajani JA, D'Amico TA, Almhanna K, Beer DG, Bentrem DJ, Besh S, et al. Gastric cancer. JNCCN. 2014;1.
24. Larghi A, Lightdale CJ, Memeo L, Bhagat G, Okpara N, Rotterdam H. EUS followed by EMR for staging of high-grade dysplasia and early cancer in Barrett's esophagus. Gastrointest Endosc. 2005;62(1):16–23.
25. Mino-Kenudson M, Brugge WR, Puricelli WP, Nakatsuka LN, Nishioka NS, Zukerberg LR, et al. Management of superfi cial Barrett's epithelium-related neoplasms by endoscopic mucosal resection: clinicopathologic analysis of 27 cases. Am J Surg Pathol. 2005;29:680–6.
26. Dunbar KB, Spechler SJ. The risk of lymph-node metastases in patients with high-grade dysplasia or intramucosal carcinoma in Barrett's esophagus: a systematic review. Am J Gastroenterol. 2012;107(6):850–62.
27. Gotoda T, Yanagisawa A, Sasako M, Ono H, Nakanishi Y, Shimoda T, et al. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. Gastric Cancer. 2000;3:219–25.
28. Moss A, Bourke MJ, Hourigan LF, Gupta S, Williams SJ, Tran K. Endoscopic resection for Barrett's high-grade dysplasia and early esophageal adenocarcinoma: an essential staging procedure with long-term therapeutic benefit. Am J Gastroenterol. 2010;105(6):1276–83.
29. Spechler SJ. Barrett esophagus and risk of esophageal cancer: a clinical review. JAMA. 2013;310(6):627–36.
30. ASGE Technology Committee, Kantsevoy SV, Adler DG, Conway JD, Diehl DL, Farraye FA, et al. Endoscopic mucosal resection and endoscopic submucosal dissection. Gastrointest Endosc. 2008;68(1):11–8.

31. Chandrasekhara V, Ginsberg G. Endoscopic mucosal resection: not your father's polypectomy anymore. Gastroenterology. 2011;141:42–9.
32. Soetikno R, Kaltenbach T, Yeh R, Gotoda T. Endoscopic mucosal resection for early cancers of the upper gastrointestinal tract. J Clin Oncol. 2005;23(20):4490–8.
33. Sato T. A novel method of endoscopic mucosal resection assisted by submucosal injection of autologous blood (blood patch EMR). Dis Colon Rectum. 2006;49(10):1636–41.
34. May A, Gossner L, Pech O, Fritz A, Günter E, Mayer G, et al. Local endoscopic therapy for intraepithelial high-grade neoplasia and early adenocarcinoma in Barrett's oesophagus: acute-phase and intermediate results of a new treatment approach. Eur J Gastroenterol Hepatol. 2002;14:1085–91.
35. May A, Gossner L, Pech O, Müller H, Vieth M, Stolte M, et al. Intraepithelial high-grade neoplasia and early adenocarcinoma in short-segment Barrett's esophagus (SSBE): curative treatment using local endoscopic treatment techniques. Endoscopy. 2002;34:604–10.
36. Qumseya BJ, Wolfsen C, Wang Y, Othman M, Raimondo M, Bouras E, et al. Factors associated with increased bleeding post-endoscopic mucosal resection. J Dig Dis. 2013;14(3):140–6.
37. Basford PJ, George R, Nixon E, Chaudhuri T, Mead R, Bhandari P. Endoscopic resection of sporadic duodenal adenomas: comparison of endoscopic mucosal resection (EMR) with hybrid endoscopic submucosal dissection (ESD) techniques and the risks of late delayed bleeding. Surg Endosc. 2014;28(5):1594–600.
38. Namasivayam V, Prasad GA, Lutzke LS, Dunagan KT, Borkenhagen LS, Okoro NI, et al. The risk of endoscopic mucosal resection in the setting of clopidogrel use. ISRN Gastroenterol. 2014;2014:494157.
39. ASGE Standards of Practice Committee, Anderson MA, Ben-Menachem T, Gan SI, Appalaneni V, Banerjee S, et al. Management of antithrombotic agents for endoscopic procedures. Gastrointest Endosc. 2009;70:1060–70.
40. Qumseya B, Panossian AM, Rizk C, Cangemi D, Wolfsen C, Raimondo M, et al. Predictors of esophageal stricture formation post endoscopic mucosal resection. Clin Endosc. 2014;47(2):155–61.
41. Machida H, Tominaga K, Minamino H, Sugimori S, Okazaki H, Yamagami H, et al. Locoregional mitomycin C injection for esophageal stricture after endoscopic submucosal dissection. Endoscopy. 2012;44(6):622–5.
42. Wu Y, Schomisch SJ, Cipriano C, Chak A, Lash RH, Ponsky JL, et al. Preliminary results of antiscarring therapy in the prevention of postendoscopic esophageal mucosectomy strictures. Surgical Endosc. 2014;28(2):447–55.
43. Pauli EM, Schomisch SJ, Furlan JP, Marks AS, Chak A, Lash RH, et al. Biodegradable esophageal stent placement does not prevent high-grade stricture formation after circumferential mucosal resection in a porcine model. Surgical Endosc. 2012;26(12):3500–8.
44. Ohki T, Yamato M, Ota M, Takagi R, Murakami D, Kondo M, et al. Prevention of esophageal stricture after endoscopic submucosal dissection using tissue-engineered cell sheets. Gastroenterology. 2012;143(3):582–8.e1-2.

45. Jovani M, Wallace M. Is complete endoscopic resection still a viable option for barrett's-related dysplasia and neoplasia? Clin Gastroenterol Hepatol. 2014. pii: S1542-3565(14)00979-3.
46. Takahashi H, Arimura Y, Okahara S, Uchida S, Ishigaki S, Tsukagoshi H, et al. Risk of perforation during dilation for esophageal strictures after endoscopic resection in patients with early squamous cell carcinoma. Endoscopy. 2011;43(3):184–9.
47. Riley SA, Attwood SEA. Guidelines on the use of oesophageal dilatation in clinical practice. Gut. 2004;53:i1–6.
48. Tomizawa Y, Iyer PG, Wong Kee Song LM, Buttar NS, Lutzke LS, Wang KK. Safety of endoscopic mucosal resection for Barrett's esophagus. Am J Gastroenterol. 2013;108(9):1440–7.
49. Ishihara R, Iishi H, Uedo N, Takeuchi Y, Yamamoto S, Yamada T, et al. Comparison of EMR and endoscopic submucosal dissection for en bloc resection of early esophageal cancers in Japan. Gastrointest Endosc. 2008;68(6):1066–72.
50. Isomoto H, Yamaguchi N, Minami H, Nakao K. Management of complications associated with endoscopic submucosal dissection/endoscopic mucosal resection for esophageal cancer. Dig Endosc. 2013;25 Suppl 1:29–38.
51. Min YW, Min BH, Kim ER, Lee JH, Rhee PL, Rhee JC, et al. Efficacy and safety of endoscopic treatment for nonampullary sporadic duodenal adenomas. Dig Dis Sci. 2013;58(10):2926–32.
52. Chennat J, Konda VJA, Ross AS, Herreros de Tejada A, Noffsinger A, et al. Complete Barrett's eradication endoscopic mucosal resection: an effective treatment modality for high-grade dysplasia and intramucosal carcinoma – an American single-center experience. Am J Gastroeterol. 2009;104:2684–92.
53. Ell C, May A, Gossner L, Pech O, Günter E, Mayer G, et al. Endoscopic mucosal resection of early cancer and high-grade dysplasia in Barrett's esophagus. Gastroenterology. 2000;118:670–7.
54. 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.
55. Waxman I, Saitoh Y. Clinical outcome of endoscopic mucosal resection for superficial GI lesions and the role of high-frequency US probe sonography in an American population. Gastroenterol Endosc. 2000;52:322–7.
56. Buttar NS, Wang KK, Lutzke LS, Krishnadath KK, Anderson MA. Combined endoscopic mucosal resection and photodynamic therapy for esophageal neoplasia within Barrett's esophagus. Gastrointest Endosc. 2001;54:682–8.
57. Pacifico RJ, Wang KK, Wongkeesong L, Buttar NS, Lutzke LS. Combined endoscopic mucosal resection and photodynamic therapy versus esophagectomy for management of early adenocarcinoma in Barrett's esophagus. Clin Gastroenterol Hepatol. 2003;1:252–7.
58. Peters FP, Kara MA, Rosmolen WD, Aalders MC, Ten Kate FJ, Bultje BC, et al. Endoscopic treatment of high-grade dysplasia and early stage cancer in Barrett's esophagus. Gastrointest Endosc. 2005;61:506–14.
59. Seewald S, Akaraviputh T, Seitz U, Brand B, Groth S, Mendoza G, 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.
60. Ell C, May A, Pech O, Gossner L, Guenter E, Behrens A, et al. Curative endoscopic resection of early esophageal adenocarcinomas (Barrett's cancer). Gastrointest Endosc. 2007;65(1):3–10.
61. 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.
62. Perry KA, Walker JP, Salazar M, Suzo A, Hazey JW, Melvin WS. Endoscopic management of high-grade dysplasia and intramucosal carcinoma: experience in a large academic medical center. Surg Endosc. 2014;28(3):777–82.
63. Park YM, Cho E, Kang HY, Kim JM. The effectiveness and safety of endoscopic submucosal dissection compared with endoscopic mucosal resection for early gastric cancer: a systematic review and metaanalysis. Surg Endosc. 2011;25(8):2666–77.
64. Hirasawa R, Iishi H, Tatsuta M, Ishiguro S. Clinicopathologic features and endoscopic resection of duodenal adenocarcinomas and adenomas with the submucosal saline injection technique. Gastrointest Endosc. 1997;46(6):507–13.
65. Apel D, Jakobs R, Spiethoff A, Riemann JF. Follow-up after endoscopic snare resection of duodenal adenomas. Endoscopy. 2005;37(5):444–8.
66. Alexander S, Bourke MJ, Williams SJ, Bailey A, Co J. EMR of large, sessile, sporadic nonampullary duodenal adenomas: technical aspects and long-term outcome (with videos). Gastrointest Endosc. 2009;69(1):66–73.
67. Kedia P, Brensinger C, Ginsberg G. Endoscopic predictors of successful endoluminal eradication in sporadic duodenal adenomas and its acute complications. Gastrointest Endosc. 2010;72(6):1297–301.
68. Giovannini M, Bories E, Pesenti C, Moutardier V, Monges G, Danisi C, Lelong B, Delpero JR. Circumferential endoscopic mucosal resection in Barrett's esophagus with high-grade intraepithelial neoplasia or mucosal cancer. Preliminary results in 21 patients. Endoscopy. 2004;36(9):782–7.

14. Endoscopic Mucosal Resection: Colon and Rectum

Tushar S. Samdani and Toyooki Sonoda

Introduction

The technique of endoscopic mucosal resection (EMR) is utilized for the removal of superficial neoplasms from the lumen of the gastrointestinal (GI) tract. In the simplest terms, EMR involves the removal of a gastrointestinal lesion through an endoscope using a snare. Of course, there are variations to this technique, and the procedure comes with a learning curve. In general, EMR is used for lesions less than 2 cm in size with a depth of invasion limited to the mucosa or submucosa, although this method can be applied to larger benign lesions in a piecemeal manner. First developed for the treatment of early gastric cancer, EMR is now widely utilized in the colon and rectum for the treatment of adenomas or early carcinomas. This chapter discusses the history, indications/contraindications, technical aspects, and complications of EMR in the large intestine.

Evolution of EMR

- 1955: Saline-assisted polypectomy was performed through a rigid proctosigmoidoscope.
- 1968: Gastric polyps were resected using high-frequency current.
- 1973: Colonic polyps were resected using a high-frequency electrosurgical unit.
- 1974: Endoscopic polypectomy was performed for pedunculated or semipedunculated early gastric cancer.

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- 1984: Strip biopsy snare resection technique with submucosal injection of physiological saline lead to the development of EMR [1].
- 1988: Endoscopic resection performed with local injection of hypertonic saline and epinephrine solution (ERHSE).
- 1992: EMR with cap-fitted panendoscope (EMRC) method was performed.
- 1997: EMR using ligation (EMR-L) technique was developed, which was subsequently extended to EMR using multi-band ligation (EMR-MBL).

Indications and Contraindications for EMR

EMR is indicated for superficial neoplasms of the GI tract with low risk of lymph node metastasis, and can be a curative procedure for these lesions. The definition of superficial invasion is the invasion of the *mucosal* or *submucosal* layers of the bowel. The assessment of low- and high-risk lesions for lymph node metastasis is critical in the selection of lesions that are amenable to EMR, since no lymph node harvest is performed with this procedure.

The risk of lymph node metastasis is negligible in mucosal carcinomas, and thus these lesions are indications for EMR. For submucosal invasion (T1 adenocarcinomas), the risk of lymph node metastasis is between 6.3 and 17.0 % [2, 3]. Factors that have been reported to increase the risk of lymph node metastasis include poor histologic grade (such as poorly differentiated, signet ring, or mucinous carcinomas), lymphovascular invasion, tumor budding, and deep submucosal invasion >1 mm [4–6]. A lesion with any one of these findings should be treated with a segmental bowel resection and not EMR. According to a Japanese collaborative study, the rate of lymph node metastasis was 0 % when submucosal invasion was limited to 1 mm in depth or less, and thus these lesions are an indication for EMR so long as the endoscopist is technically proficient [5].

In cases of potential submucosal invasion, EMR should accomplish a complete en bloc resection in one piece, as this allows for accurate histopathologic analysis. For lesions with significant submucosal invasion, the EMR specimen then becomes the “biopsy,” after which patients are referred for a segmental resection. For lesions larger than 2 cm, an en bloc polypectomy may be difficult, and in these cases endoscopic submucosal dissection (ESD) may be required. ESD, however, is a much

more technically challenging and time-consuming procedure compared to EMR, with higher complication rates. A more practical approach to larger and defiant sessile polyps, in cases where a lesion appears to be benign, is to apply EMR in a piecemeal fashion.

The assessment of deep submucosal invasion can be predicted by the morphologic appearance of the lesion through the endoscope, but this requires a highly trained endoscopist. Extensive research in Japan has led to accurate preoperative characterization and staging of neoplastic lesions of the GI tract. Excavated lesions (Paris 0-III) or nonpolypoid lesions (Paris 0-II) with a non-granular surface or invasive pit pattern on magnified chromoendoscopy suggest deeper submucosal invasion [7] and should be excluded from consideration of EMR.

A non-lifting sign, or when a polyp fails to lift upon submucosal injection, is a highly accurate predictor of deep submucosal invasion [8] and EMR should not be attempted in these patients. Not only will EMR risk undertreatment of cancer, but also the chance of perforation is increased in this setting. The exception to this rule, however, is in patients who have had prior EMR, where non-lifting is due to submucosal fibrosis and not tumor invasion. If the original pathology was benign, then EMR can proceed cautiously, but a piecemeal resection with smaller specimens may be required to prevent perforation. Uncorrectable coagulopathy is also a contraindication for EMR.

Techniques of EMR

The technique of EMR is widely divided into three categories: (1) injection-assisted, (2) suction-assisted, and (3) band-assisted. The injection-assisted, or "saline lift," EMR is by far the most common method of EMR in the colon and rectum, and is covered in this chapter. It is performed by injecting fluid underneath the mucosal layer, creating a submucosal bleb which raises the lesion off of the muscularis propria, after which a snare is passed over the lesion and the lesion is removed using electrical current (Fig. 14.1). The lesion is then retrieved using an endoscopic net such as a Roth Net® (US Endoscopy, Mentor, OH). This is also known as the "strip biopsy" method. The injection of solution provides a cushion to minimize the chance of deep thermal injury to the bowel.

The instruments helpful for a successful EMR are:

- High-definition (HD) colonoscope.
- Electrosurgical unit.

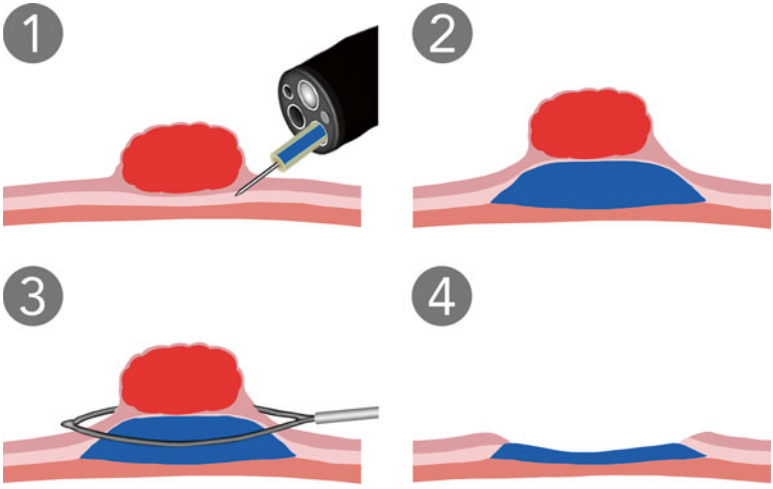

Fig. 14.1. The steps of an injection-assisted EMR: (1) An injection needle is advanced into the submucosal plane. (2) A submucosal bleb is created, which protects the muscularis propria from thermal injury. (3) A snare is passed over the lesion. (4) A snare polypectomy is completed.

- CO_2 insufflator.
- Injection needle.
- Injection solution.
- Snares (assortment of small, standard, or jumbo, and "non-slip").
- Net for specimen retrieval, such as the Roth Net® (US Endoscopy, Mentor, OH).

The strip biopsy method and can also be performed using a double-channel colonoscope (the injection-lift-cut method). In this double-channel method, both a snare and a grasping forceps are advanced through two separate scope channels; the lesion is grasped by the forceps and pulled gently into the open snare, after which the lesion is snared off using electrical current.

The suction-assisted and band-assisted EMR techniques are utilized more commonly in the upper GI tract. Suction-assisted, or cap-assisted mucosal resection (EMRC), is performed with a specialized transparent plastic cap that is fitted to the tip of the endoscope. Lesions are typically

lifted first with a submucosal injection. A snare is opened and positioned on the internal circumferential ridge at the tip of the cap. The mucosa is suctioned into the cap and the snare is then closed to capture the lesion. The lesion is resected with a snare excision. Resected pieces can be collected into the cap and retrieved.

Ligation-assisted EMR utilizes a variceal band ligation device, which is used to create a "polyp" out of a flat lesion. The band is not strong enough to pull in the muscularis propria, and the lesion is snared off in the submucosal plane either above or below the band.

Submucosal Injection

The importance of a good submucosal injection is often underestimated in EMR. This includes both the *choice of injection solution,* as well as the *technique of mucosal elevation*. Although normal saline solution (0.9 %) with or without epinephrine is inexpensive and most commonly utilized for EMR, the downside is that it quickly dissipates. As more saline is injected, the mucosa becomes edematous, at times severely limiting visualization.

Therefore, a more viscous injection fluid can be helpful, and many different solutions have been utilized for this purpose, sometimes in combination, all with pros and cons. These include hyaluronic acid (expensive), hydroxypropyl methylcellulose (or hypromellose, which is used in artificial tears), glycerol, dextrose/fructose, albumin, fibrinogen, or autologous blood. It is important to remember that some hypertonic solutions (such as hyaluronic acid and hydroxypropyl methylcellulose) must be diluted to prevent local inflammation and tissue damage upon injection. It is also helpful to add indigo carmine dye at a concentration of 0.005 % to the injection solution. The light blue discoloration of this solution allows for better demarcation of the mucosal edges of the polyp, and better defines the submucosal layer.

If a polyp is large or located behind a fold, it is helpful to inject the proximal (oral) side of the polyp first, which brings the area most difficult to visualize into view. Subsequent injections of the distal side are then performed. A retroflexion of the colonoscope in the cecum may also be helpful to visualize and inject the proximal aspect of a difficult flat polyp in the right colon, especially one that extends around a fold.

Complex EMR

It is preferable in EMR to remove a colonic lesion in one piece (en bloc resection) with negative margins, but this is not always possible. Many endoscopists elect to perform piecemeal polypectomy for lesions larger than 2 cm by ensnaring multiple adjacent portions of a complex lesion in a sequential manner (Fig. 14.2). However, this piecemeal resection tends to result in higher rates or recurrence compared to en bloc excision. Mannath et al. reported that piecemeal polypectomy increases the chance of recurrent polyp by 5.5 times (95 % CI: 1.1–30.48, $p=0.045$) that of an en bloc resection [9]. Thus, after an EMR, a repeat colonoscopy is advisable in 3–6 months to look for recurrence. After EMR, one must not forget to place a tattoo adjacent to the polypectomy wound as there could be no detectable wound at the follow-up colonoscopy.

In order to decrease the chance of a polyp recurring at its margin, the edges of the polyp can be ablated with thermal therapy. This can be performed with electrocoagulation using a hot biopsy forceps or the tip of a snare, or with argon plasma coagulation (APC). The literature is inconclusive whether the use of complimentary APC reduces the polyp recurrence rate after EMR. One randomized study revealed a lower polyp recurrence rate (63.6 % non-APC vs. 10.0 % APC, $p=0.02$) when APC was used as a routine adjunct to seemingly complete piecemeal polypectomy. However, in this same study, when APC was used to treat the edges of an incompletely resected polyp, the recurrence rate remained high at 46 % [10]. On a practical note, small areas of potential residual adenomatous tissue that remain after EMR, whether treated in a piecemeal manner or not, should be ablated with the aforementioned thermal therapy or resected using a small precise snare such as the Exacto® cold snare (US Endoscopy, Mentor, OH). One often finds that a large snare in this setting does not grab tissue well.

Fig. 14.2. (continued) portion of the polyp after submucosal injection. The *blue* dye solution in the submucosal plane helps define the edges of the polyp. (**e, f**) Snare polypectomy of an adjacent mound of polypoid tissue. (**g**) The edges of the polypectomy wound are treated with thermal therapy using a hot biopsy forceps. (**h**) Polypectomy wound and removal of polyp pieces in a specimen net.

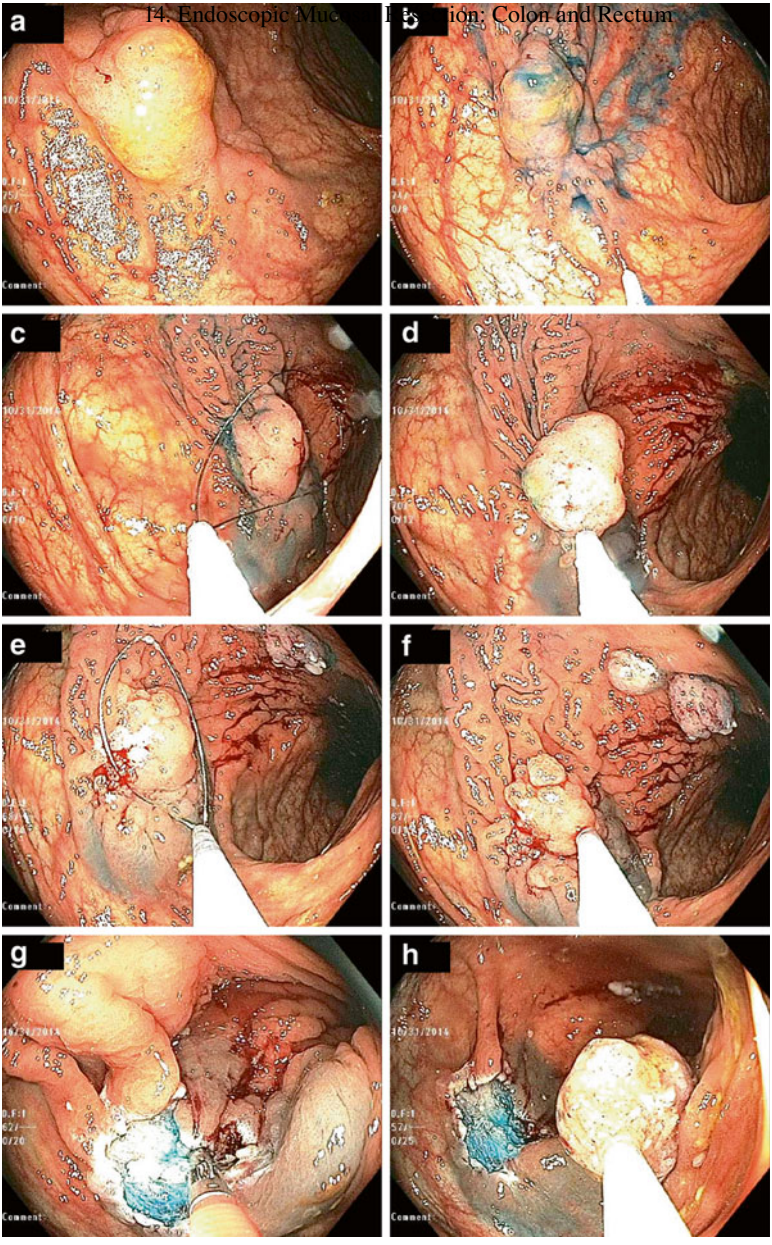

Fig. 14.2. Example of a piecemeal EMR. (**a**) Tubulovillous adenoma with high-grade dysplasia in the hepatic flexure. (**b**) Chromoendoscopy with dilute indigo carmine dye solution highlights the irregular margins of the polyp.This is a difficult polyp for en bloc resection. (**c**, **d**) Snare polypectomy of the largest

Complications

The most common complication after EMR is *bleeding*. Although some large series report rates of post-polypectomy bleeding of 1 % or less, the average rate of bleeding after EMR and ESD appears to be about 10 %. The bleeding can be immediate after the procedure, or occur in a delayed manner (>48 h afterward). In a study that examined the risk factors for bleeding after EMR in 288 patients, the overall rate of post-procedure bleeding was 7 %, and increased risk for bleeding was seen for right-sided colonic lesions (odds ratio [OR] 4.4, $p=0.01$) and use of aspirin (OR 6.3, $p=0.005$). All bleeding occurred before aspirin was restarted, however [11]. In another large prospective multicenter study of over 1000 patients undergoing endoscopic resection for large colonic lesions in Japan, the rate of post-procedure bleeding was only 1.6 % [12].

When post EMR bleeding does occur, the treatment depends on the severity of the bleeding and may range from conservative observation to endoscopic reintervention. Hemostasis is obtained by the placement of hemostatic clips, application of coagulation, or either after injection of epinephrine-containing saline solution (in cases of severe hemorrhage).

Perforation with EMR occurs at two different times: during the procedure and in a delayed manner. Intra-procedure perforation typically occurs in less than 1 % of patients [12], and when recognized at the time of the procedure can usually be managed successfully with the application of endoclips. Delayed perforation can be a manifestation of deep thermal injury and has an increased chance of peritonitis. In these patients the chances of successful intraluminal therapy is small, and most patients will need surgical intervention.

Conclusion

EMR initially emerged as an endolumenal method for the removal of early gastric tumors, and has evolved to now commonly find application in the colon and rectum. Both dysplastic and selected submucosal adenocarcinomas are candidates for EMR so long as there are no adverse features or massive submucosal invasion, as the risk of lymph node metastasis in these lesions is low. Significant training is needed to diagnose and accurately stage a lesion prior to EMR, as well as to safely carry out the

procedure. Patient selection is critical, and is based on both patient factors and endoscopist skill. Complications of EMR can be serious as well as the consequences of a mismanaged early-stage colorectal cancer. Thus an advanced endoscopic skillset is requisite for successful EMR application.

References

1. Tada M, Karita M, Yanai H, Takemoto T. Endoscopic therapy of early gastric cancer by strip biopsy. Gan To Kagaku Ryoho. 1988;15:1460–5. Japanese.
2. Yamamoto S, Watanabe M, Hasegawa H, Baba H, Yoshinare K, et al. The risk of lymph node metastasis in T1 colorectal carcinoma. Hepatogastroenterology. 2004; 51(58):998–1000.
3. Son HJ, Song SY, Lee WY, Yang SS, Park SH, et al. Characteristics of early colorectal carcinoma with lymph node metastatic disease. Hepatogastroenterology. 2008; 55(85):1293–7.
4. Ueno H, Mochizuki H, Hashiguchi Y, Shimazaki H, Aida S, et al. Risk factors for an adverse outcome in early invasive colorectal carcinoma. Gastroenterology. 2004; 127(2):385–94.
5. Kitajima K, Fujimori T, Fujii S, Takeda J, Ohkura Y, et al. Correlations between lymph node metastasis and depth of submucosal invasion in submucosal invasive colorectal carcinoma: a Japanese collaborative study. J Gastroenterol. 2004;39(6): 534–43.
6. Beaton C, Twine CP, Williams GL, Radcliffe AG. Systematic review and meta-analysis of histopathological factors influencing the risk of lymph node metastasis in early colorectal cancer. Colorectal Dis. 2013;15(7):788–97.
7. Matsuda T, Fujii T, Saito Y, Nakajima T, Uraoka T, et al. Efficacy of invasive/non-invasive pattern by magnifying chromoendoscopy to estimate the depth of invasion of early colorectal neoplasms. Am J Gastroenterol. 2008;103(11):2700–6.
8. Uno Y, Munakata A. The non-lifting sign of invasive colon cancer. Gastrointest Endosc. 1994;40(4):485–9.
9. Mannath J, Subramanian V, Singh R, Telakis E, Ragunath K. Polyp recurrence after endoscopic mucosal resection of sessile and flat colonic adenomas. Dig Dis Sci. 2011;56(8):2389–95.
10. Brooker JC, Saunders BP, Shah SG, Thapar CJ, Suzuki N, Williams CB. Treatment with argon plasma coagulation reduces recurrence after piecemeal resection of large sessile colonic polyps: a randomized trial and recommendations. Gastrointest Endosc. 2002;55(3):371–5.
11. Metz AH, 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(6):506–11.
12. Wada Y, Kudo SE, Tanaka S, Saito Y, Ishii H, et al. Predictive factors for complications in endoscopic resection of large colorectal lesions: a multicenter prospective study. Surg Endosc. 2015;29(5):1216–22.

15. Endoscopic Submucosal Dissection: Upper Gastrointestinal Tract

Amit Bhatt, Seiichiro Abe, Arthi Kumaravel, Ichiro Oda, John Vargo, and Yutaka Saito

Introduction

Endoscopic submucosal dissection (ESD) is an advanced endoscopic technique that allows for potentially curative resection of early cancerous lesion of the esophagus and stomach [1–3]. The technique was developed greater than a decade ago in Japan and has become the standard of care there for the treatment of early esophageal and gastric cancer [4, 5]. These techniques allow for the removal of lesions in an en bloc fashion, allowing for precise histopathologic analysis and confirmation of curative resection similar to a surgically removed specimen (Fig. 15.1). As the technique was initially developed for the treatment of early gastric cancer, a condition that is rare in the West, initial Western interest in ESD was limited. With extension of ESD indications to esophageal and colonic lesion Western interest is now increasing.

Comparison to Traditional Endoscopic Mucosal Resection

Traditional endoscopic mucosal resection (EMR) is a well-established technique. It allows for safe and efficient resection of mucosal lesions. Its disadvantage is poor control of lateral margin dissection, and as the size of a lesion increases, EMR's ability to resect it in an en

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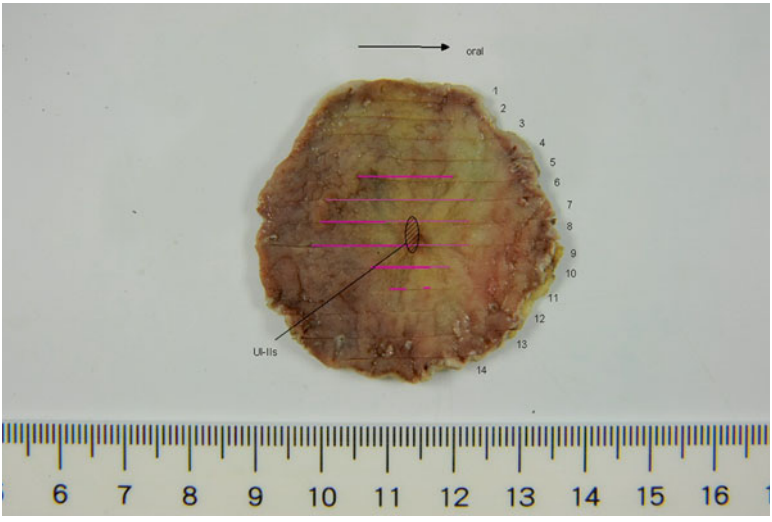

Fig. 15.1. An en bloc-resected specimen of early gastric cancer allowing for precise histopathologic analysis. *Red lines* represent submucosal invasion and *pink lines* represent intramucosal cancer.

Table 15.1. Comparison of EMR to ESD in esophageal SCC.

Size (mm)	EMR en bloc (%)	EMR local recurrence (%)	ESD en bloc (%)	ESD local recurrence (%)
<10	100	0	100	0
11–20	54.5	4.5	96	0
>20	4.5	13.6	97.2	0

SCC squamous cell carcinoma, *EMR* endoscopic mucosal resection, *ESD* endoscopic submucosal dissection

bloc fashion decreases (Table 15.1) [6]. For lesions greater than 2 cm, piecemeal EMR resection is generally required, which is associated with a high risk of local recurrence (Table 15.1) [6]. A large meta-analysis study has compared ESD with EMR, and found higher en bloc and curative resection rates with ESD (Table 15.2) [7]. These advantages of ESD come at a price of a longer procedure time, and higher risk of bleeding and perforation [7].

Table 15.2. Meta-analysis comparing ESD and EMR.

En bloc resection	Favors	Odds ratio (95 % CI)
Esophagus	Favors ESD	24.36 (6.22.95.37)
Stomach	Favors ESD	12.06 (8.40.17.30)
Curative resection		
Esophagus	Favors ESD	6.85 (2.48, 18.97)
Stomach	Favors ESD	2.95 (1.39, 6.25)

EMR endoscopic mucosal resection, *ESD* endoscopic submucosal dissection, *CI* confidence interval

ESD Indications

The main curative difference between endoscopic and surgical resection of cancer is the absence of lymph node dissection with endoscopic technique. Thus endoscopic resection can only be considered in lesions with a negligible risk of lymph node metastasis. This is the driving principle that decides which lesions are amendable to ESD resection and those which require surgery. The risk of lymph node metastasis with early cancer is largely based on the depth of invasion and histology of the lesion. The precise depth of invasion will not be known until the specimen is resected and an important part of our preoperative endoscopic assessment is estimating a lesion's depth of invasion.

Gastric ESD Indications

Gastric cancer is one of the most common cancers in Japan. Due to national screening programs, greater than 50 % of gastric cancer is diagnosed as early gastric cancer [8–10]. Analysis of large series of gastrectomy specimens for early gastric cancer revealed that based on histology, depth of invasion, and presence or absence of an ulcer, certain gastric cancers had a negligible risk of lymph node metastasis. [11–13]. These cancers make up the indications for gastric ESD (Table 15.3) [14].

Esophageal ESD Indications

Factors that need to be weighed when considering esophageal ESD are the unique lymphatics of the esophagus, risk of stricture formation, and the mortality rate associated with esophagectomy. The esophagus is a

Table 15.3. Indications for gastric ESD.

	Mucosal					
	Ulcer (−)		Ulcer (+)		Submucosal	
Pathology	**≤2 cm**	**>2 cm**	**≤3 cm**	**>3 cm**	**≤3 cm**	**Any size**
Differentiated type	ESD/EMR	ESD	ESD	Surgery	ESD	Surgery
Undifferentiated type	ESD	Surgery	Surgery	Surgery	Surgery	Surgery

Adapted from Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines [13]

Table 15.4. Japanese Esophageal Society guidelines for esophageal ESD.

Absolute indications	T1a esophageal cancer involving epithelium or lamina propria	<2/3 the circumference of the esophagus
Relative indications Allow even space between columns	Esophageal cancer involving the muscularis mucosa or < 200 microns Allow even space between columns of the submucosa	

Adapted from guidelines for diagnosis and treatment of carcinoma of the esophagus [20]

unique organ in the gastrointestinal tract, in that the lymphatics penetrate through the muscularis mucosa and reach the lamina propria beneath the basement membrane [15]. This theoretically means that there is a higher risk of lymph node metastasis with early esophageal cancer. Circumferential mucosal resection in the esophagus is associated with a high risk of recalcitrant esophageal stricture formation [16, 17]. The alternative to esophageal ESD is esophagectomy that has a mortality rate of approximately 3 % [18–20]. The Japanese Esophageal Society guidelines recommended that absolute indications for esophageal ESD are intramucosal cancers involving the epithelium and lamina propria occupying less than 2/3 the lumen of the esophagus (Table 15.4) [21]. Relative indications are cancers involving the muscularis mucosa or less than 200 μm invasion of the submucosa (Table 15.4) [21]. Patients who undergo esophageal ESD under a relative indication may need additional treatment with an additional modality due to the higher risk of lymph node metastasis. It should be noted that these guidelines are largely based on the Japanese experience with squamous cell carcinoma (SCC), and esophageal adenocarcinoma (EAC) is the predominant malignancy in the West. Western studies looking at esophagectomy specimens for early EAC showed that the risk of lymph node metastasis ranged from 0 to 2.6 % with T1a cancer [18–20]. This is less than the mortality rate associated with esophagectomy and it seems reasonable to consider ESD in this group.

Preoperative Assessment

The preoperative assessment for ESD is focused on estimating the depth of invasion and precisely defining lateral borders of the lesion. The depth of invasion is estimated based on the macroscopic type and endoscopic features of the lesion as well as high-frequency miniprobe examination [22–24]. The macroscopic type analysis is based on the Japanese Classification of Gastric Carcinoma or the Paris classification that is more commonly known in the West [23, 24]. The lateral borders of early gastric cancer are delineated by using a combination of narrow band imaging and chromoendoscopy with 0.2 % indigo carmine solution. Chromoendoscopy with iodine defines the lateral borders of esophageal SCC, which is an iodine-avoiding lesion. The combination of high-definition white light endoscopy and narrowband imaging is used to define the lateral borders of EAC.

ESD Equipment

The specialized equipment necessary for ESD includes distal attachments, lifting solutions, ESD knives, coagulation devices, and high-performance electrosurgical generators.

Distal Attachments

Distal attachments are clear plastic caps that are placed to the end of the endoscope. They aid in visualization by maintaining distance from the target tissue. They also allow for the counter traction necessary for the endoscope to enter into the submucosal space. Distal attachments are available in different firmness and shape [25]. Straight soft distal attachments work well for gastric and esophageal ESD.

Lifting Solutions

Lifting solutions expand the submucosal layer creating a safe plan for dissection. While normal saline is inexpensive and universally available, it produces a short duration lift as it rapidly diffuses into the surrounding tissues. Glycerol is a hypertonic solution of 10 % glycerin and 5 % fructose. Glycerol produces a soft, long-lasting lift that facilitates

safe ESD [26]. Glycerol is not commercially available in the United States but may be compounded by hospital pharmacies. Hyaluronic acid has high water retention capabilities, and produces an exceptionally long-lasting lift [26, 27]. Inadvertent injection of hyaluronic acid into the muscular layer may obscure visualization, and it is best to confirm the submucosal layer with injection of normal saline or glycerol first. Sodium hyaluronate (MucoUp; Johnson and Johnson, Tokyo, Japan) is commonly used in Japan for ESD but it is not commercially available in the West. It can be compounded by hospital pharmacies. An alternative is to use a mixture of 15 mL hydroxypropyl methylcellulose (Gonak 2.5 %; Akorn Inc, Somerset, NJ) and 85 mL of normal saline [28]. Indigo carmine can be added to the lifting solution used to help define the submucosal layer for dissection.

ESD Knives

There are now a large variety of ESD knives available. The traditional ESD knife types are insulated tip (IT) knives and needle-type knives. These are also the currently available ESD knife types in the West. IT knives have an insulated ceramic ball at the end of the knife, and cut with the blade of the knife (Fig. 15.2). IT knives allow for fast dissection, but the plane of dissection is not always directly visualized and may have to be estimated based on the contour of the muscle layer. Needle-type knives have no insulated component, and cut with the tip of the knife (Fig. 15.2). Needle-type knife dissection is generally slower than IT knife dissection, but allows for direct visualization of the dissection plane. While most knives can be used for gastric ESD, due to the delicate muscular layer of the esophagus, only certain knives are typically used for esophageal ESD to limit the risk of perforation. IT knife nano (Olympus KD-612L/U, Tokyo, Japan), dual knife (Olympus KD-650L/KD-650U, Tokyo, Japan), and hook knife (Olympus KD-620LR/KD-620UR, Tokyo, Japan) are all suitable for esophageal ESD (Fig. 15.2).

Coagulation Devices

Bleeding is common during ESD, and control of bleeding is key to maintaining visualization and ultimately performing successful ESD. Bleeding is mainly treated with coagulation devices, and mechanical devices like hemoclip placement may obstruct the dissection plane for

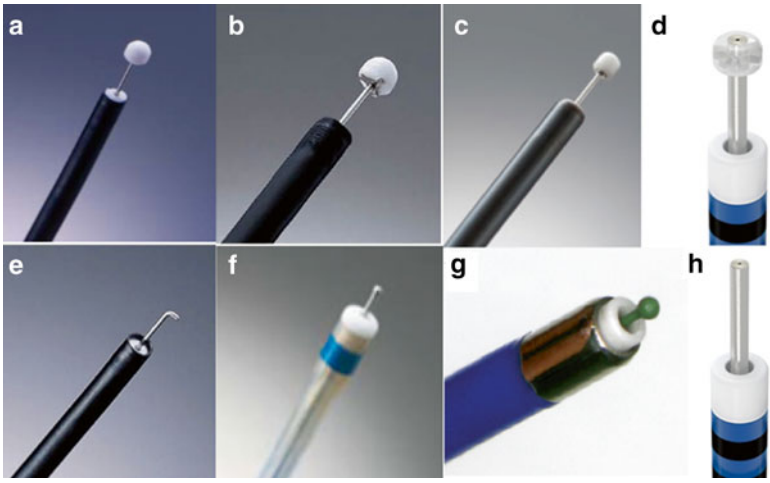

Fig. 15.2. Insulated tip knives (**a**–**d**). Needle-type knives (**e**–**h**). (**a**) IT knife (Olympus KD-612L, Tokyo Japan). (**b**) IT knife 2 (Olympus KD-611L, Tokyo Japan). (**c**) IT knife nano (Olympus KD-612L/U, Tokyo Japan). (**d**) HybridKnife O-Type (ERBE, Germany). (**e**) Hook knife (Olympus KD-620LR/KD-620UR, Tokyo Japan). (**f**) Dual knife (Olympus KD-650L/KD-650U, Tokyo Japan). (**g**) B-knife (B-knife; XEMEX Co.) a ball-tip bipolar needle knife. (**h**) HybridKnife I-type (ERBE, Germany).

further ESD. Excessive coagulation can make subsequent dissection difficult and increases the risk of both immediate and delayed perforation. It is thus important to limit coagulation by precisely identifying the bleeding source and applying focused coagulation to limit tissue damage. Coagulation of vessels is performed with coagulation forceps like monopolar Coag-gaspers (Olympus FD-410LR/FD-411UR, Tokyo Japan), hot biopsy forceps (FD-1L-1; Olympus, Tokyo, Japan), and bipolar HemoStat-Y (H-S2518/H-S2522; Pentax, Tokyo, Japan).

High-Frequency Electrogenerators

A high-performance electrosurgical generator is required to provide the modulated currents necessary for ESD. The commonly used generators include ERBE VIO 200S (ERBE, Tuebingen, Germany), ERBE VIO 300D (ERBE, Tuebingen, Germany), and ESG 100 (Olympus, America). The electrosurgical generator settings vary based on a number

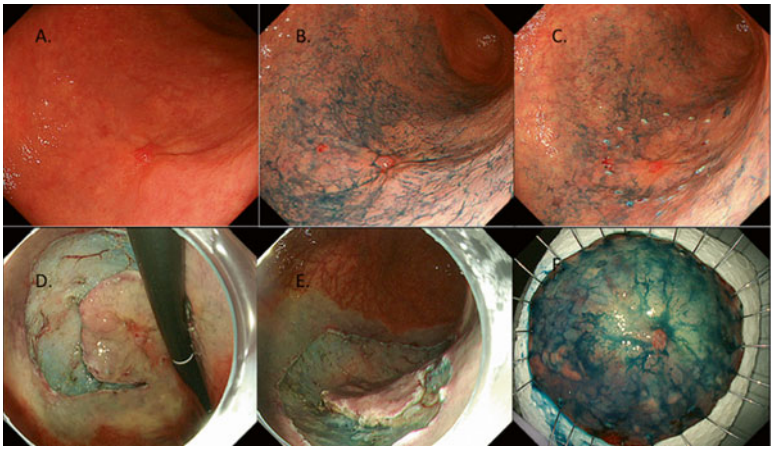

Fig. 15.3. Early gastric cancer. (**a**) High-definition white light endoscopy. (**b**) Chromoendoscopy 0.2 % indigo carmine. (**c**) Mucosal incision. (**d**) Circumferential mucosal incision. (**e**) Resected specimen.

of factors including knife type used, the location of the lesion, and nature of the lesion. As setting may need to be adjusted based on tissue effect, one should contact the manufacturer of their generator to understand electrosurgical generator settings.

Gastric ESD Technique

The steps of ESD involve (1) marking of lateral margins, (2) circumferential incision, and (3) submucosal dissection (Fig. 15.3).

Marking

It is important to mark the lateral margins of a tumor, as these margins become obscured once fluid injection and lateral margin dissection is performed. Marking may be made with either argon plasma coagulation or the tip of a needle-type knife. For early gastric cancer we make marking 5 mm away from the borders, as there can be subepithelial spread of these tumors.

Circumferential Incision

In gastric ESD, a circumferential incision is generally performed around the lesion separating it from the rest of the gastric mucosa. A lifting solution is first injected around the lesion. An initial incision is made with a needle type knife to gain access to the submucosal layer. This initial incision is extended circumferentially with the use of either a needle type knife or IT knife, separating the lesion from the adjacent mucosa. Sometimes, based on the location of the lesion, only a partial circumferential incision is performed prior to submucosal dissection. This is further described in the esophageal ESD technique section below.

Submucosal Dissection

The submucosal layer beneath the lesion is expanded with injection of a lifting solution. The endoscope is advanced beneath the mucosa, and the submucosal layer is dissected with an ESD knife. Care is made to perform dissection parallel to the muscular plane to avoid inadvertent muscular injury.

Esophageal ESD Technique

The narrow lumen of the esophagus limits endoscopic maneuverability making esophageal ESD more technically challenging to perform than gastric ESD. The thin muscle layer of the esophagus increases the risk of perforation, and precise dissection is needed during esophageal ESD (Fig. 15.4).

Marking

Perforations may occur during marking for esophageal ESD due to the thin wall of the esophagus. Marking with APC, or a retracted dual knife or hook knife are acceptable methods for safe marking.

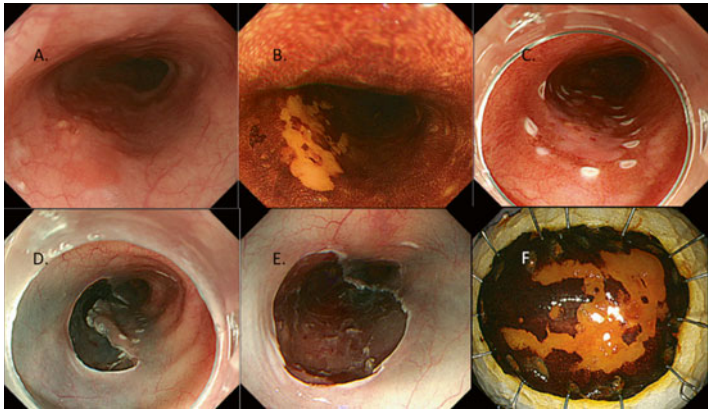

Fig. 15.4. Early esophageal squamous cell carcinoma. (**a**) High-definition white light endoscopy. (**b**) Chromoendoscopy iodine. (**c**) Marking. (**d**) Partial circumferential incision. (**e**) ESD scar after resected specimen. (**f**) Resected specimen.

Circumferential Incision

During esophageal ESD we normally perform only a partial circumferential incision prior to starting submucosal dissection. The partial circumferential incision limits escape of fluid from the submucosal layer allowing for a safer plane of dissection. Initially the oral (proximal) and anal (distal) incisions are made. Mucosal incision along the left lateral border mucosal lesion is then performed allowing the lesion to retract away from the water that may pool on the gravity-dependent side. After partial submucosal dissection is performed, circumferential incision of the right lateral wall is completed.

Submucosal Dissection

After mucosal incision, the exposed submucosal layer is expanded with the injection of lifting solution. In esophageal ESD we prefer a combination of glycerol and hyaluronic acid for a sustained submucosal lift. The submucosa can be dissected with an IT knife nano (Olympus KD-612L/U, Tokyo Japan) or hook knife (Olympus KD-620LR/KD-620UR, Tokyo Japan) by hooking and cutting the submucosa, or by direct contact with the tip of a dual knife (Olympus KD-650L/KD-650U, Tokyo Japan).

Adverse Events

Bleeding

ESD bleeding can be separated into immediate bleeding occurring during the procedure and delayed bleeding occurring after the procedure. Bleeding is common during ESD and managing immediate bleeding is part of performing successful ESD. Significant immediate bleeding has been defined as ≥2 g/dL drop in hemoglobin as compared to pre-procedure values [29]. The risk of immediate bleeding is approximately 7 % with gastric ESD [29]. Bleeding is more common in the proximal stomach due to the larger diameter submucosal vessels in this area. The risk of delayed bleeding with gastric ESD is approximately 5.5 % and is more common in the first 24 h after ESD [29]. The use of proton pump inhibitors and prophylactic coagulation of vessels in the base of the ESD defect has been shown to reduce the risk of delayed bleeding after gastric ESD [30, 31]. Second-look endoscopy was routinely performed to prevent delayed bleeding when gastric ESD was introduced. This practice has largely been discontinued because a randomized controlled trial showed that second-look endoscopy had no clinical benefit to the prevention of delayed bleeding after gastric ESD [32]. Significant bleeding is less common in the esophagus, likely secondary to there being less submucosal vessels in this area [1].

Perforations

Most perforations experienced occur during the ESD procedure itself but delayed perforations may occur. The risk of immediate perforation varies by locations and is 1.6–5.2 % in gastric ESD and 0–6 % in esophageal ESD [3, 29]. The majority of these perforations are small in size can be managed endoscopically with hemoclip closure.

Stricture

Strictures are mainly an adverse event of esophageal ESD but may sometimes occur in the gastric cardia and antrum [16, 33]. Both the size and circumference of mucosal resection in the esophagus are associated with the risk of stricture formation [16]. Both oral and injected steroids have been shown to reduce the risk of post ESD stricture formation [34, 35].

Conclusion

ESD is an advanced endoscopic resection technique allowing for potentially curative resection of early cancerous lesions of the esophagus and stomach while avoiding the mortality and morbidity associated with surgery. It has distinct advantages over traditional EMR technique, especially when a lesion's size is greater than 2 cm. ESD is indicated for treatment of superficial esophageal and gastric cancers greater than 2 cm with a negligible risk of lymph node metastasis. It is now the standard of care in Japan for treatment of early cancers in the esophagus and stomach. Initial Western adoption of the technique was slow due to its flat learning curve and device availability. Many of these barriers have now been overcome and we are seeing an increasing interest and practice of ESD in the West.

References

1. Gotoda T, Ho KY, Soetikno R, Kaltenbach T, Draganov P. Gastric ESD: current status and future directions of devices and training. Gastrointest Endosc Clin N Am. 2014;24(2):213–33.
2. 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.
3. Ono S, Fujishiro M, Koike K. Endoscopic submucosal dissection for superficial esophageal neoplasms. World J Gastrointest Endosc. 2012;4(5):162–6.
4. Hirao M, Masuda K, Asanuma T, Naka H, Noda K, Matsuura K, et al. Endoscopic resection of early gastric cancer and other tumors with local injection of hypertonic saline-epinephrine. Gastrointest Endosc. 1988;34(3):264–9.
5. Gotoda T, Kondo H, Ono H, Saito Y, Yamaguchi H, Saito D, et al. A new endoscopic mucosal resection procedure using an insulation-tipped electrosurgical knife for rectal flat lesions: report of two cases. Gastrointest Endosc. 1999;50(4):560–3.
6. Yamashita T, Zeniya A, Ishii H, Tsuji T, Tsuda S, Nakane K, et al. Endoscopic mucosal resection using a cap-fitted panendoscope and endoscopic submucosal dissection as optimal endoscopic procedures for superficial esophageal carcinoma. Surg Endosc. 2011;25(8):2541–6.
7. Cao Y, Liao C, Tan A, Gao Y, Mo Z, Gao F. Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract. Endoscopy. 2009;41(9):751–7.
8. Nakamura K, Ueyama T, Yao T, Xuan ZX, Ambe K, Adachi Y, et al. Pathology and prognosis of gastric carcinoma. Findings in 10,000 patients who underwent primary gastrectomy. Cancer. 1992;70(5):1030–7.

9. Nashimoto A, Akazawa K, Isobe Y, Miyashiro I, Katai H, Kodera Y, et al. Gastric cancer treated in 2002 in Japan: 2009 annual report of the JGCA nationwide registry. Gastric Cancer. 2013;16(1):1–27.
10. Shimizu S, Tada M, Kawai K. Early gastric cancer: its surveillance and natural course. Endoscopy. 1995;27(1):27–31.
11. Yamao T, Shirao K, Ono H, Kondo H, Saito D, Yamaguchi H, et al. Risk factors for lymph node metastasis from intramucosal gastric carcinoma. Cancer. 1996;77(4): 602–6.
12. Gotoda T, Yanagisawa A, Sasako M, Ono H, Nakanishi Y, Shimoda T, et al. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. Gastric Cancer. 2000;3(4):219–25.
13. Hirasawa T, Gotoda T, Miyata S, Kato Y, Shimoda T, Taniguchi H, et al. Incidence of lymph node metastasis and the feasibility of endoscopic resection for undifferentiated-type early gastric cancer. Gastric Cancer. 2009;12(3):148–52.
14. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). Gastric Cancer. 2011;14(2):113–23.
15. Rice TW, Bronner MP. The esophageal wall. Thorac Surg Clin. 2011;21(2):299–305.
16. Katada C, Muto M, Manabe T, Boku N, Ohtsu A, Yoshida S. Esophageal stenosis after endoscopic mucosal resection of superficial esophageal lesions. Gastrointest Endosc. 2003;57(2):165–9.
17. Sato H, Inoue H, Kobayashi Y, Maselli R, Santi EG, Hayee B, et al. Control of severe strictures after circumferential endoscopic submucosal dissection for esophageal carcinoma: oral steroid therapy with balloon dilation or balloon dilation alone. Gastrointest Endosc. 2013;78(2):250–7.
18. Markar SR, Karthikesalingam A, Thrumurthy S, Low DE. Volume-outcome relationship in surgery for esophageal malignancy: systematic review and meta-analysis 2000-2011. J Gastrointest Surg. 2012;16(5):1055–63.
19. Liu L, Hofstetter WL, Rashid A, Swisher SG, Correa AM, Ajani JA, et al. Significance of the depth of tumor invasion and lymph node metastasis in superficially invasive (T1) esophageal adenocarcinoma. Am J Surg Pathol. 2005;29(8):1079–85.
20. Li Z, Rice TW, Liu X, Goldblum JR, Williams SJ, Rybicki LA, et al. Intramucosal esophageal adenocarcinoma: primum non nocere. J Thorac Cardiovasc Surg. 2013;145(6):1519–24. 1524.e1–3.
21. Kuwano H, Nishimura Y, Ohtsu A, Kato H, Kitagawa Y, Tamai S, et al. Guidelines for diagnosis and treatment of carcinoma of the esophagus. Esophagus. 2008;5:61–73.
22. Abe S, Oda I, Shimazu T, Kinjo T, Tada K, Sakamoto T, et al. Depth-predicting score for differentiated early gastric cancer. Gastric Cancer. 2011;14(1):35–40.
23. Japanese Gastric Cancer A. Japanese classification of gastric carcinoma – 2nd English edition. Gastric Cancer. 1998;1(1):10–24.
24. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Participants, in the Paris Workshop. Gastrointest Endosc. 2003;58(6 Suppl):S3–43.
25. Sanchez-Yague A, Kaltenbach T, Yamamoto H, Anglemyer A, Inoue H, Soetikno R. The endoscopic cap that can (with videos). Gastrointest Endosc. 2012;76(1): 169–78.e1–2.

26. Uraoka T, Saito Y, Yamamoto K, Fujii T. Submucosal injection solution for gastrointestinal tract endoscopic mucosal resection and endoscopic submucosal dissection. Drug Des Devel Ther. 2009;2:131–8.
27. Yamamoto H, Kawata H, Sunada K, Sasaki A, Nakazawa K, Miyata T, et al. Successful en-bloc resection of large superficial tumors in the stomach and colon using sodium hyaluronate and small-caliber-tip transparent hood. Endoscopy. 2003;35(8):690–4.
28. 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.
29. Oda I, Suzuki H, Nonaka S, Yoshinaga S. Complications of gastric endoscopic submucosal dissection. Dig Endosc. 2013;25 Suppl 1:71–8.
30. Uedo N, Takeuchi Y, Yamada T, Ishihara R, Ogiyama H, Yamamoto S, et al. Effect of a proton pump inhibitor or an H2-receptor antagonist on prevention of bleeding from ulcer after endoscopic submucosal dissection of early gastric cancer: a prospective randomized controlled trial. Am J Gastroenterol. 2007;102(8):1610–6.
31. Takizawa K, Oda I, Gotoda T, Yokoi C, Matsuda T, Saito Y, et al. Routine coagulation of visible vessels may prevent delayed bleeding after endoscopic submucosal dissection – an analysis of risk factors. Endoscopy. 2008;40(3):179–83.
32. Mochizuki S, Uedo N, Oda I, Kaneko K, Yamamoto Y, Yamashina T, et al. Scheduled second-look endoscopy is not recommended after endoscopic submucosal dissection for gastric neoplasms (the SAFE trial): a multicenter prospective randomized controlled non-inferiority trial. Gut. 2015;64(3):397–405.
33. Coda S, Oda I, Gotoda T, Yokoi C, Kikuchi T, Ono H. Risk factors for cardiac and pyloric stenosis after endoscopic submucosal dissection, and efficacy of endoscopic balloon dilation treatment. Endoscopy. 2009;41(5):421–6.
34. Yamaguchi N, Isomoto H, Nakayama T, Hayashi T, Nishiyama H, Ohnita K, et al. Usefulness of oral prednisolone in the treatment of esophageal stricture after endoscopic submucosal dissection for superficial esophageal squamous cell carcinoma. Gastrointest Endosc. 2011;73(6):1115–21.
35. Hanaoka N, Ishihara R, Takeuchi Y, Uedo N, Higashino K, Ohta T, et al. Intralesional steroid injection to prevent stricture after endoscopic submucosal dissection for esophageal cancer: a controlled prospective study. Endoscopy. 2012;44(11):1007–11.

16. Endoscopic Submucosal Dissection: Colon and Rectum

Emre Gorgun

Introduction

Colonoscopy is the gold standard for imaging in the colon and rectum. It is widely used for screening, cancer and polyp surveillance, as well as evaluation of symptomatic patients; development of colon cancer screening programs in many countries has led to increasing numbers of patients undergoing optical colonoscopy. Screening colonoscopy and polypectomy have been shown to reduce colorectal cancer related deaths in the USA. Colorectal polyp removal is associated with low recurrence, morbidity, and mortality [1, 2]. Asymptomatic lesions incidentally discovered during screening colonoscopy and symptomatic polyps are removed at endoscopists' discretion. While majority of polyps are easily eliminated, some lesions may not be amenable for colonoscopic removal. Up to 15 % of colonic polyps require more advanced polypectomy techniques due to their size, location, and or appearance [3–5]. Nevertheless a significant percentage of patients are referred to surgeons for colorectal resection. In these circumstances an oncological or "radical" colorectal resection is advised since a significant percentage (5–22 %) of these polyps may harbor invasive cancers [6, 7]. There is a continuing debate on whether polyps that are large and broad based in appearance, awkwardly placed, incapable of being elevated for complete removal, and/or suspicious of carcinoma should be removed via oncological formal resection or polypectomy with colotomy. To help answer this question we recently conducted a study at our institution where we estimated the cancer risk in patients with endoscopically benign unresectable colonic polyps referred for surgery. During 15-year study period, 439 patients underwent colectomy due to polyps deemed unsuitable for endoscopic removal. Final pathology revealed high-grade

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dysplasia in 20 % and invasive cancer in 8 % of patients. Endoscopic diagnosis misses cancer in at least 8 % of cases. All apparently benign polyps that cannot be removed endoscopically should be resected via colorectal resection in accordance with oncologic principles. However for more than 90 % of patients, an oncologic colorectal resection is over treatment and bowel resection is associated with major complications and mortality. Therefore advanced polypectomy techniques such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) have been successfully utilized at our institution to remove large colorectal polyps/lesions.

Evaluation of polyp characteristics is the initial step in decision making for the most applicable removal technique. Morphology of polyp (pedunculated, flat, or depressed) and mucosal appearance are calculated to determine the ideal approach. There are several morphologic and histologic assessments such as Haggitt, Paris, Kudo, and Kikuchi's classification in decision making when managing colorectal polyps. Cancer risk may increase in patients with large, sessile, or non-polypoid lesions [8].

Haggitt classification is used for pedunculated and sessile polyps to determine risk of cancer invasion [9, 10]. The level of invasion within the layers was shown to correlate well with prognosis. Haggitt's classification categorizes neoplastic invasion into four levels from the tip to the base of the polyp. Radical surgery is recommended for Higgitt's level 4 lesions [11]. Histological features of neoplasms including tumor differentiation, lymphovascular invasion, and surgical margins should be considered regardless of invasion degree [12, 13].

Non-protruding lesions have varying potential with regard to invasion into the submucosa. While flat adenomas have mostly benign features, depressed-type lesions are considered more aggressive. An international group of endoscopists, surgeons, and pathologists gathered in Paris for an intensive workshop designed to develop endoscopic classification of superficial neoplastic lesions of the GI tract. Paris classification basically relies on morphologic features of tumors. Lesions are divided in to two groups based on polypoid or non-polypoid appearance. Non-polypoid lesions are then subdivided into four as slightly elevated, flat, slightly depressed, and excavated (ulcer) lesions [14].

Pitting pattern is another morphologic feature which aids colorectal mucosal lesions to be evaluated in detail. Kudo's classification represents a risk adjustment by describing five different pitting patterns where type III to V indicates neoplasia [15, 16].

Muscularis mucosae is used as a landmark to determine invasive cancer and T1 colorectal cancer has an overall 10 % risk of lymph node metastasis [17, 18]. Classification of invasion levels of T1 tumors within the submucosal layers has changed the management approach for early colorectal tumors. Kikuchi's classification divides submucosal plan into three sections vertically. While early neoplasms invading upper third (SM1) submucosa can safely be treated endoscopically, endoscopic removal of tumors invading mid (SM2) and lower thirds (SM3) of the submucosa is controversial due to risk of higher lymph node metastases [19].

Advanced technology and refinements in scopes and instruments allow endoscopist to manage difficult gastrointestinal polyps more effectively. Currently both adult and pediatric colonoscopes have wide working channel and HD image quality. Additional techniques including submucosal injection, use of transparent distal disposable cap and endoknives are used. "Suck and cut" is one of the techniques for difficult polypectomy [20–22]. Ideally, the polyp is situated at the 5 o'clock position. According to location and feature of lesion, retroflexion, use of an upper endoscope or pediatric endoscope may be used alternatively [5, 23]. Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are alternative techniques for removing large/difficult polyps not suitable for standard polypectomy. These two techniques involve elevation of submucosal plane by endoscopic injection followed by intraluminal removal/dissection techniques. If intraluminal endoscopic techniques fail, combined endoscopic laparoscopic surgery (CELS) using laparoscopic assisted polyp removal can be achieved prior to oncological colorectal resections [22]. We will discuss different types of advanced polypectomy techniques but mainly ESD.

Tools Used in Endoscopic Submucosal Dissection and Technique

One technique of EMR involves the use of a variceal banding technology where a lesion is suctioned into a distal banding cap, and a flat lesion is turned into a pedunculated lesion. The narrow neck is then snared, and the lesion is removed easily. However, ESD involves a more advanced technique where submucosal injection and elevation of tissue planes are first achieved, followed by submucosal dissection using various types of needle knives. The advantage of ESD is that it allows an en bloc resection of an intestinal lesion, regardless of the size. This technique was first popularized in Japan for the treatment of early

esophageal and gastric cancers [23]. The ESD method is widely used in the field of the upper gastrointestinal tract, especially in the stomach, because an en bloc resection not only offers postoperative organ preservation but exact histopathological diagnoses as well. In Japan, ESD is routinely performed for the treatment of early gastric carcinoma and superficial esophageal carcinoma.

The use of ESD for colorectal lesions has not yet been established as a standard therapeutic method; however, the use of ESD for colorectal lesions has been successful and studies are ongoing. Many types of endoscopic knives have been introduced and are available for use in colorectal ESD. Currently in the USA, there is no extensive experience with ESD. Our institution recently presented our early experience with ESD at the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) annual meeting in 2013 [24]. Since this presentation, we have increased our experience in colonic ESD. A total of 33 patients were referred to us for oncologic colorectal resection for large colorectal lesions and were attempted for ESD. The median age of the patients was 62 (range 50–88), median ASA score was 3 (2–4), and median body mass index (BMI) was 30 kg/m^2 (18–46). Lesions were located in the cecum (40 %), splenic flexure (20 %), sigmoid colon (20 %), transverse colon (10 %), and rectum (10 %). ESD was possible in 27 of 33 lesions. Median operating time was 105 min (62–196). In seven patients, ESD could not be technically performed due to non-lifting of the lesion, and either laparoscopic resection or endoscopic full thickness excision with laparoscopic repair of the defect was performed. There was no perforation or bleeding after ESD. The median length of hospital stay was 1 day (0–5). No recurrence was observed at postoperative third or 6 months colonoscopy. While perforation and bleeding are the major complications, colonoscopy related complications including splenic injury, postpolypectomy syndrome, mesenteric hemorrhage, diverticulitis, appendicitis, and pancreatitis can be seen after ESD. Close postoperative follow-up is required postoperatively. We usually observe patients at least 3–4 h after ESD, and make sure a full meal is well tolerated before discharge. In complicated and larger lesion requiring ESD overnight stay is preferred. Tolerance of meals without nausea or vomiting, recovery of bowel functions, adequate pain control with oral analgesia and independent ambulation are the discharge criteria. In summary we performed ESD technique with good success and insignificant complications. Our initial experience in the USA at the Cleveland Clinic proved that ESD is feasible and effective with low complication rates and can avoid unnecessary oncologic segmental bowel resections. All studied

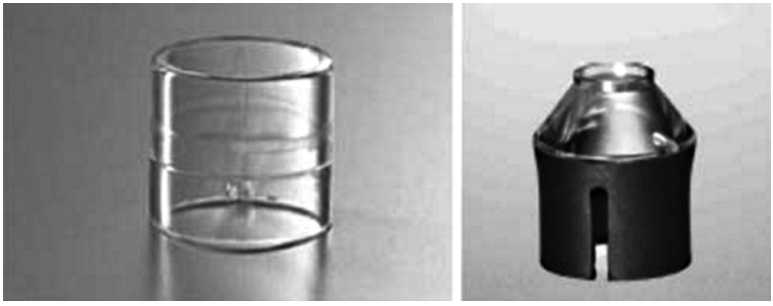

Fig. 16.1. A disposable cap used for endoscopic submucosal dissection (courtesy of Olympus).

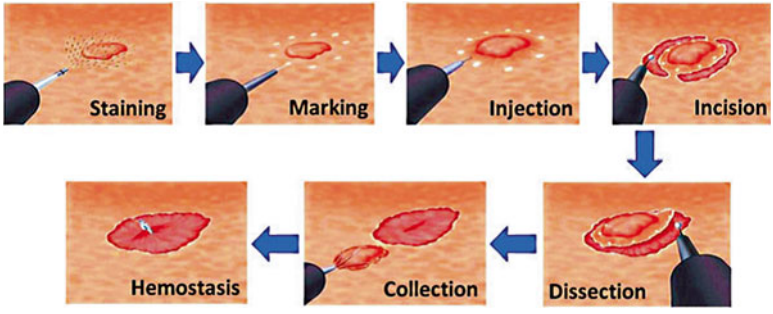

Fig 16.2. Sequential steps of endoscopic submucosal dissection (ESD) (courtesy of Olympus).

patients were offered initial ESD in the operating room with possible bowel resection if ESD could not be successfully completed. A pediatric colonoscope (Olympus America Inc., Center Valley, PA) was used, and a transparent distal disposable cap was attached to the tip of the endoscope (Fig. 16.1). The lesion was first critically visualized either by dye injection, narrowband imaging, or direct view. After this step, circumferential marking of the lesion with electrocoagulation was performed (Fig. 16.2). This was followed by submucosal injection using a mixture of saline, 2.5 % Hypromellose (HUB Pharmaceuticals, LLC, Rancho Cucamonga, CA) (Fig. 16.3) and indigo carmine solution. This raises the submucosal plane and allows the procedure to be performed safely. The next step was mucosal incision with the dual knife, followed by submucosal dissection. The submucosal dissection (Fig. 16.4) was carried by the alternating use of the DualKnifeTM, HookKnifeTM, and

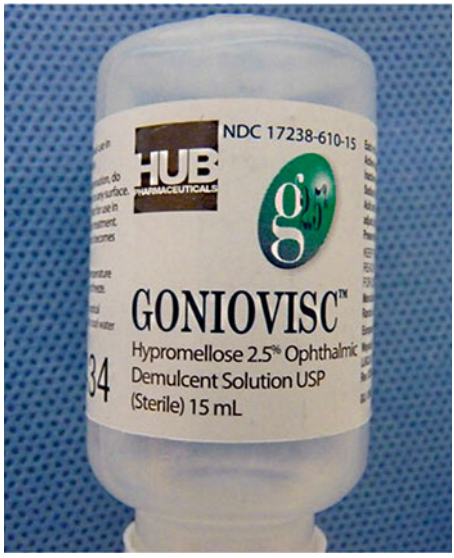

Fig. 16.3. Hypromellose solution. A hyperosmolar injection solution provides superior lift to a polyp compared to saline.

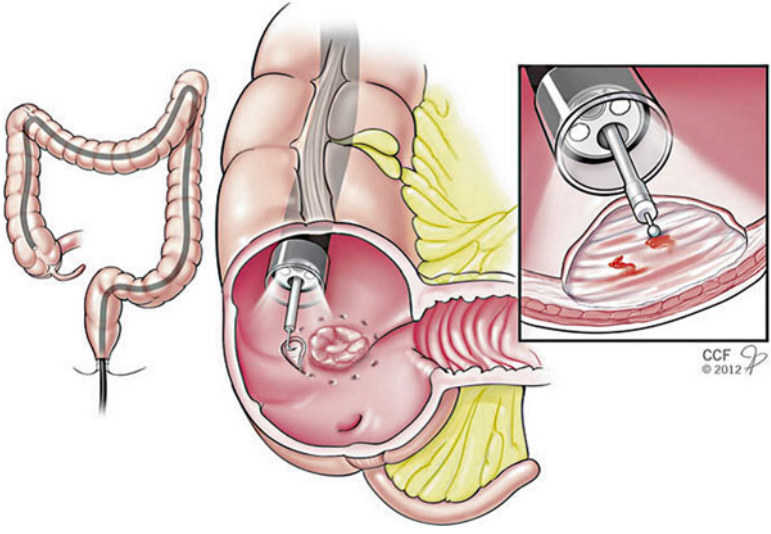

Fig. 16.4. Endoscopic submucosal dissection (ESD) in the colon with a transparent tip cap (reprinted with permission, Cleveland Clinic, Center for Medical Art & Photography © 2011–2014. All Rights Reserved).

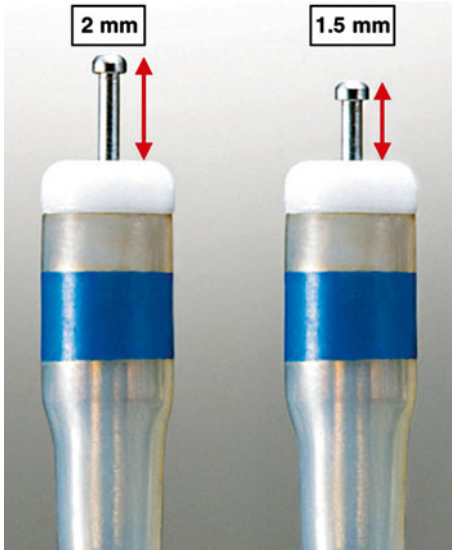

Fig. 16.5. Dual knife: Useful for marking and dissection in ESD (courtesy of Olympus).

Coagrasper TM (Olympus America Inc., Center Valley, PA) (Figs. 16.5, 16.6, and 16.7). The disposable distal cap facilitated the dissection in the correct submucosal plane. Once the entire lesion was dissected free, en bloc tissue retrieval was achieved and finally hemostasis was completed. The following items are useful in ESD. Our personal experience has been to use each of the following tools for different particular steps and maneuvers.

Dual Knife

The single-use Olympus DualKnife™ (Olympus America Inc., Center Valley, PA) electrosurgical knife features an adjustable two-step knife length and a dome-shaped cutting section designed to simplify marking and enable incision and dissection in all directions (Fig. 16.5). Distinct blue markers are visible on the sheath to provide endoscopic verification of cutting depth. The channel diameter is 2.8 mm, and working length is 165 cm for the upper gastrointestinal and 230 cm for the lower gastrointestinal system. Cutting knife length is 2.0 mm for upper

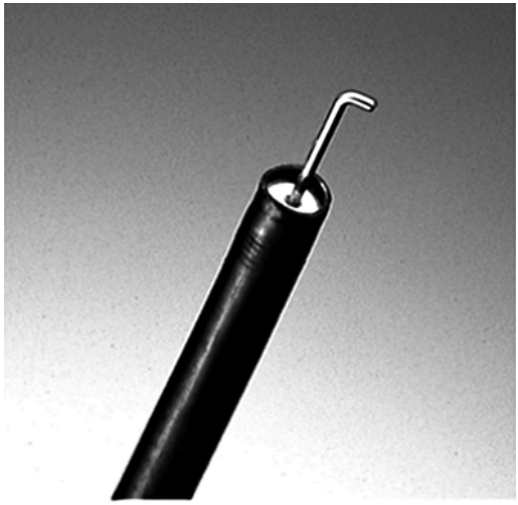

Fig. 16.6. Hook knife: Controls depth of penetration as tissues are pulled away while energy is applied (courtesy of Olympus).

Fig. 16.7. Coagrasper: Helpful for larger submucosal vessels (courtesy of Olympus).

gastrointestinal purposes and 1.5 mm for colonic applications. The purpose of the difference in cutting lengths is to prevent accidental bowel perforation due to wall thickness variance between the stomach and colon. When the handle is closed and the tip is pulled into the sheath, this

facilitates the functions of marking and hemostasis. When the handle is open and the knife is deployed, this facilitates incision and dissection.

Hook Knife

The HookKnife™ (Olympus America Inc., Center Valley, PA) is a distal L-shaped hook with rotational function that allows for precise incision and dissection in longitudinal and lateral directions (Fig. 16.6). This type of tool is used to hook the tissue and draw it away from the mucosa while diathermy is applied, thus minimizing the risk of perforation. The turn and lock feature is simple to deploy and ensures the cutting wire is locked at the desired position during the procedure. A choice of lengths allows the endoscopist to choose a working length based on procedural technique or lesion location.

Coagrasper

Coagrasper™ (Olympus America Inc., Center Valley, PA) provides precise and effective hemostasis by grasping a bleeding point or a visible vessel and coagulating it (Fig. 16.7). Excellent rotation function increases the accuracy of the grasper. Two types of cup shape and opening width are available for use in both the upper and lower gastrointestinal tracts. The single-use Coagrasper™ hemostatic forceps delivers targeted monopolar coagulation that creates hemostasis at the precise site of bleeding. A combination of mechanical and energy-based hemostasis device, the Coagrasper will isolate the vessel from the healthy surrounding mucosa so that thermal coagulation occurs only where needed.

Distal Disposable Cap

Distal disposable cap is a transparent tip hood (Fig. 16.1) that is critical for tissue manipulation in colorectal ESD. A disposable distal attachment (Olympus America Inc., Center Valley, PA) is placed onto the tip of the colonoscope and aids in entry into the submucosa and lifts up the mucosa as to provide traction and countertraction during dissection. Additionally, the distal disposable cap adds stability during incision and improves the visual field by holding down the mucosa when needed.

Submucosal Injection Solution

Hypromellose injection solution and indigo carmine blue dye play a central role in ESD (Fig. 16.3). The hyperosmolar injection solutions facilitate adequate submucosal elevation and safe dissection. The hyperosmolar feature allows the solution to remain in the submucosal plane for a long time compared to saline without dissipating too quickly. This is essential during a lengthy polypectomy. Although variable in practice, my preference is to dilute Hypromellose six- to eightfold using saline and mix small amounts of indigo carmine blue dye. The blue coloration of the submucosal plane provides better visualization of the structures and vasculature.

CO_2 Insufflation

Gas insufflation is necessary to obtain optimal visualization of the intestinal surface during colonoscopy. However, insufflated air during colonoscopy remains in the bowel for a long time and results in prolonged bowel distension, abdominal pain, and discomfort. During and toward the end of a colonoscopy, the insufflated air cannot be completely suctioned, and the remaining air is not easily absorbed by the intestinal mucosa. On the other hand, the transluminal absorption of carbon dioxide (CO_2) is much faster (40–100 times) compared to air, improving patient comfort.

This advantage is further magnified in the operating room, where intraluminal CO_2 insufflation has been noted to be advantageous when simultaneously combined with CO_2 laparoscopy by limiting bowel distension. The CO_2 regulation unit is simple to operate and can be run with no additional technical support. Most CO_2 units feature a single button on the front panel to start and stop the flow of CO_2. It is easily set up by connecting to a gas cylinder with a dedicated cylinder hose or by connecting directly to the hospital's medical gas supply.

The units are usually small and compact and can fit easily into a standard endoscopy workstation. My recommendation is to use CO_2 insufflation for any lengthy polypectomy procedure.

When intraoperative colonoscopy is needed as an adjunct to colorectal surgery, a downside of using air insufflation is prolonged bowel distension and obstructed surgical exposure. To test the safety of simultaneous CO_2 colonoscopy and laparoscopy, we conducted a case-matched study

where the outcomes of patients undergoing laparoscopic intestinal resection with and without intraoperative colonoscopy were compared. The postoperative recovery and rate of complications were similar, and there were no complications related to CO_2 colonoscopy [25].

Treatment Algorithm

ESD is technically demanding and requires advanced endoscopy skills due to anatomic features of the colon. Under supervision, endoscopists in training can perform ESD with minimal morbidity. Current research should focus on ESD indications in the colon and rectum and the role of ESD for colonic lesions in a treatment algorithm. Based on our clinical experience and outcomes we follow the algorithm in the management of difficult colorectal lesions as summarized in Fig. 16.8.

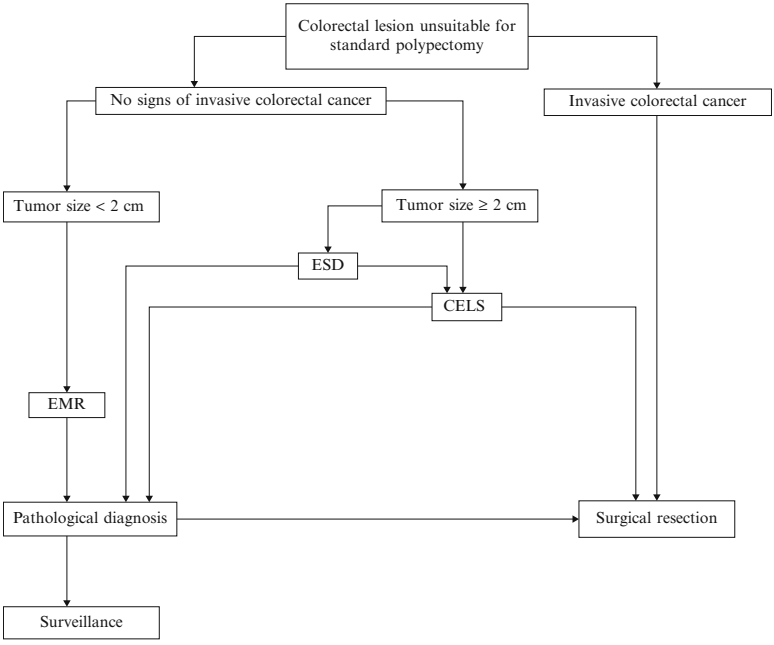

Fig. 16.8. ESD algorithm for mucosal/submucosal tumors. *EMR* endoscopic mucosal resection, *ESD* endoscopic submucosal dissection, *CELS* combined endoscopic laparoscopic surgery.

CELS

Combined endoscopic laparoscopic surgery (CELS) is another emerging technique in which intraoperative colonoscopy plays a key role. Laparoendoscopic polyp resection has been suggested as an alternative to segmental bowel resection for complete removal of large polyps. With this technique, laparoscopic instruments are used to manipulate and stabilize the polyp-bearing segment of bowel from the serosal aspect, improving exposure for the endoscopist and increasing the chance of a successful endoscopic polypectomy (Fig. 16.9). Intraoperative CO_2 colonoscopy is extremely helpful in these combined procedures by limiting the amount of bowel distension and rendering clamping of the terminal ileum unnecessary.

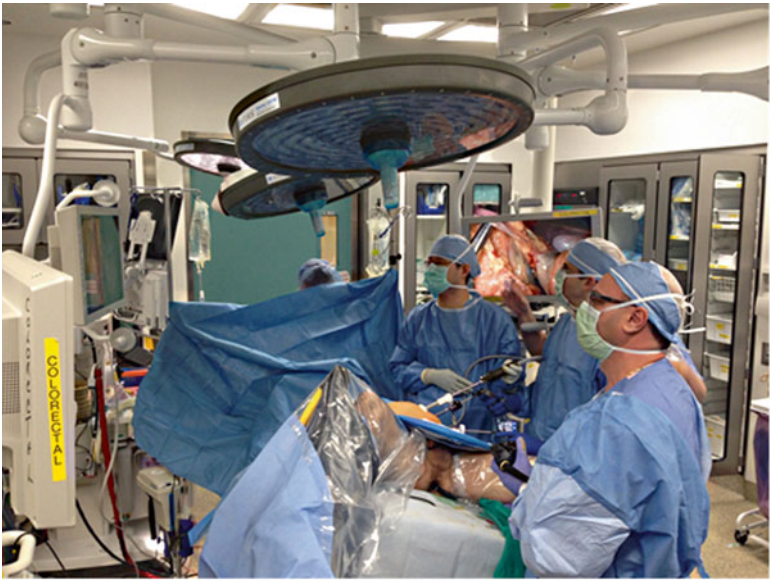

Fig. 16.9. Patient, surgeon, and endoscopist performing CELS.

Conclusion and Future Directions

ESD is a safe and useful technique in carefully selected patients. With ESD training courses and increasing experiences, this approach will gradually expand and potentially more commonly performed for large colonic lesions among American surgeons and endoscopists.

References

1. Winawer SJ, Zauber AG, Ho MN, O'Brien MJ, Gottlieb LS, Sternberg SS, Waye JD, Schapiro M, Bond JH, Panish JF. Prevention of colorectal cancer by colonoscopic polypectomy. N Engl J Med. 1993;329:1977–81.
2. Zauber AG, Winawer SJ, O'Brien MJ, Lansdorp-Vogelaar I, van Ballegooijen M, Hankey BF, Shi W, Bond JH, Schapiro M, Panish JF. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med. 2012;366:687–96.
3. Waye JD. Advanced polypectomy. Gastrointest Endosc Clin N Am. 2005;15: 733–56.
4. Gallegos-Orozco JF, Gurudu SR. Complex colon polypectomy. Gastroenterol Hepatol (N Y). 2010;6:375–82.
5. Zhang M, Shin EJ. Successful endoscopic strategies for difficult polypectomy. Curr Opin Gastroenterol. 2013;29:489–894.
6. Hurlstone DP, Sanders DS, Cross SS, Adam I, Shorthouse AJ, Brown S, Drew K, Lobo AJ. Colonoscopic resection of lateral spreading tumours: a prospective analysis of endoscopic mucosal resection. Gut. 2004;53:1334–9.
7. Conio M, Repici A, Demarquay J, Blanchi S, Dumas R, Filiberti R. EMR of large sessile colorectal polyps. Gastrointest Endosc. 2004;60:234–41.
8. Soetikno RM, Kaltenbach T, Rouse RV, Park W, Maheshwari A, Sato T, Matsui S, Friedland S. Prevalence of nonpolypoid (flat and depressed) colorectal neoplasms in asymptomatic and symptomatic adults. JAMA. 2008;299:1027–35.
9. Haggitt RC, Glotzbach RE, Soffer EE, Wruble LD. Prognostic factors in colorectal carcinomas arising in adenomas: implications for lesions removed by endoscopic polypectomy. Gastroenterology. 1985;89:328–36.
10. Kikuchi R, Takano M, Takagi K, Fujimoto N, Nozaki R, Fujiyoshi T, Uchida Y. Management of early invasive colorectal cancer. Dis Colon Rectum. 1995;38: 1286–95.
11. Marzouk O, Schofield J. Review of histopathological and molecular prognostic features in colorectal cancer. Cancers. 2011;3:2767–810.
12. Volk EE, Goldblum JR, Petras RE, Carey WD, Fazio VW. Management and outcome of patients with invasive carcinoma arising in colorectal polyps. Gastroenterology. 1995;109:1801–7.
13. Kafka NJ, Coller JA. Endoscopic management of malignant colorectal polyps. Surg Oncol Clin N Am. 1996;5:633–61.

14. Inoue H, Kashida H, Kudo S, Sasako M, Shimoda T, Watanabe H, Yoshida S, Guelrud M, Lightdale C, Wang K. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc. 2003;58:S3–43.
15. Kudo S, Hirota S, Nakajima T, Hosobe S, Kusaka H, Kobayashi T, Himori M, Yagyuu A. Colorectal tumours and pit pattern. J Clin Pathol. 1994;47:880–5.
16. Kobayashi Y, Kudo S, Miyachi H, Hosoya T, Ikehara N, Ohtsuka K, Kashida H, Hamatani S, Hinotsu S, Kawakami K. Clinical usefulness of pit patterns for detecting colonic lesions requiring surgical treatment. Int J Colorectal Dis. 2011;26:1531–40.
17. Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. Dis Colon Rectum. 2002;45:200–6.
18. Kobayashi H, Mochizuki H, Morita T, Kotake K, Teramoto T, Kameoka S, Saito Y, Takahashi K, Hase K, Oya M. Characteristics of recurrence after curative resection for T1 colorectal cancer: Japanese multicenter study. J Gastroenterol. 2011;46:203–11.
19. Tytherleigh M, Warren B. Management of early rectal cancer. Br J Surg. 2008; 95:409–23.
20. Seitz U, Seewald S, Bohnacker S, Soehendra N. Advances in interventional gastrointestinal endoscopy in colon and rectum. Int J Colorectal Dis. 2003;18:12–8.
21. Kedia P, Waye JD. Colon polypectomy: a review of routine and advanced techniques. J Clin Gastroenterol. 2013;47:657–65.
22. Cruz RA, Ragupathi M, Pedraza R, Pickron TB, Le AT, Haas EM. Minimally invasive approaches for the management of “difficult” colonic polyps. Diagn Ther Endosc. 2011;2011:682793.
23. Ono H, Kondo H, Gotoda T, Shirao K, Yamaguchi H, Saito D, Hosokawa K, Shimoda T, Yoshida S. Endoscopic mucosal resection for treatment of early gastric cancer. Gut. 2001;48:225–9.
24. Gorgun E, Remzi F. Endoscopic submucosal dissection for large non pedunculated lesions of the colon: early experience in the United States. Baltimore, MD: SAGES; 2013.
25. Gorgun IE, Aytac E, Manilich E, Church JM, Remzi FH.Intraoperative colonoscopy does not worsen the outcomes of laparoscopic colorectal surgery: a case-matched study.Surg Endosc. 2013 Oct;27(10):3572–6. doi: 10.1007/s00464-013-2928-1. Epub 2013 Mar 22.

17. Peroral Endoscopic Myotomy (POEM)

Joel M. Sternbach and Eric S. Hungness

Abbreviations

DES	Distal esophageal spasm
DI	Distensibility index
EGD	Esophagogastroduodenoscopy
EGJ	Esophagogastric junction
EMR	Endoscopic mucosal resection
EPT	Esophageal pressure topography
ES	Eckardt score
ESD	Endoscopic submucosal dissection
FLIP	Functional lumen imaging probe
GERD	Gastroesophageal reflux disease
HRIM	High-resolution impedance manometry
HRM	High-resolution manometry
LES	Lower esophageal sphincter
NOTES	Natural orifice transluminal endoscopic surgery
POEM	Peroral endoscopic myotomy
TBE	Timed barium esophagram

Indications

Achalasia

Achalasia is a rare disease characterized by failure of relaxation of the lower esophageal sphincter (LES) and loss of coordinated peristalsis in the esophageal body. Despite being the most common primary esophageal

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motor disorder, the annual incidence is estimated at only 1 per 100,000 individuals [1]. Initially described in 1674 by Sir Thomas Willis, our current understanding of the etiology of achalasia has developed thanks to histopathologic analysis over the last two decades. Immunohistochemical studies have suggested an autoimmune response, potentially triggered by a neurotropic virus such as herpes simplex virus 1 in genetically susceptible hosts, with selective loss or impairment of ganglions in the myenteric plexus resulting in unopposed cholinergic stimulation of the distal esophagus and LES [2]. Presenting symptoms include dysphagia to solids and liquids (>90 %), regurgitation of undigested food and saliva (76–91 %), weight loss (35–91 %), and chest pain (25–64 %). Patients may also report respiratory complications of aspiration, such as nocturnal cough and pneumonia, as well as heartburn and esophagitis secondary to stasis [3]. There is no known cure for achalasia. Current treatment options are aimed at palliation of symptoms through elimination of outflow obstruction at the EGJ.

Emerging Indications

Based on case series reporting excellent early results, POEM operators have applied the minimally invasive technique to esophageal motor disorders other than type I and type II achalasia, including type III achalasia, distal esophageal spasm (DES), Jackhammer (hypercontractile) esophagus, and hypertensive LES [4, 5]. In general, EGJ outflow obstruction caused by high LES pressure responds favorably to division of the obstructing muscle fibers, whereas symptoms such as chest pain, attributed to esophageal body contraction (DES and type III achalasia), have lower rates of symptom remission following myotomy [6]. POEM has also been utilized as a salvage operation following failed laparoscopic Heller myotomy (LHM), with dissection and myotomy occurring in the 4–6 o'clock position.

History/Background

In the 100 years since Dr. Heller first described the "transabdominal, extramucosal cardioplasty performed onto the anterior and posterior walls of the cardia," the procedure has been transformed by laparoscopy, modified in length, and augmented by anti-reflux procedures [7]. In the last 10 years, however, the complementary fields of natural orifice translumenal

endoscopic surgery (NOTES) and endoscopic submucosal dissection (ESD) have expanded from simple proof-of-concept studies to a broad variety of fully incision-less operations in use today. Early animal models demonstrated the feasibility of both safe access to the submucosal space using the mucosal flap technique and endoscopic myotomy [8, 9]. Based on these techniques, Dr. Haruhiro Inoue performed the first human POEM procedure in Japan in 2008 and presented his results at the 2009 Digestive Diseases Week in Chicago with subsequent publication in Endoscopy in 2010 [10]. Following his landmark publication, the procedure as described by Inoue grew exponentially with an estimated number of POEM cases exceeding 2000 worldwide by the end of 2012, when the global experience in POEM was summarized in the international POEM survey (IPOEMS), leading up to and during the NOSCAR conference in July 2012 [6].

Patient Selection

Symptom Assessment Questionnaires

Validated, disease-specific questionnaires can help establish the diagnosis of achalasia, assess disease severity, and establish baseline values to allow postoperative evaluation of treatment effect. The most widely used and reported instrument for achalasia is the four-item Eckardt score that evaluates the frequency of occurrence of chest pain, regurgitation, dysphagia, and amount of weight loss on a 0–3 scale [11]. Higher scores represent increasingly severe disease, while post-intervention scores less than or equal to three are associated with treatment success [12]. While simple to obtain, the ES does not measure disease impact on overall quality of life. More extensive and sensitive surveys include the Mayo Dysphagia Questionnaire-30, Achalasia Disease-Specific Quality of Life measure, Visceral Sensitivity Index, and EORTC QLQ-OES18 [13].

Physiologic Tests

Timed Barium Esophagram

Timed barium esophagram (TBE) (Fig. 17.1), comprised of chest radiographs obtained 1, 2, and 5 min after ingestion of 200–250 ml of dilute barium contrast, is useful for evaluation of both esophageal body

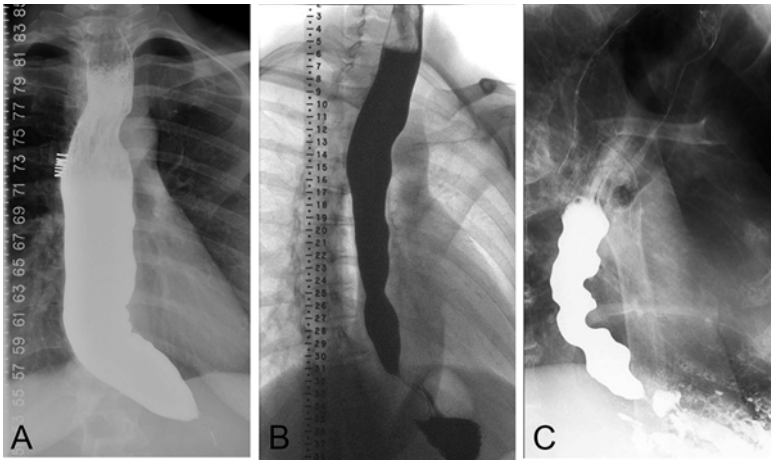

Fig. 17.1. Timed barium esophagram. Characteristic findings in achalasia include (**a**) increased esophageal width as seen in a patient with type I achalasia, (**b**) so-called bird's beak appearance of the contrast column as it tapers in the distal esophagus of a patient with type II achalasia, and (**c**) retained contrast with a "corkscrew" appearance seen in type III achalasia and other spastic disorders of the esophagus such as DES.

and EGJ anatomy (classic appearance of the "bird-beak" esophagus). TBE provides quantification of a baseline height of the barium column, degree of esophageal emptying, if any, and esophageal width. TBE also allows detection of sigmoid esophagus (representing so-called end-stage achalasia), hiatus hernia, and epiphrenic diverticula.

Esophagogastroduodenoscopy

Esophagogastroduodenoscopy (EGD) is required as part of the preoperative work-up of all patients prior to treatment for achalasia to rule out pseudo-achalasia (EGJ outflow obstruction secondary to an infiltrating malignancy). If the index of suspicion remains high for pseudo-achalasia (older patients with prominent weight loss and a short duration of symptoms), despite a negative EGD, adjunctive studies such as endoscopic ultrasound or computed tomography scan should be performed [14]. EGD also allows for assessment of retained solids or liquids, stasis, or reflux esophagitis and candidiasis.

High-Resolution Manometry

Manometry is considered the "gold standard" for the diagnosis of idiopathic achalasia. This diagnostic modality has had significant improvement in resolution and evaluation of esophageal motility over the last 10 years with the introduction of solid-state, high-resolution manometry (HRM) catheters utilizing 36 or more pressure sensors at 1 cm intervals. The increased resolution offered by HRM catheters has been accompanied by the development of esophageal pressure topography (EPT), or Clouse plots, to display pressure data in a more accessible format than traditional line tracings. Based on manometric profiles, Pandolfino et al. proposed the Chicago classification, dividing patients into three subtypes of achalasia (Fig. 17.2), with well-described prognostic implications [15, 16]. Type I, or "classic" achalasia, is defined by absent peristalsis and impaired EGJ relaxation in response to swallowing, quantified as a 4-s integrated relaxation pressure (IRP) >10 mmHg. Type II achalasia is diagnosed by the presence of panesophageal pressurization (>30 mmHg) and is associated with the best outcomes following myotomy. Type III achalasia, associated with premature, spastic contractions of the distal esophagus (two or more swallows with a distal latency of <4.5 s), and impaired EGJ relaxation, has the least reliable response to myotomy or pneumatic dilatation [16].

EndoFLIP

The functional lumen imaging probe, or EndoFLIP (Crospon, Galway, Ireland), is a novel diagnostic catheter that utilizes impedance planimetry, with sensors positioned at 0.5–1 cm intervals within a distensible balloon to generate a geometric representation of the lumen of the esophagus and LES (Fig. 17.3). When combined with a pressure sensor in the distal portion of the balloon, the FLIP allows quantification of the EGJ response to volumetric distention, calculated as the distensibility index (DI) = cross-sectional area/intra-balloon pressure. Recent publications have suggested a role for intraoperative EndoFLIP measurements to allow real-time evaluation of myotomy adequacy during LHM and POEM [17].

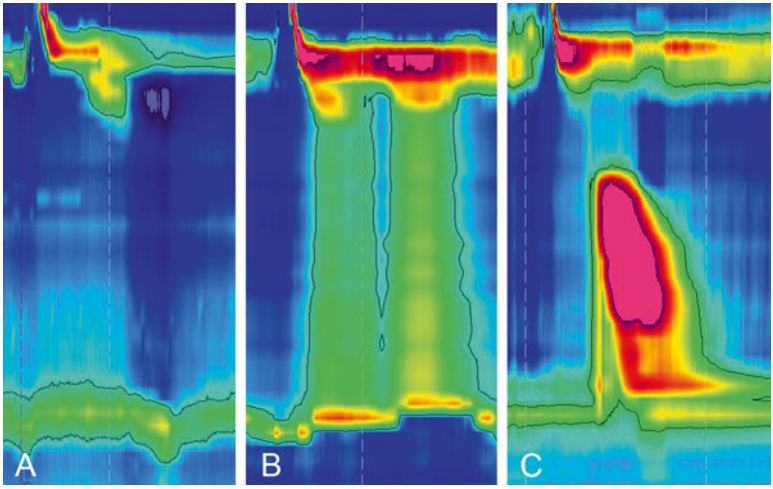

Fig. 17.2. High-resolution manometry. Distinct manometric patterns are observed in the subtypes of achalasia according to the Chicago classification. In the setting of elevated 4-s integrated relaxation pressures, (**a**) type I patients are recognizable by the absence of peristalsis, (**b**) type II patients exhibit pan-esophageal pressurization at the 30 mmHg isobaric contour, and (**c**) type III patients are defined by a spastic distal esophageal contraction with a distal latency less than 4.5 s.

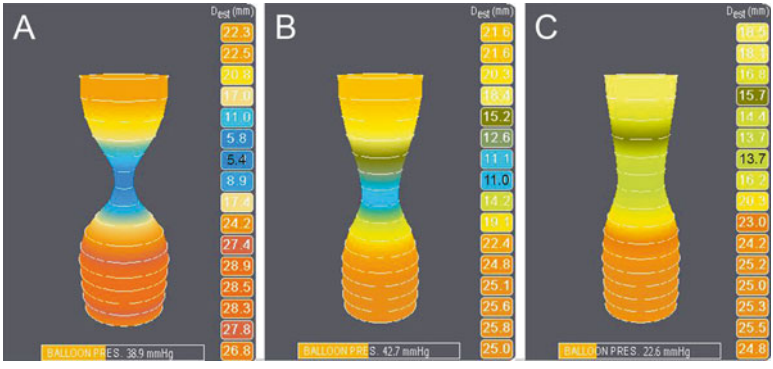

Fig. 17.3. Intraoperative EndoFLIP: The lower esophageal sphincter is identified on EndoFLIP by the characteristic "hourglass" shape (**a**) following induction of general anesthesia during a POEM procedure. Increased distensibility is noted after (**b**) creation of the submucosal tunnel, with a doubling of the minimum diameter and (**c**) completion of myotomy; final EndoFLIP measurements revealed a further increase in diameter and a nearly 50 % pressure decrease at the EGJ.

Contraindications

Patient Factors

Patients should undergo evaluation in a preoperative clinic in coordination with anesthesiology and additional work-up as indicated. The less invasive nature of the POEM procedure minimizes the list of comorbidities that preclude the procedure. Absolute contraindications to POEM include the inability to tolerate general anesthesia, secondary to prohibitive cardiopulmonary disease, uncorrectable coagulopathy/thrombocytopenia, and the presence of advanced cirrhosis, with or without evidence of esophageal varices. Additionally, the POEM procedure relies on the ability to access the submucosal space, so extensive fibrosis secondary to external-beam radiation to the mediastinum, extensive mucosal ablations, or prior EMR generally prohibit the operation. Published reports have included patients ranging in age from 3 to 97 years old [6]. Prior treatments that can cause inflammation and/or fibrosis of the submucosal space such as botulinum toxin injection, pneumatic dilation, prior LHM, or prior POEM can all contribute to the difficulty of the dissection and in some cases increase the rate of inadvertent mucosotomies or duration of the procedure. While none of the prior treatment modalities, other than esophagectomy, represent absolute contraindications to POEM, the added complexity should preclude such cases from being attempted during the initial learning curve [18].

Technical/Training

Safe conduct of the POEM procedure relies on the availability of all necessary equipment, adequately trained and well-coordinated support staff, and sufficient preclinical training. Prior experience with EMR/ESD techniques and/or NOTES procedures has been reported as helpful, as have simulations using live animal, ex vivo models, and cadavers. Most operators reported having expert proctoring during the initial human cases (median 2, range 1–7) [6].

Preoperative Care

Prior to surgery, a multidisciplinary team including gastroenterologists and minimally invasive surgeons should evaluate the patient.

Patient Instructions

Preoperatively, the patient is prescribed Nystatin swish-and-swallow for an empiric 3-day course, instructed to maintain a clear liquid diet starting 24 h, and to remain NPO for 12 h, prior to surgery. Some centers report conducting routine EGD 1–3 days preoperatively to screen for candidiasis. Management of perioperative medications should be performed in consultation with the preoperative clinic, cardiology, and the patient's primary care provider. In general, we continue beta blockers perioperatively, as well as Aspirin when indicated for a history of stent placement, coronary artery disease, or coronary artery bypass graft. Prophylactic Aspirin and Plavix are typically held for 7 and 5 days preoperatively, respectively, and decisions regarding management of therapeutic anticoagulation are made on an individual basis.

Anesthetic Considerations

Preoperative and intraoperative coordination with the anesthetic team is crucial to safe conduct of the POEM procedure. Issues of particular importance include positioning and securing the endotracheal tube as far laterally as possible and potentially utilizing a pre-formed, right-angled Oral RAE™ tracheal tube (Moore Medical, Farmington, CT). The anesthesia team should be aware of the potential for unplanned extubation given the frequent passage of the endoscope through the oropharynx, with the equipment necessary for re-intubation readily available. It is also helpful to discuss blood pressure management, specifically maintaining the systolic blood pressure below 100–110 mmHg, if feasible, as this is anecdotally associated with fewer bleeding complications.

Room Setup and Equipment

For a list of equipment recommended for POEM, see Table 17.1. Sequential compression devices are utilized for thromboprophylaxis and a second-generation cephalosporin or comparable preoperative antibiotic (Ancef/Flagyl at our institution) is given. After successful induction of general anesthesia and secured positioning of an endotracheal tube, the patient is positioned supine, flush with the head of the OR table, the right arm is supported on an arm board, and the left arm is appropriately padded and tucked next to the torso. The bed should be lowered and step

Table 17.1. Equipment checklist.

Room setup	Forward viewing, high-definition gastroscope with 2.8 mm working port (GIF-H180, Olympus)
	Clear cap with ¼″ tape to secure at the end of the gastroscope
	Carbon dioxide (CO_2) insufflation system (Olympus)
	High-frequency electrosurgical generator (ERBE)
Intraoperative tools	Bite-block
	60–90 ml syringes with saline for irrigation ± simethicone
	Indigo carmine injection solution with epinephrine
	Indigo carmine injection solution without epinephrine
	Dilute bacitracin irrigation
	¼″ Red tape to mark insertion depth for endoscopic instruments
	Sterile toothbrush for cleaning knife
Endoscopic instruments	Endoscopic injection/sclerotherapy needle (Olympus)
	Triangular-tip endoscopic submucosal dissection knife (Olympus)
	Coagrasper hemostatic forceps (Olympus)
	QuickClip2 (Olympus) hemostatic clips
	Instinct Hemoclips (Cook) for closure of wider mucosal defects
	OverStitch (Apollo Endosurgery) endoscopic suturing system

stools positioned at the head of the bed as needed to minimize strain and fatigue on the part of the operator. An endoscopy tower, equipped with a forward-viewing, 2.8 mm single-channel, high-definition flexible gastroscope (GIF-H180; Olympus America, Inc., Center Valley, PA), with carbon dioxide (CO_2) insufflation, is positioned near the midpoint of the OR table and the cautery foot pedal is placed within reach of the operator. A minimum of one assistant is required to coordinate the operation of the injector and triangular-tip ESD knife and should be positioned to the left of the operator. A second assistant, to the right of the operator, can stabilize the endoscope at the mouth allowing simultaneous manipulation of the deflection wheels and the injector or cautery knife. The second assistant can also assist with passage of intraoperative measurement devices such as the EndoFLIP catheter. A time-out should be performed prior to the procedure to confirm patient identity, procedure, and availability of endoscopic equipment (clips, coagulation forceps, etc.) and ensure that the endoscopy tower is utilizing CO_2 insufflation and that correct electrocautery levels are set.

Operative Technique (Fig. 17.4)

Diagnostic Endoscopy

Once the anesthesiologist is satisfied with the positioning and security of the endotracheal tube, the abdomen is prepped and draped to provide access in the event that Veress needle decompression of a capnoperitoneum is required. A bite-block is placed to facilitate passage of the endoscope (Fig. 17.4a). Thorough clearance of impacted food is required for complete assessment of the esophageal mucosa (Fig. 17.4b) and to minimize soilage of the submucosal tunnel. Placement of a 16 or 18 French orogastric tube can facilitate clearance, as can availability of 60–90 ml flushes or a power-flush system for the working port. It is not uncommon to encounter copious frothy sputum in the esophagus (Fig. 17.4c), a condition that resolves quickly with irrigation using dilute simethicone. Initial EGD is performed to assess for the presence of active candidiasis (Fig. 17.4d), an indication to abort the procedure and reschedule the myotomy pending resolution of the infection. Following a visual inspection of the esophagus and stomach, note should be made of the location of the esophagogastric junction as determined by the distance from the incisors to the squamocolumnar junction (Fig.17.4e) using the external markings on the endoscope for reference. In the absence of a hiatal hernia, the SCJ is typically located between 38 and 42 cm from the incisors.

Mucosal Lift and Mucosotomy

In the case of a standard length myotomy (extending 6–7 cm proximal to the EGJ), the mucosotomy should be made 12–14 cm above the EGJ. The majority of operators participating in the IPOEMS reported creating an anterior submucosal tunnel in the 1–2 o'clock position [6]. An endoscopic needle is inserted just below the mucosa and a 3–4 cm wheal is raised using 10 ml of solution containing indigo carmine (0.2 mg/ml), epinephrine (5 mcg/ml), and 0.9 % saline (Fig. 17.4f). A longitudinal mucosotomy is created (using a few drops of liquid to create a meniscus to assess positioning relative to the most anterior aspect, designated 12 o'clock). Mucosotomy length should be just large enough to accommodate the clear cap on the endoscope (Fig. 17.4g), as excessive length will add time and cost to the procedure during clip closure of the mucosotomy.

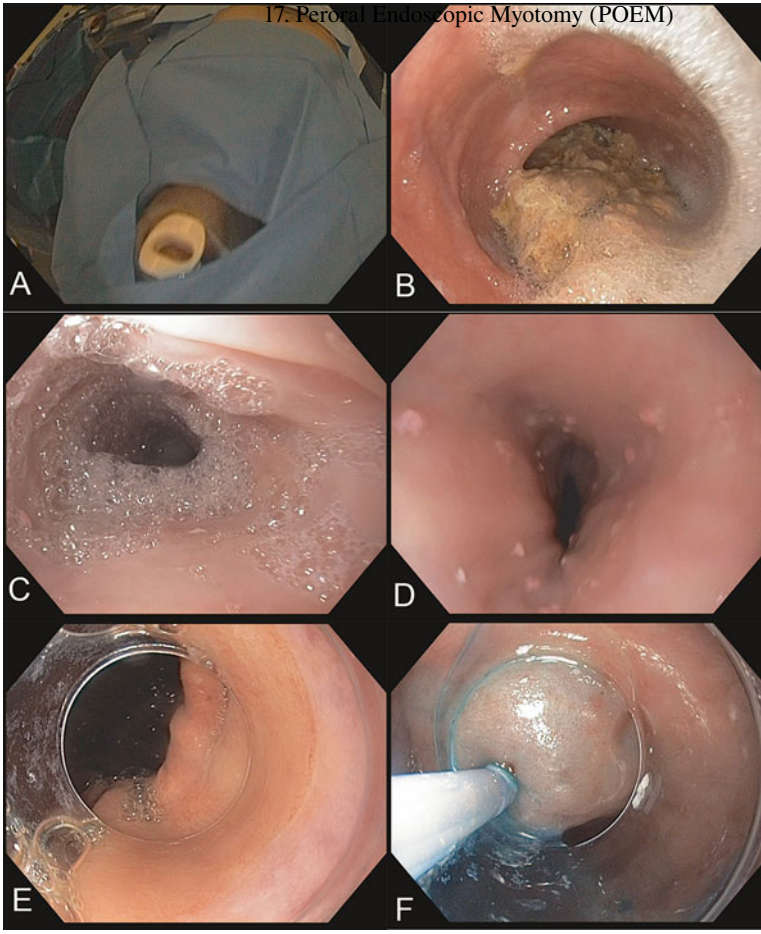

Fig. 17.4. (**a**–**i**) Operative steps for POEM: Patients are (**a**) prepped and draped with the abdomen exposed and a bite-block is placed to facilitate passage of the endoscope. Findings during initial EGD can include (**b**) impacted food and (**c**) copious frothy sputum that should both be cleared to allow for detection of (**d**) active candidiasis. Identification of the (**e**) squamocolumnar junction provides an approximation distance to the EGJ. A combination of dilute epinephrine and indigo carmine is injected to (**f**) elevate the mucosa. The submucosal space is accessed through (**g**) creation of a longitudinal mucosotomy. The submucosal tunnel is extended distally with a combination of (**h**) dilute indigo carmine injection for marking and hydrodissection and (**i**) cautery to divide the tissue of the submucosa. Withdrawal from the tunnel and retroflexion in the stomach allow (**j**) endoluminal verification of adequate extension onto the gastric cardia. Starting 6–7 cm proximal to the EGJ, (**k**) a selective myotomy of the inner, circular muscle layer is performed to 2–3 cm distal to the EGJ. After ensuring hemostasis and irrigation of the submucosal tunnel with dilute bacitracin, (**l**) endoscopic clips are used for mucosotomy closure.

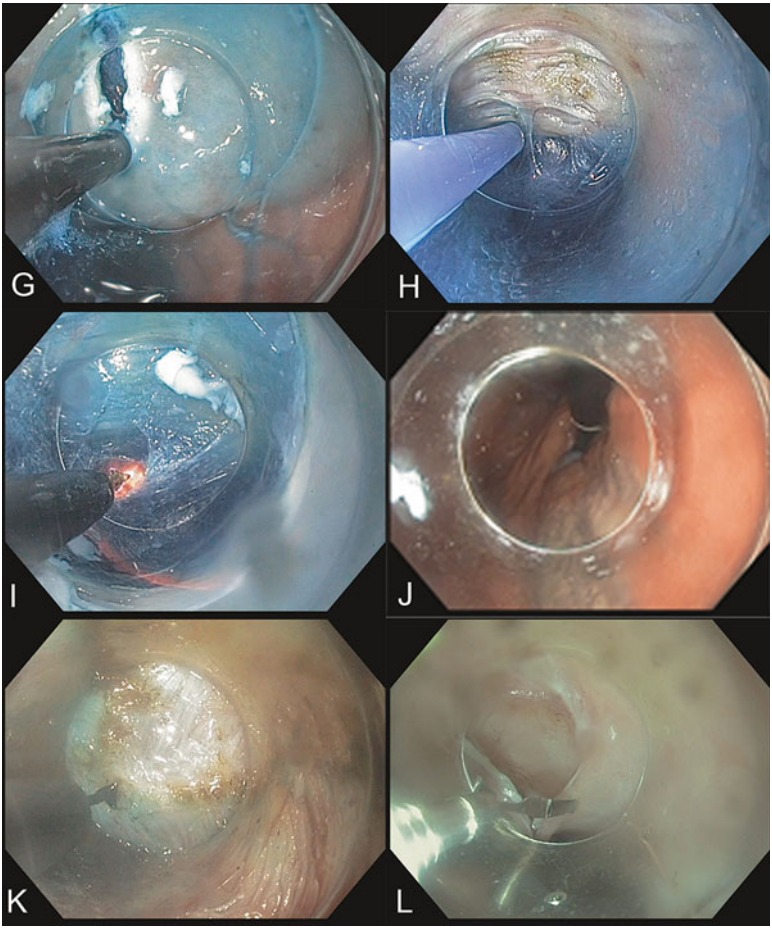

Fig. 17.4. (continued)

Creation of the Submucosal Tunnel

After the initial mucosal lift, subsequent injections during the creation of the submucosal tunnel should be diluted dye without epinephrine to limit total exposure to the adrenergic agent. Distal progression of the submucosal tunnel is facilitated by alternating hydro-dissection to enlarge the submucosal space (Fig. 17.4h) and cautery to divide the thin fibers connecting the mucosa to the inner, circular muscle layer

(Fig. 17.4i). Careful advancement of the endoscope and slight posterior deflection of the cap can be used to put the submucosal fibers on stretch and guide dissection. Frequent reference to fluid meniscus can help prevent spiraling as the tunnel is carried distally on the esophagus. Extra care should be taken near the EGJ as this area is prone to inadvertent mucosotomy given the increased muscular tone and anecdotally described "stickiness," attributed to prior episodes of inflammation or previous treatment modalities. Beyond the EGJ, switching back to an injection solution containing both dye and dilute epinephrine can aid in demarcating the distal extent of the submucosal tunnel. To confirm adequate extension onto the gastric cardia, the endoscope can be withdrawn from the submucosal tunnel and passed into the stomach lumen to obtain a retroflex view of the EGJ (Fig. 17.4j).

Anterior Myotomy of the Circular Muscle Layer

Using the endoscopic markings, the selective myotomy of the circular muscle layer should be initiated 6 cm proximal to the EGJ for a standard length myotomy. Variations in myotomy length have been suggested when treating conditions that predominantly affect the esophageal body, such as type III achalasia or jackhammer esophagus; in these cases, the myotomy can be started just proximal to the spastic segment, ensuring at least 2–3 cm of mucosal flap coverage in the submucosal tunnel [19]. Once the plane between the inner circular muscle layer and thin, outer, longitudinal muscle layer is accessed, the triangular-tip ESD knife can be used to hook the circular muscle fibers and extend the myotomy distally (Fig. 17.4k). Full-thickness myotomy or splaying of the thin, outer longitudinal muscle fibers is common, especially around the EGJ. The myotomy should be extended 2–3 cm distal to the EGJ onto the gastric cardia. At the conclusion of the myotomy, after assuring hemostasis in the tunnel, irrigation is performed with dilute bacitracin solution.

A variety of intraoperative techniques have been described to evaluate for adequacy of myotomy in relieving esophageal outflow obstruction at the level of the EGJ. These range from purely subjective, based on laparoscopic inspection or ease of passage of the endoscope during EGD post-myotomy, to quantitative, but time consuming, in the case of intraoperative manometry. At least three centers in the USA currently employ the EndoFLIP device described earlier, in the diagnostic testing section, for intraoperative assessment of myotomy adequacy as measured by an increase in EGJ distensibility index [17].

Closure of Mucosotomy

Mucosotomy width will help guide initial clip selection, with the Instinct™ Endoscopic Hemoclip (Cook Medical, Winston-Salem, NC, USA) or Resolution Clip (Boston Scientific, Marlborough, MA, USA) being helpful in cases of wider mucosal defects and the QuickClip2 (Olympus, Tokyo, Japan) offering a smaller overall size following deployment (Fig. 17.4l). Alternative methods of closure have been described utilizing proprietary endoscopic suturing devices such as the OverStitch (Apollo Endosurgery, Austin, TX, USA), to allow a running closure of longer mucosotomy defects.

Avoiding Complications

Aspiration

Preoperative dietary restriction to clear liquids in preparation for the procedure as well as utilization of a "rapid-sequence" intubation technique by anesthesia (limited pre-oxygenation/bag-masking) can help minimize the risk of aspiration during induction. If needed, awake fiberoptic intubation in the upright position can be utilized in high-risk patients.

Capnothorax

Given the frequency of full-thickness myotomy or splaying of the outer, longitudinal muscle fibers, development of unilateral or bilateral capnothorax is common [6]. There is no data supporting routine postoperative chest X-rays, assuming CO_2 is utilized for insufflation in place of air. Capnothorax progressing to tension physiology or hemodynamic compromise is exceedingly rare but the instruments should be available as well as staff capable of performing an emergent needle or tube thoracostomy, if needed. Self-limited subcutaneous emphysema is also common with expected resolution within 24 h postoperatively. In addition, roughly 50 % of POEM cases are accompanied by the development of some degree of capnoperitoneum secondary to CO_2 tracking from the mediastinum or full-thickness gastric myotomy [6]. Capnoperitoneum can be differentiated from an insufflated stomach by the presence of isolated epigastric fullness in the latter; the diffuse abdominal distension

of the former, when accompanied by hemodynamic instability or impaired ventilation, is an indication for decompression with a Veress needle (typically in the right upper quadrant, just inferior to the costal margin) or laparoscopic port. While not necessarily complications, the relative frequency with which insufflation-related events are encountered highlights the necessity of utilizing CO_2 insufflation during POEM.

Bleeding

Based on the global POEM experience to date, bleeding, if it occurs, is most commonly encountered during dissection across and distal to the EGJ. As previously discussed, even mild hypertension will compound the bleeding risk inherent to the increased vascularity in the submucosal space of the EGJ and gastric cardia. Mild bleeding can typically be controlled with application of monopolar electrocautery. Brisker bleeding, or unavoidable division of larger bridging vessels, should be approached with coagulation forceps. Submucosal tunnel bleeding that obscures endoscopic visualization can occasionally be temporized by removal of the endoscope from the tunnel and application of direct pressure with the scope or cap from the esophageal lumen for 10–20 min. Alternative techniques include hemostatic clip application and judicious injection of dilute epinephrine. Case reports have suggested the option of utilizing tamponade devices such as Sengstaken-Blakemore, Minnesota, or Linton Tubes (All Bard Medical) to staunch brisk bleeding. Given the disastrous consequences of this in the setting of a partial or full-thickness myotomy, these high-pressure balloons should not be considered as part of the endoscopic armamentarium when approaching bleeding during the POEM procedure.

Full-Thickness Perforation

Entry into the mediastinum at the level of the mucosotomy, either during initial access of the submucosal space or subsequently, should prompt close attention to mucosal closure technique, including consideration of alternative methods of closure such as endoscopic suturing [20] or utilization of larger clips. Blunt dissection of the submucosal space has been described in both animal models and human case series as a means to expedite tunnel creation and decrease procedure duration. This technique is associated with increased rates of inadvertent mucosotomy,

particularly in the area just proximal to the EGJ, where relative tethering of the mucosa can occur and predispose the proximal tissue to perforation when approached blindly. Significant mucosal defects that occur prior to myotomy creation should prompt consideration of aborting the procedure and/or attempting submucosal tunnel and myotomy in an alternate position on the esophagus (i.e., posterolateral). Small mucosal defects and those that occur during or after myotomy should be closed from the lumenal side with endoscopic clips or suture. Note that mucosal injuries, especially in the region of the EGJ, can lead to the development of strictures and recurrent dysphagia.

Postoperative Care

At the conclusion of the case, patients are extubated in the operating room and transferred to the post-anesthesia care unit (PACU). During the initial recovery phase in the PACU, patients are given standing intravenous antiemetics and analgesia as needed and kept nil per os (NPO) pending further evaluation. If the patient is sufficiently recovered from the effects of anesthesia and not experiencing chest pain, fever, or tachycardia, sips of clear liquids are initiated in the evening of surgery. In the absence of concerning symptoms or signs that suggest leak, patients are given a tray of clear liquids in the morning and advanced to a full liquid diet for lunch. Discharge typically occurs in the afternoon of the first postoperative day (POD#1) after response to lunch is evaluated. Among the IPOEMS centers, the weighted mean length of stay was 3.1 days (range 1–7), with the six US centers generally reporting earlier discharges postoperatively [6]. Patients are discharged on twice-daily proton pump inhibitors that are continued until physiologic testing is performed at 6 months to assess for the presence or degree of gastroesophageal reflux. Many centers advocate routine imaging (water-soluble or thin barium esophagram) on POD#1 with some centers performing second-look EGD prior to diet initiation or hospital discharge [6]. During our initial experience, the postoperative care pathway included obtaining a POD#1 esophagram, but the lack of impact on patient management and low leak rate have led to abandonment of asymptomatic screening of all patients postoperatively. There are descriptions of postoperative computed tomography scans of the chest being routinely obtained; however, following the same logic that led to abandonment of routine esophagram use, there is no clear evidence to support the cost or radiation exposure associated with routine screening CT scans.

Follow-Up

Patients should be seen 2–6 weeks postoperatively to evaluate treatment response and detect potential early failures. In the absence of recurrent symptoms, full physiologic testing with TBE, HRIM, EndoFLIP, and pH-impedance is postponed until the 6-month follow-up appointment. TBE in particular has been shown to have significant prognostic value following pneumatic dilation in detecting patients with symptomatic relief that are at increased risk for early treatment failure [21]. Patients are seen again at 1 year and then annually for life, with completion of validated questionnaires and intermittent physiologic testing to track long-term outcomes. Long-term follow-up protocols can also incorporate routine or symptom-triggered screening for esophageal malignancy.

Review of Existing Literature

Efficacy

To date, no prospective, randomized trials comparing POEM to LHM or pneumatic dilatation have been published. The IPOEMS reported overall treatment success of 98 % at a mean follow-up of 9.3 months, with 40 % of patients having failed prior treatments [6]. The multicenter, prospective trial by Von Renteln et al. showed a decline in success rate over time, from 97.1 % at 3 months to 82.4 % at 1 year [22], although this may reflect a learning curve issue as many of the cases in this report were performed during the early portion of POEM series at participating centers.

Rates of GERD

Richards et al. demonstrated in 2004 that in the absence of a concurrent fundoplication, complete division of the lower esophageal sphincter and gastric sling fibers during Heller's cardiomyotomy results in debilitating reflux [23]. Neither partial nor complete fundoplication is performed following POEM and concern has been raised regarding the potential for higher long-term rates of GERD. While long-term data is forthcoming, based on visualization of erosive esophagitis on EGD or abnormal pH studies during short-term follow-up (<1 year), the

estimated prevalence of GERD following POEM may be in the range of 20–46 % [6]. Comparable rates have been reported in patients undergoing LHM with anterior (Dor) fundoplication in multicenter, prospective, randomized trials [24, 25]. Similar to the argument put forth by proponents of anterior (Dor) fundoplication, the lack of posterior mediastinal dissection and preservation of the phreno-esophageal ligament during POEM may mitigate the absence of a surgical anti-reflux barrier. Preservation of the angle of His may also contribute to the anatomic anti-reflux barrier when the 1–2 o'clock position is used for myotomy during POEM, as the natural course of the esophagus (clockwise rotation and right-to-left sweep) favors dissection onto the lesser curve and division of the clasp fibers with maintenance of the sling fibers.

References

1. Mayberry JF. Epidemiology and demographics of achalasia. Gastrointest Endosc Clin N Am. 2001;11:235–48. PMID: 11319059.
2. Kahrilas PJ, Boeckxstaens G. The spectrum of achalasia: lessons from studies of pathophysiology and high-resolution manometry. Gastroenterology. 2013;145(5): 954–65. PMID: 23973923.
3. Moonen A, Boeckxstaens G. Current diagnosis and management of achalasia. J Clin Gastroenterol. 2014;48(6):484–90. PMID: 24926623.
4. Kandulski A, Fuchs KH, Weigt J, Malfertheiner P. Jackhammer esophagus: high-resolution manometry and therapeutic approach using peroral endoscopic myotomy (POEM). Dis Esophagus. 2014;27. PMID: 24460870.
5. Minami H, Inoue H, Haji A, et al. Per-oral endoscopic myotomy: emerging indications and evolving techniques. Dig Endosc. 2015;27(2):175-81. PMID: 25040806.
6. Stavropoulos SN, Modayil R, Friedel D, et al. The International Per Oral Endoscopic Myotomy Survey (IPOEMS): a snapshot of the global POEM experience. Surg Endosc. 2013;27:3322–38. PMID: 23549760.
7. Fisichella PM, Patti MG. From Heller to POEM (1914-2014): a 100-year history of surgery for achalasia. J Gastrointest Surg. 2014;18(10):1870–5. PMID: 24878993.
8. Pasricha PJ, Hawari R, Ahmed I, et al. Submucosal endoscopic esophageal myotomy: a novel experimental approach for the treatment of achalasia. Endoscopy. 2007;39:761–4. PMID: 17703382.
9. Rajan E, Gostout CJ, Feitoza AB, et al. Widespread EMR: a new technique for removal of large areas of mucosa. Gastrointest Endosc. 2004;60:623–7. PMID: 15472695.
10. Inoue H, Minami H, Kobayashi Y, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42:265–71. PMID: 20354937.
11. Eckardt VF. Clinical presentations and complications of achalasia. Gastrointest Endosc Clin N Am. 2001;11(2):281–92. PMID: 11319062.

12. Hungness ES, Teitelbaum EN, Santos BF, et al. Comparison of perioperative outcomes between peroral esophageal myotomy (POEM) and laparoscopic Heller myotomy. J Gastrointest Surg. 2012. PMID: 23054897.
13. Harnish JL, Darling GE, Diamant NE, et al. Patient-centered measures for achalasia. Surg Endosc. 2008;22(5):1290–3. PMID: 18027052.
14. Fisichella PM, Raz D, Palazzo F, Niponmick I, Patti MG. Clinical, radiological, and manometric profile in 145 patients with untreated achalasia. World J Surg. 2008;32:1974–9. PMID: 18575930.
15. Pandolfino JE, Kwiatek MA, Nealis T, et al. Achalasia: a new clinically relevant classification by high-resolution manometry. Gastroenterology. 2008;135:1526–33. PMID: 18722376.
16. Rohof WO, Salvador R, Annese V, et al. Outcomes of treatment for achalasia depend on manometric subtype. Gastroenterology. 2012. PMID: 23277105.
17. Rohof WO, Hursch DP, Kessing BF, et al. Efficacy of treatment for patients with achalasia depends on the distensibility of the esophagogastric junction. Gastroenterology. 2012;143(2):328–35. PMID: 22562023.
18. 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. PMID: 23394838.
19. Roman S, Pioche M, Mion F. Per oral endoscopic myotomy (POEM) for all spastic esophageal disorders? Endosc Int Open. 2015;3(3):E202–4. PMID: 26171431.
20. Modayil R, Friedel D, Stavropoulos SN. Endoscopic suture repair of a large mucosal perforation during peroral endoscopic myotomy for treatment of achalasia. Gastrointest Endosc. 2014;80(6):1169–70. PMID: 24830579.
21. Vaezi MF, Baker ME, Achkar E, et al. Timed barium oesophagram: better predictor of long term success after pneumatic dilation in achalasia than symptom assessment. Gut. 2002;50:765–70. PMID: 12010876.
22. von Renteln D, Fuchs KH, Fockens P, et al. Peroral endoscopic myotomy for the treatment of achalasia: an international prospective multicenter study. Gastroenterology. 2013;145:309–11. PMID: 23665071.
23. Richards WO, Torquati A, Holzman MD, et al. Heller myotomy versus Heller myotomy with Dor fundoplication for achalasia: a prospective randomized double-blind clinical trial. Ann Surg. 2004;240(3):405–12. PMID: 15319712.
24. Rebecchi F, Giaccone C, Farinella E, Campaci R, Morino M. Randomized controlled trial of laparoscopic Heller myotomy plus Dor fundoplication versus Nissen fundoplication for achalasia: long-term results. Ann Surg. 2008;248(6):1023–30. PMID: 19092347.
25. Rawlings A, Soper NJ, Oelschlager B, et al. Laparoscopic Dor versus Toupet fundoplication following heller myotomy for achalasia: results of a multicenter, prospective, randomized-controlled trial. Surg Endosc. 2012;26:18–26. PMID: 21789646.

18. Endoscopic Interventions for the Thoracic Esophagus: Zenker's and Other Diverticula

Emily A. Speer and Lee L. Swanstrom

Introduction

Esophageal diverticula are outpouchings or herniations from the esophageal wall that may be found anywhere along the esophageal lumen. They are typically classified as either true (all layers of the esophagus) or false, and treatment is heavily influenced by their location (upper, middle, or lower), which often portends their etiology. A wide variety of operative approaches have been described, and largely due to the rarity of this condition, no large studies comparing one approach with another currently exist. In this chapter, we focus on the operative techniques of endoscopic treatment of esophageal diverticula, with a majority focus on the most common—Zenker's diverticulum.

Background

As previously mentioned, esophageal diverticula are classified as either true or false, and are grouped according to location (upper, middle, or lower). True diverticula involve all layers of the esophageal wall and are usually fall into the category of "traction diverticula," those that form in response to pull forces from an inflammatory or fibrotic mediastinal process. They are usually associated with cancer or chronic infection such as tuberculosis, with resulting lymph node reaction. True diverticula tend to occur in the mid-esophagus. On the other hand, false diverticula occur most frequently in the upper and lower esophagus. False diverticula, which contain only mucosa and submucosa that herniate

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through weaknesses in muscularis, are termed pulsion diverticula. These are formed as a result of increased intraluminal pressure mainly due to primary motility disorders or outflow obstruction. They can also occur as a result to planned or accidental perforation such as post dilation perforations or as a long-term sequelae of Heller myotomy when it extends into the unsupported thoracic esophagus. Upper esophageal diverticula are sometimes called "C6" diverticula, and they are most frequently Zenker's diverticula or less commonly Killian–Jamieson diverticula. Lower esophageal ones are termed epiphrenic diverticula.

Upper Esophageal Diverticulum

History

The most commonly encountered esophageal diverticula are, again, Zenker's diverticula. In 1877, the first recorded attempt of surgical treatment of a Zenker's was performed by Nicoladoni, who created a fistula between the patient's pouch and skin [1]. Subsequently, diverticulectomy, diverticulopexy, and diverticulum inversion were described. Endoscopic (ridged) diverticulotomy was actually described quite early on in 1917 by Mosher, but this approach was quickly abandoned after an unacceptably high rate of mediastinitis was encountered. It wasn't until over 40 years later that endoscopic treatment made its reappearance when Dolman and Mattson presented promising results with electrosurgical endoscopic diverticulotomy in 1960. Yet endoscopy was slow to gain popularity after its initial discouraging results. Over 20 years later, in 1984, Overbeek et al. described flexible endoscopic laser diverticulotomy, and in 1993, Collard and Hirsch simultaneously reported diverticulotomy using a ridged endoscope and transoral stapling device [2]. Great progress has been made after initially disappointing results and the endoscopic treatment of esophageal diverticula is rapidly advancing along with the advent of new surgical innovations.

Upper, aka C6 diverticula are largely false diverticula caused by inappropriately high intraluminal pressure during deglutition. The most common are Zenker's and Killian–Jamieson diverticula. A Killian's diverticulum is formed by weakness in the Killian–Jamieson triangle located inferiorly to the cricopharyngeus muscle. It is located more laterally than a Zenker, which forms above the cricopharyngeus muscle through Killian's triangle (Fig. 18.1). Killian–Jamieson diverticula occur in a 1:4 ratio with Zenker's diverticula, and they are often misdiagnosed

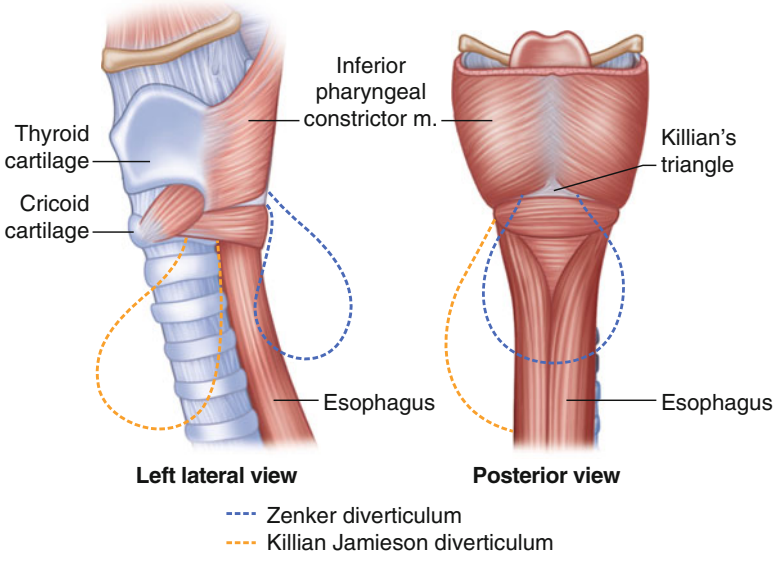

Fig. 18.1. Anatomic position of proximal esophageal diverticula.

as Zenker's. They are usually smaller, however, and are less likely to be symptomatic than Zenker's (19 % versus 62 %) [3]. As a pulsion diverticulum, Killian–Jamieson diverticula are thought to be due to high intraluminal pressures during swallowing caused by inappropriately robust proximal esophageal circular muscle contraction while the cricopharyngeus simultaneously closes above the Killian–Jamieson triangle. While Killian–Jamieson diverticula have been treated by both open and endoscopic means, some feel endoscopic repair may be inferior since it does not allow adequate visualization of the recurrent laryngeal nerve, which inserts at the bottom of the Killian–Jamieson triangle [4]. Currently, however, both open and endoscopic treatments are viable options.

Zenker's diverticula are by far the most common esophageal diverticula, and they have certainly generated the most endoscopic surgical interest. Zenker's diverticulum is a false diverticulum formed due to high intrapharyngeal pressure from uncoordinated and impaired relaxation of the cricopharyngeus (upper esophageal sphincter) during deglutition. Killian's triangle, just proximal to the cricopharyngeus, is an area of relative weakness, and is thusly the site of mucosal and submucosal herniation (Fig. 18.1). The neck of the diverticulum is midline, and in

approximately 90 % of cases it extends inferiorly and toward the patient's left. Although the exact etiology of the disease is unknown, fibrosis of the cricopharyngeus muscle is a prominent histologic finding. Gastroesophageal reflux disease is associated with Zenker's diverticula, and this is thought to be due to GERD contributing to cricopharyngeal dysfunction perhaps as a secondary protective compensation to the defective lower esophageal sphincter [5].

Presentation

Upper esophageal diverticula present most commonly with dysphagia in the early phase of deglutition (80–90 %), chronic cough (30–40 %), regurgitation of undigested food or pills (leading to poor absorption), weight loss, aspiration pneumonia, and halitosis. They can lead to iatrogenic perforation from nasogastric tubes, or act as a reservoir and incarceration of endoscopic capsules, and even lost dentures have been reported [5]. They have been found to harbor squamous cell cancer in 0.4–1.5 %, and careful endoscopic examination is always warranted. Zenker's diverticula have a prevalence of approximately 0.01–0.11 % overall, and are more common in elderly males in the seventh to ninth decades of life [5]. Diagnosis is made with either upper endoscopy or contrast swallow study (Fig. 18.2).

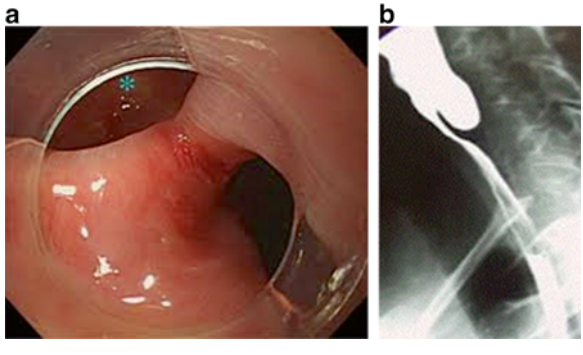

Fig. 18.2. (**a**) Endoscopic visualization of Zenker's. (**b**) Barium X-ray of Zenker's diverticulum.

Treatment

Definitive treatment of Zenker's involves dealing with both the anatomic outpouching and, treating the underlying cause of the disorder, the hypertensive cricopharyngeal sphincter. The primary goal of treatment of Zenker's diverticulum should be a cricopharyngeal myotomy. The cricopharyngeal bar, which is also the common wall of the diverticulum and esophagus, consists of mucosa, submucosa, connective tissue, and the cricopharyngeus muscle. Therefore, division of the common wall endoluminally effectively achieves both sphincter division and ablates the diverticulum by creating a common channel. This allows for rapid drainage of the diverticulum into the upper esophagus. Diverticulotomy has been found to be effective at returning intrabolus and upper esophageal sphincter pressures toward normal [6]. This was previously unrecognized, as initial diverticulum surgeries focused on diverticulum resection, suspension, or inversion often without myotomy. Without myotomy, long-term recurrence rates are very high [7].

An open operation via cervical incision has traditionally been utilized for treatment of Zenker's diverticulum. However, this approach is associated with longer hospital stays and higher morbidity compared to newer endoluminal approaches. Additionally, the cervical approach has a higher risk of damage to the recurrent laryngeal nerve and hypoglossal, and requires general anesthesia. As Zenker's diverticulum is largely a disease of elderly patients who often have relative contraindications to surgery, endoscopic therapies have become increasingly attractive to surgeons, otolaryngologists, and gastrointestinal endoscopists alike [6].

Transoral approaches utilize either rigid or flexible endoscopes. A variety of energy devices may be used to divide the Zenker's bar and use of different devices continue to be reported. These include laparoscopic staplers, monopolar needle knife or hook knife electrocautery, monopolar forceps, ultrasonic shears (Harmonic), bipolar devices (Liga-Sure or BELA), argon plasma coagulation, and carbon dioxide lasers. In general, stapling, ultrasonic scalpels, rigid bipolar devices, and carbon dioxide lasers are utilized for the myotomy through a rigid endoscope; monopolar needle-knife, argon plasma coagulators, and emerging devices such as flexible bipolar forceps may be used through a flexible endoscope.

If a Zenker's diverticulum is small and asymptomatic, no treatment is needed; if larger or symptomatic, treatment may be advisable. The optimal approach for repair is debated, but patient comorbidity, size of

diverticulum, neck mobility, and local expertise are all factors that go into deciding the best procedure. Flexible endoscopy is especially useful in patients whose anatomy precludes adequate visualization with rigid endoscopy (for example, severe kyphosis, unfavorable dentition, and small oropharyngeal cavities). Many experts advocate that if the diverticulum is less than 3 cm, flexible endoscopy may be ideal; if 3–5 cm stapled cricopharyngotomy may be best; and if >5 cm in healthy patients, open diverticulectomy with myotomy might be preferable. Additionally, patients with recurrent Zenker's after prior open repair are likely to be best served by endoscopic cricopharyngomyotomy in order to avoid reoperating around important cervical structures such as the recurrent laryngeal and hypoglossal nerves [6].

Stapling

Stapling is currently the most frequently performed transoral approach to Zenker's diverticulum [6]. The simultaneous cut and seal function of the stapler makes this approach attractive, particularly to surgeons. This approach is thought to be optimal for diverticula from 3 to 5 cm since the nonfunctioning end of the stapler can be difficult to fit in smaller pouches and leaves at least a residual 1 cm of undivided common wall. The technique may vary, but, in general, is as follows:

1. General endotracheal anesthesia is induced.
2. Antibiotics (typically a second generation cephalosporin) and a dose of steroids (to minimize mucosal edema) are administered in accordance with surgeon preference.
3. The patient is positioned supine with neck hyper-extension using a shoulder roll. This position helps maintain the straight hypopharyngeal pathway needed for in-line passage of the rigid endoscope.
4. Teeth are protected.
5. A rigid bivalve endoscope (such as a Karl Storz Weerda diverticuloscope) is used (Fig. 18.3). A light source and optical scope are usually fixed to the diverticuloscope to aid visualization. The diverticuloscope is inserted in closed position into the esophageal inlet under constant direct visualization. This is slowly retracted and opened to expose the common wall. The scope is gently advanced again until the anterior blade enters the esophagus and the posterior blade lies in the diverticulum, exposing the Zenker's cricopharyngeal bar.

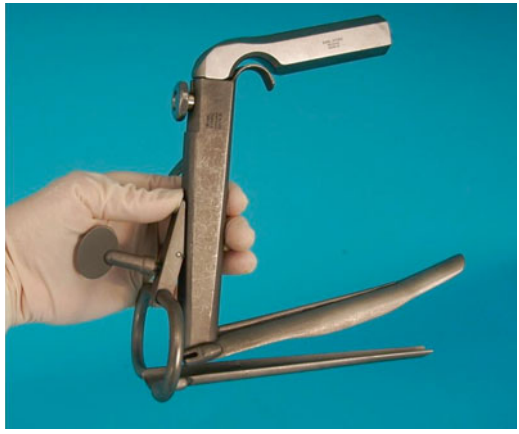

Fig. 18.3 Weerda ridged laryngeal retractor.

6. The laparoscopic endostapler is introduced through the scope and across the cricopharyngeal bar, with the cartridge arm in the esophagus and the anvil arm in the diverticulum. Care must be taken not to perforate the back end of the diverticulum. A 35 mm stapler with 2.5 mm staple height is commonly used. The stapler is fired, simultaneously cutting and sealing, and thus eliminating all but about 1–1.5 cm of the septum. In larger diverticulum, this will effectively divide the cricopharyngeal sphincter. In an attempt to minimize the nonfunctional distal tip, some authors have advocated trimming the end of the anvil arm of the stapling device (Fig. 18.4). Needle knife electrocautery may also be used to complete the end of the myotomy. Alternatively, retraction sutures (using endostitch or overstitch) may be placed on the lateral edges of the cricopharyngeal bar to provide proximal traction as the stapler is engaged [6].

Ultrasonic Shears and Bipolar (Liga-Sure)

Using similar techniques as stapled diverticulotomy, 5 mm laparoscopic tools such as ultrasonic scalpels and bipolar electrosurgical sealing devices, have also been used to divide the common wall of the Zenker [8]. The main advantage of these devices over endostaplers is

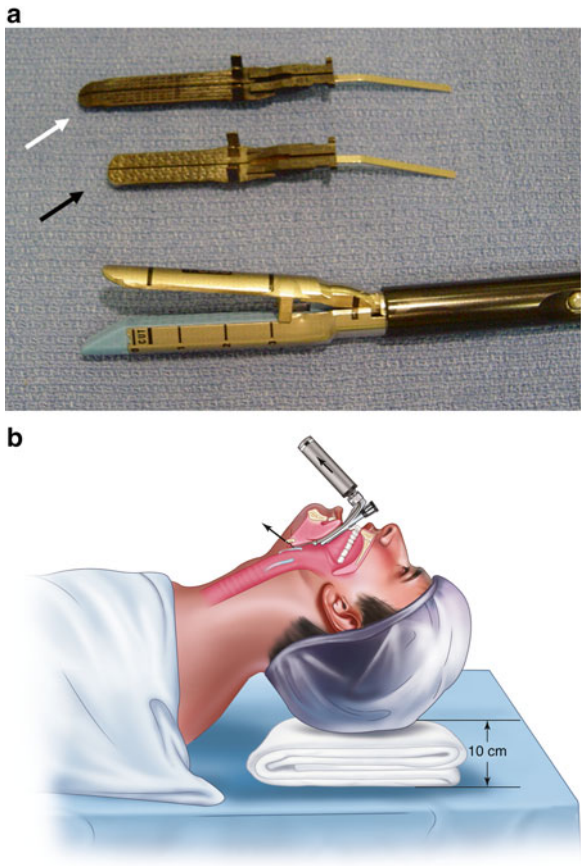

Fig. 18.4. Endoscopic staplers can be used to divide the cricopharyngeal septum. They are often modified by grinding off the anvil blade to extend the cut further down the tip of the diverticulum (**a**). (**b**) One blade is placed in the diverticulum and the other in the esophagus.

that the cutting surface extends all the way to the distal tip and their much smaller profile (5 mm versus 12 mm) markedly improves visualization. Additionally, the small diameter of these tools allows them to fit into smaller diverticula. Recently, the use of a flexible overtube fashioned into a soft diverticuloscope in lieu of a traditional bivalved rigid endoscope has been described. This modified "duck-beak diverticuloscope" provides exposure of the cricopharyngeal bar while

Fig. 18.5. A bivalved flexible overtube can be used for exposure for either rigid or flexible Zenker's diverticulectomy. ZD overtube (Cook Endoscopy, Winston-Salem, North Carolina).

simultaneously protecting the posterior wall of the diverticulum and anterior wall of the esophagus from inadvertent electrical burns (Fig. 18.5) [9]. The soft diverticulascope overtube also allows one to use a flexible scope with the small laparoscopic instruments yielding a true "hybrid" procedure.

"Laser" Diverticulectomy

In 1981, van Overbeek described the use of a CO_2 laser for septal division [10]. His technique allowed the use of a smaller-diameter rigid diverticuloscope than stapled cricopharyngotomy (since the laser is thinner than a stapler), and it also enables a very precise transection using a micromanipulator. Another advantage of using laser is its very minimal lateral thermal spread [11]. Steps to this procedure were:

1. General endotracheal anesthesia was introduced, and the patient was prepared in similar fashion to that of the stapled technique.
2. A special rigid diverticuloscope was introduced and the common wall was isolated.

An operating microscope with a 400 mm lens and CO_2 laser micromanipulator at 5–10 W was used to divide the cricopharyngeal bar in its midline from the top down to the base. Care is taken to fully divide the septum, as it is fairly easy for one to misjudge where the bottom of the bar lies [6, 11].

"Laser Zenker's diverticulectomy" enjoyed a brief enthusiastic popularity before rather quickly completely fading away, due to the equipment cost, the cumbersome nature of the laser, credentialing issues and a few, rather spectacular reports of endotracheal fires. It is today, only of historical interest.

Flexible Endoscopic Zenker's Treatment

In 1995, Ishioka et al. and Mulder et al. simultaneously reported the first use of flexible endoscopy for treatment of Zenker's diverticulum [12, 13]. This has subsequently transformed treatment of Zenker's diverticulum in that it made it feasible to treat patients who were poor risks for open surgery, as it allowed surgery without the need for general endotracheal anesthesia or inpatient hospital stays, and also was a minimally invasive alternative for patients who were not candidates for ridged transoral approaches due to anatomic constraints such as rigid kyphosis, previous spine surgery, micrognathia, etc. The basic procedure remains the same; namely, division of the common wall, provides a cricopharyngeal myotomy and creates a common cavity to prevent anatomic "hang up." Surgeons can use either "freehand" techniques or, more commonly, accessories such as hoods, caps, and soft diverticuloscopes to aid in visualization and protect against inadvertent esophageal electrocautery injury. Technology advances, particularly those in the evolving fields of ESD, full-thickness resection and NOTES, continue to transform how the flexible endoscope is used for the treatment of Zenker's diverticulum.

The needle knife, hook knife, and triangle tip direct current monopolar instruments have all been described for flexible endoscopic cricopharyngomyotomy. Variations in technique exist, but the procedure is generally set up as follows:

1. The patient can be placed in left lateral decubitus position or supine.
2. General endotracheal intubation is primarily used, in order to provide a stable operative field but mainly to protect from aspiration in these fairly at-risk patients.
3. A standard flexible upper endoscope is used to clear the diverticula of debris. Great care is taken to intubate the esophagus under direct endoscopic visualization to avoid iatrogenic perforation. A large bore 16–18 french nasogastric tube may be inserted into the esophagus under endoscopic visualization to help stent the anterior esophageal wall away from the cricopharyngeal bar and to decompress the stomach. Carbon dioxide insufflation is important both for post procedure patient comfort and to prevent complications including pneumothorax or substantial and long-lasting sub-Q emphysema. A soft diverticuloscope such as the ZD overtube (Cook Endoscopy) may also be used to expose and protect the working area (see Fig. 18.5). This duck-beaked tube is inserted such that the longer end protects the

Fig. 18.6. Dissecting caps are a useful adjunct to provide retraction and exposure.

anterior esophagus and the shorter end shields the posterior diverticular wall. The overtube is advanced over the endoscope into the position, and the black line signals the approximate location (16 cm) that the overtube usually rests at the teeth [6]. We have found however, that the exposure benefits are often outweighed by the restricted endoscope motion the device entails—both from friction and the diameter constraints. Alternatively, clear dissecting caps, as are used for procedures like ESD or POEM, can be used to provide retraction and exposure (Fig. 18.6).

4. Using a soft coagulation current, it is important to mark the midpoint of the cricopharyngeal/common wall as well as the endpoint of the diverticulum as identified under full insufflation. We tend to add extra marks between these two points to map out the path of maximal apposition between the esophagus and diverticulum.
5. The endoscopist inserts the needle-knife or hook-knife through the working channel and division of the septum begins. An endocut (alternating cut/coag) setting is used for the mucosa and a blended or pure coagulation current is usually used for the muscle layers. Most surgeons begin division at the top of the septum and end at the base

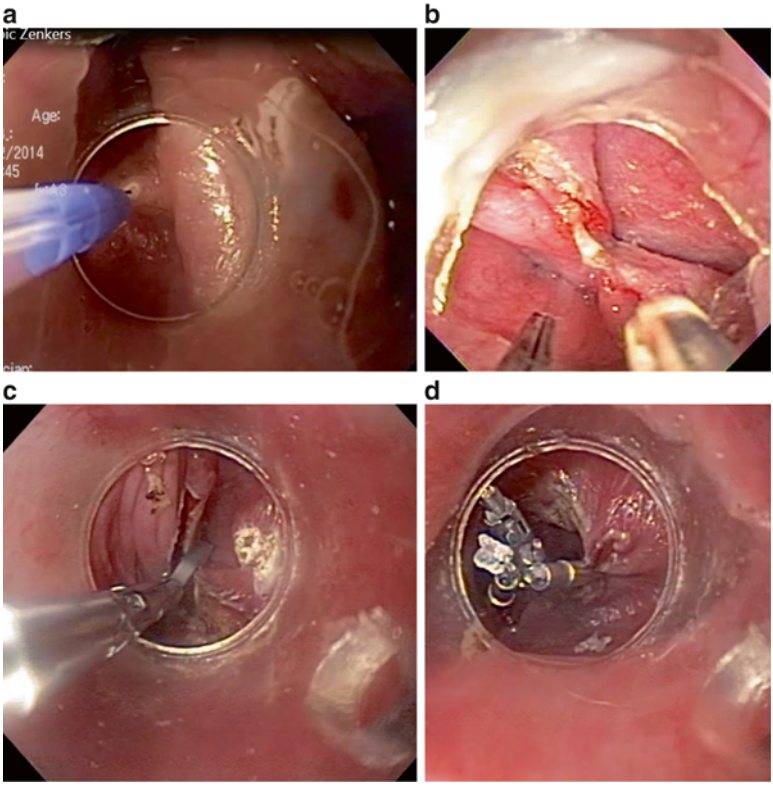

Fig. 18.7. (**a**) The midpoint of the cricopharyngeal bar, the tip of the diverticulum and a corresponding point on the esophagus are marked with the cautery. (**b**) The common wall is then divided with the needle-knife or hook cautery. (**c**) The Apex of the diverticula incision and esophageal incision is clipped. (**d**) Additional clips reapproximate the mucosa over the divided muscle on the sides.

(Fig. 18.7). However, concerns have been raised that incomplete myotomy might be more common using a strictly freehand technique (as evidenced by a reported 20 % recurrence rate in some studies) [6]. This may be due to distorted anatomy following separation of the cricopharyngeal muscle, or perhaps fear of perforating freely into the neck and causing complications. Some endoscopists advocate using a hook knife to start hooking tissue at the caudal aspect of the cricopharyngeal bar and working upward to ensure complete myotomy. We prefer to do an extended esophageal myotomy for 1–2 cm onto the wall of the esophagus to avoid any chance of an incomplete myotomy.

6. Clips are then used to close the mucosa over the divided muscle, to prevent leaks into the neck or mediastinum, to minimize the risk of bleeding from the raw muscle edges and to decrease the chance that the muscle will heal back together [14]. Some even advocate a "clip and cut" technique whereupon a clip is placed on either size of the line of dissection prior to incision [15]. Although some divide the common wall and leave it open, we prefer to close as infection and postoperative bleeding remain significant possibilities. We have found that by avoiding extending the esophageal mucosal incision the full length of the myotomy (i.e., raising a flap), closure is relatively easy.

Argon Plasma Coagulation

Argon Plasma Coagulation, like laser, is an alternative to monopolar electrocoagulation that appears to have similar risks and benefits [16]. Setup is virtually identical to that of needle-knife diverticulotomy. Again, conscious sedation may be used. A nasogastric tube or flexible diverticuloscope may be used. Clips may also be used. Typical APC settings are ERBE 200 ICC 120/A60, 1.2 L/min [6].

Future Devices

A number of devices that are either in development or being used in animal models show promise for future endoscopic Zenker's treatment. Flexible bipolar forceps (BELA, Ethicon Endosurgery) (Fig. 18.8) originally developed for natural orifice surgery has been used to perform diverticulotomy in porcine models. This device was inserted through the working port of an endoscope and had promise as it both sealed ("welds") and divided the tissue [17]. Flexible endoscopic stapling devices are also in development, and these may also prove the ultimate device for cricopharyngotomy and Zenker's cure (Fig. 18.9).

Postoperative Care

After endoscopic cricopharyngotomy, patients are typically discharged on postoperative day number 1. For uncomplicated outpatient procedures, some patients may be discharged as quickly as 6 h postprocedure. Our institution routinely obtains postoperative water-soluble

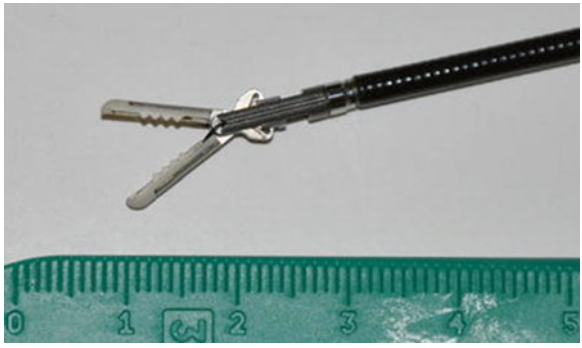

Fig. 18.8. The Bela bipolar coagulation device (Ethicon, Blue Ash, OH) is a flexible cut and seal device that has been shown to be useful for Zenker's.

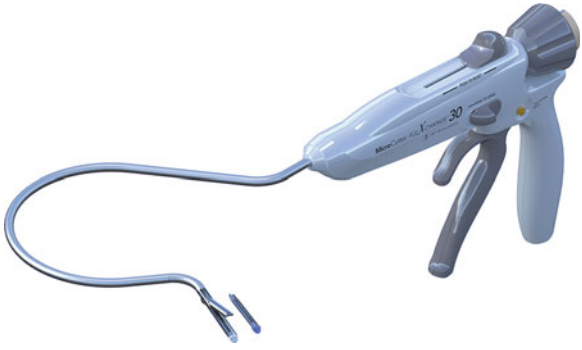

Fig. 18.9. In the future, 3 or 5 mm flexible endoscopic stapling devices may be the ultimate answer for treating Zenker's.

contrast esophagrams to evaluate for clearance or leaks. It should be noted, however, that these studies may not be reliable for ruling out very small leaks, and clinical judgment is prudent. We also routinely recommend a clinical evaluation for gastroesophageal reflux and an endoscopy to look for retained clips or residual diverticula at 6 months. In patients with continued dysphagia symptoms at the 6-month follow-up, our practice is to perform a Savary dilation if there is no residual diverticulum or retained clips.

Outcomes

Outcomes comparing ridged endoscopic, flexible endoscopic and open diverticulotomy have been historically difficult to quantify given the rarity of the Zenker's diverticulum diagnosis and the lack of standardization in technique. In a recent article by Leong et al., 585 transoral stapled diverticulotomy patients were reviewed, and overall good results were reported. Overall, 92 % of the endoscopic stapling procedures were completed successfully. Symptoms improved or resolved in 91 %, the complication rate was 9.6 %, and overall recurrence rate was 12.8 % (most of these went on to repeat stapling) [18]. Most retrospective analyses of both flexible and ridged endoscopic Zenker's treatment cite clinical success rates from 80 to 100 % with mean recurrence rates of 6 % (versus 5 % for open procedures) [6].

Complications

Complications of endoscopic Zenker's diverticulotomy include bleeding in up to 10 % (which may be decreased by closing the mucosa with clips or staplers), leaks (most of which can be treated conservatively with NPO and intravenous antibiotics), mediastinitis, aspiration pneumonia, temporary subcutaneous or mediastinal emphysema (23 %), transient fever, septum recurrence, and missed malignancy (due to a non-excised pouch) [6]. Other risks include dental injury, thermal injury to recurrent laryngeal nerves, cervical spinal cord trauma and death in approximately 0.2 %. This compares favorably to the mortality rate from open procedures (1.6–3 %) [19].

Mid-esophageal Diverticulum

Esophageal diverticula in the middle third are unique from other esophageal diverticula in that they are commonly true diverticula (involving all layers of the esophageal wall). These are often traction diverticula, which are caused by a nearby inflammatory reaction pulling on the esophageal wall and frequently are associated with either chronic severe infectious disease or cancer. It should be remembered that pulsion diverticula can still present in the mid-esophagus, and, motility disorders have been found to be associated with 80–100 % of these patients. For

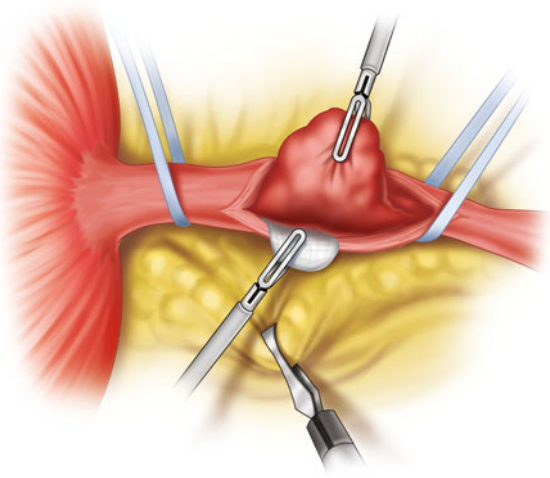

Fig. 18.10. Mid and distal esophageal diverticula are best treated with a thoracoscopic or laparoscopic approach, including resection and a distal myotomy. Art by Michael Leonard.

this reason, endoscopic diverticulotomy and distal myotomy by a POEM (per-oral endoscopic myotomy) technique might be a feasible for symptom relief in ill or elderly patients who are unfit for surgery. Although not widely accepted, there has been case reports of endoscopic diverticulotomy through a flexible endoscope [20] as well as treatment by distal endoscopic myotomy. The standard approach for these diverticula remains laparoscopic/thoracoscopic diverticulectomy with distal myotomy via a laparoscopic or thoracoscopic approach (Fig. 18.10).

Distal Esophageal (Epiphrenic) Diverticulum

Background

Lower esophageal diverticula, or epiphrenic diverticula, are false diverticula arising in the lower 1/3 of the esophagus, near the diaphragm. Their estimated incidence is 1:500,000 per year, and their prevalence is thought to be between 0.015 and 2.0 % [21, 22]. As is common with many false diverticula, they are thought to arise from a combination of downstream obstruction (either functional or mechanical) and a point of

weakness in the muscular layer of the esophagus. An estimated 75–90 % of epiphrenic diverticula are associated with motility disorders, most commonly achalasia and diffuse esophageal spasm [22]. They have a propensity to develop in the right posterior esophageal wall, 4–8 cm above the cardia [21]. The most common presenting symptom is dysphagia, although regurgitation, weight loss, aspiration, heartburn, and cough may also be present. Most lower esophageal diverticula are asymptomatic, but diverticula larger than 5 cm are usually symptomatic and need repair. Cancer incidence in these diverticula is elevated and is estimated to be around 0.6 % (6/100,000) [21, 22].

Diagnosis and Treatment

The diagnosis of epiphrenic diverticula is usually made by esophagram or upper endoscopy during a workup of dysphagia. Almost all experts advocate obtaining esophageal manometry to evaluate for concurrent motility disorder, due to evolving evidence that these diverticula are almost always associated with a sever esophageal motility disorder.

Treatment options range from symptom control with medical management (PPI and solid diet restriction) to open thoracotomy with diverticulectomy and myotomy. Endoscopic options for treatment of symptomatic epiphrenic diverticula include empiric dilation, botox injection, stenting, and per oral endoscopic myotomy. The importance of myotomy as an integral adjunct in treating lower esophageal diverticula has gradually become more evident. In a study of 21 patients out of Mayo Clinic, patients who underwent open or laparoscopic diverticulectomy alone had high recurrence and leak rates compared to those who underwent diverticulectomy with myotomy (19 % and 24 % versus 0 % and 0 %, respectively) [22]. This finding can be explained by considering the physiologic outflow obstruction that often leads to the formation of these pulsion diverticula. While transabdominal and transthoracic approaches remain the most commonly used approaches, severe mediastinal inflammation from adhesions around the diverticular wall, an operative morbidity of 20 %, and a mortality of 5 % all make surgical intervention less enticing. This is especially true when presented with elderly frail patients. This has led clinicians to attempt a multitude of endoscopic interventions aimed at alleviating the relative outflow obstruction in an attempt to stabilize or even shrink diverticula. Again, dilation, botox, stenting, and endoscopic myotomy have all been reported as case studies. The authors have also attempted overstitch

closure of these diverticula, and this, in conjunction with endoscopic myotomy, may be a potential treatment in the future [21–23].

Conclusions

Esophageal diverticula are a rare entity, and the literature regarding their endoscopic treatment is largely composed of small retrospective reviews and case studies. Accordingly, convincing evidence regarding the optimal endoscopic approach is currently lacking. Local surgeon expertise, anatomic considerations, and patient comorbidities are the strongest influencers of treatment choice. Zenker's diverticulum, by far the most common esophageal diverticulum, has appropriately generated the most endoscopic data to date. A number of therapeutic strategies (including endostapling, ultrasonic and bipolar energy devices, carbon dioxide lasers, monopolar electrocoagulators, and argon plasma coagulators) are available, all hinging on the key concept of cricopharyngeal myotomy and opening the diverticulum into the esophageal lumen. New technologies and innovations continue to emerge. Given the elderly and often frail patient demographic that are generally afflicted by these conditions, it seems likely that endoscopic treatments will be first-line in the future.

References

1. Ferguson MK. Evolution of therapy for pharyngoesophageal (Zenker's) diverticulum. Ann Thorac Surg. 1991;51:848–52.
2. Chang CY, Payyapilli RJ, Scher RL. Endoscopic staple diverticulostomy for Zenker's diverticulum: review of literature and experience in 159 consecutive cases. Laryngoscope. 2003;113:957–65.
3. Chea CH, et al. Killian-Jamieson diverticulum: the rarer cervical esophageal diverticulum. Med J Malaysia. 2011;66(1):73–4.
4. Boisvert RD, Bethune DC, Acton D, Klassen DR. Bilateral Killian-Jamieson diverticula: a case report and literature review. Can J Gastroenterol. 2010;24:173–4.
5. Naprawa G, Bialkowska J. Foreign body in a Zenker's diverticulum (looking for the lost dentures). Prz Gastroenterol. 2014;9(4):254–8.
6. Bizotto A, et al. Zenker's diverticulum: exploring treatment options. Acta Otorhinolaryngol Ital. 2013;33:219–29.
7. Gutschow CA, Hamoir M, Rombaux P, et al. Management of pharyngoesophageal (Zenker's) diverticulum: which technique? Ann Thorac Surg. 2002;74:1677–83.
8. Fama AF, Moore EJ, Kasperbauer JL. Harmonic scalpel in the treatment of Zenker's diverticulum. Laryngoscope. 2009;119:1265–9.

9. González N, et al. Zenker's diverticulum by LigaSure scalpel. Endoscopy. 2014;46:E229–30.
10. Van Overbeek JJ. Pathogenesis and methods of treatment of Zenker's diverticulum. Ann Otol Rhinol Laryngol. 2003;112:583–93.
11. Verhaegen VJ, et al. Endoscopic carbon dioxide laser diverticulostomy versus endoscopic staple-assisted diverticulostomy to treat Zenker's diverticulum. Head Neck. 2011;33:154–9.
12. Ishioka S, et al. Endoscopic incision of Zenker's diverticula. Endoscopy. 1995;27:433–7.
13. Mulder CJ, et al. Flexible endoscopic treatment of Zenker's diverticulum: a new approach. Endoscopy. 1995;27:438–42.
14. Case DJ, Baron TH. Flexible endoscopic management of Zenker diverticulum: the Mayo Clinic experience. Mayo Clin Proc. 2010;85:719–22.
15. Tang SJ, Jazrawi SF, Chen E, et al. Flexible endoscopic clip-assisted Zenker's diverticulotomy: the first case series. Laryngoscope. 2008;118:1199–205.
16. Rabenstein T, et al. Argon plasma coagulation for flexible endoscopic Zenker's diverticulotomy. Endoscopy. 2007;39:141–5.
17. Rieder E, Martinec DV, Dunst CM, Swanstrom LL. Flexible endoscopic Zenkers diverticulotomy with a novel bipolar forceps: a pilot study and comparison with needleknife dissection. Surg Endosc. 2011;25(10):3273–8.
18. Leong SC, Wilkie MD, Webb CJ. Endoscopic stapling of Zenker's diverticulum: establishing national baselines for auditing clinical outcomes in the United Kingdom. Eur Arch Otorhinolaryngol. 2012;269:1877–84.
19. Bonafede JP, Lavertu P, Wood BG, et al. Surgical outcome in 87 patients with Zenker's diverticulum. Laryngoscope. 1997;107:720–5.
20. Schubert D, et al. Endoscopic treatment of a mid-esophageal diverticulum. Endoscopy. 2004;36(8):735–7.
21. Abdollahimohammad A, et al. Epiphrenic esophageal diverticula. J Res Med Sci. 2014;19(8):795–7.
22. Zaninotto G, et al. Therapeutic strategies for epiphrenic diverticula: systematic review. World J Surg. 2011;35:1447–53.
23. Aiolfi A, Bona D, Bonavina L. Endoscopic treatment of an epiphrenic diverticulum using a fully covered self-expanding metal stent. Endoscopy. 2013;45:E101.

19. Endoscopic Retrograde Cholangiopancreatography (ERCP)

Kristy L. Kummerow and Benjamin K. Poulose

Historical Perspective

The use of endoscopy to access the pancreaticobiliary tree for diagnostic and therapeutic purposes has become one of the most common minimally invasive procedures performed by both surgeons and gastroenterologists alike. The first endoscopic cholangiogram was described by McCune and colleagues in 1968 [1]. Five years later, Classen and Demling reported the first endoscopic sphincterotomy [2]. The term endoscopic retrograde cholangiopancreatography (ERCP) is attributed to Cotton [3, 4]. Since its introduction as a diagnostic and therapeutic alternative, ERCP has become widely utilized, with associated advances in tools and techniques. Even in the age of advanced laparoscopic techniques, ERCP remains the mainstay of therapeutic intervention for the pancreaticobiliary tree. ERCP is technically demanding, with high volume centers and experienced endoscopists reporting greatest selective cannulation success, fewer complications, and decreased hospital utilization [5–7].

Indications

ERCP is typically used to gain access to the biliary and pancreatic ductal systems using a minimally invasive, transoral approach. Ideally, a clear therapeutic goal should be defined prior to each ERCP procedure. The use of diagnostic ERCP should be rare, as less invasive methods (magnetic resonance cholangiopancreatography (MRCP), and endoscopic ultrasound (EUS)) can often provide adequate imaging capability with

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less inherent risk. Diagnostic ERCP is most often used when precise clarity is needed in defining ductal anatomy and pathology, often preceding surgical intervention. The most common indications for ERCP include the management of calculous disease of the biliary tract, the management of complications after hepatopancreaticobiliary operations, and the evaluation and stenting of strictures.

Diagnostic ERCP

The diagnostic capability of ERCP combines both techniques in endoscopy and radiology. Evaluation begins with a scout radiograph taken of the upper abdomen. This image can help identify clips, drains, and other pathology that can assist in overall management. Unlike traditional forward-viewing endoscopes, duodenoscopes have limited capacity to view the esophagus and stomach but are designed to evaluate the duodenal bulb, ampulla, and second portion of the duodenum well.

In select situations, ERCP may be used as the primary means to diagnose pancreaticobiliary disease without plans for intervention. These cases should be carefully selected and minimized mainly due to the known risk of post-ERCP pancreatitis in 10 % of cases [8]. Contrast injection into the common bile duct can be used to define the intra- and extrahepatic biliary system (Fig. 19.1). The caliber and course of the

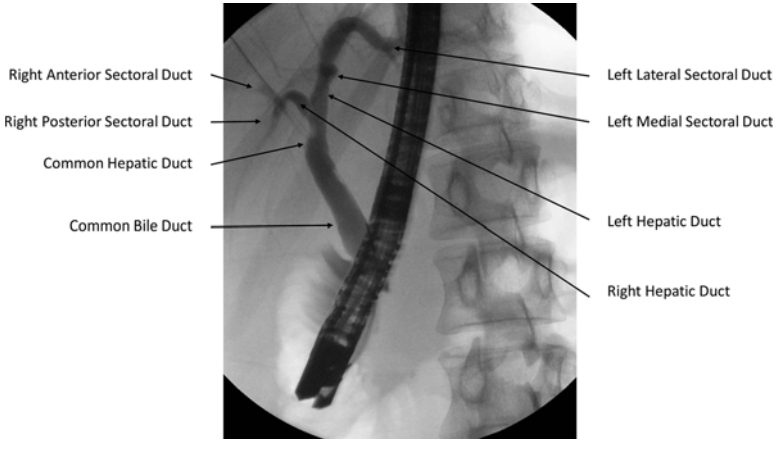

Fig. 19.1. Diagnostic cholangiogram.

common bile duct, common hepatic duct, right and left hepatic ducts, and sectoral branches should be described and documented. The diameter of the typical therapeutic duodenoscope (13 mm at its distal end) provides a convenient size reference in viewing films. Filling defects, strictures, or areas of extravasation are noted. The pancreatic ductal system is not routinely evaluated unless there is a specific clinical need. The pancreatogram may be used to define abnormal pancreatic ductal anatomy including pancreas divisum, annular pancreas, traumatic disruption, and pancreatic lesions that communicate with the ductal system, including some pancreatic tumors (e.g., intraductal papillary mucinous neoplasm (IPMN)) and pseudocysts with pancreatic ductal communication [9]. An additional useful endoscopic finding in IPMN is expression of mucin from the ampulla [10] (Fig. 19.1).

Choledocholithiasis

ERC is often used to treat choledocholithiasis, and can be done preoperatively, intraoperatively, or postoperatively with respect to cholecystectomy. Based on available evidence, ERC performed preoperatively or intraoperatively is equivalent to laparoscopic common bile duct exploration (LCBDE) with respect to stone clearance, morbidity, and mortality. A recent Cochrane review found a slight increased incidence of retained stones with postoperative ERC compared to LCBDE in conjunction with laparoscopic cholecystectomy [11]; however, quality of LCBDE for stone detection is more variable than ERC, and included studies may not be representative of general practice [12–14]. An analysis of cost and quality-adjusted life years favors ERC when experienced and reliable endoscopic teams are readily available and the risk of post-ERC pancreatitis is not excessive [15]. In practice, the decision to use ERC versus LCBDE is often dictated by available resources, institutional practice standards, surgeon experience, and endoscopist experience [16, 17].

Cholangitis

ERC is used to decompress the biliary system in cases of cholangitis secondary to biliary obstruction. Cholangitis is diagnosed based on presence of right upper quadrant pain, jaundice, and fever, which constitute the classic clinical finding of Charcot's triad [18]. Common bile duct

dilation will be apparent on imaging. Cholangitis with biliary sepsis is one of the few interventional emergencies that benefit from ERC. Generally, stenting is performed in the emergent setting to relieve the obstruction, and the causative pathology is managed on a less emergent basis once the patient has stabilized clinically.

Biliary Strictures

Biliary strictures can be diagnosed and often successfully treated with ERC. In evaluating a luminal narrowing in the biliary tree, it is important to establish whether the lesion is benign or malignant, if it is intrinsic to the bile duct or caused by external compression, and the precise anatomic location of the lesion. Intrinsic stricture disease includes pancreatic and biliary malignancies as well as benign strictures secondary to cholecystectomy, chronic pancreatitis, or sclerosing cholangitis. Multiple imaging modalities can be useful, including ultrasound, CT, MRI, MRCP, and radioscintigraphy in addition to ERC [17]. The evaluative algorithm is dependent on the specific clinical circumstances and available resources. ERC is useful for delineating anatomy, obtaining brushings of the luminal surface to evaluate for malignancy, and endoscopic intervention in the case of benign lesions or palliative intent [19]. Peroral cholangioscopy may add value in some cases where further information is needed to guide diagnosis or management, as targeted biopsies can be performed and anatomy clarified to determine surgical resectability [20].

Post-cholecystectomy Indications

ERC can be used to diagnose and treat post-cholecystectomy symptoms, which may be related to retained stones, bile duct stricture or occlusion, bile leak, sphincter of Oddi dysfunction, or an alternate gastrointestinal problem; however, ERC should not be considered the first evaluative step. It is important to approach post-cholecystectomy problems in a systematic fashion, starting with a careful history and physical exam and laboratory assessment including complete blood count and metabolic panel with liver tests. Ultrasound is often the first imaging modality used, as it is a noninvasive way to detect right upper quadrant fluid collections and abnormal biliary ductal dilation. A contrast-enhanced CT scan can also be useful for assessing pres-

ence of fluid collections and anatomic abnormalities. If hepatic transaminases are elevated, CT angiography should be included to assess arterial flow to the liver. The initial goal in management is to drain any intraperitoneal bile, which may be a source of sepsis. Then, one must establish the integrity of the biliary system. This is typically accomplished by means of imaging modalities including MRCP, radionuclide scintigraphy, and ERC. The selection of a noninvasive versus and invasive imaging modality will depend on the pretest suspicion that an intervention will be needed. If there is a high likelihood of intervention, ERC should be performed. With ERC, biliary strictures may be successfully treated endoscopically using balloon dilation and/or stent placement [19]. Stenting and sphincterotomy can be used to treat bile leaks by creating a low resistance route of bile flow into the small bowel [21, 22]. Finally, ERC may be used to evaluate persistent biliary-type pain of unclear etiology after cholecystectomy, which may be related to Sphincter of Oddi dysfunction or occult retained stones [23].

Acute Biliary Pancreatitis

ERC may be beneficial in some circumstances of acute biliary pancreatitis, although available evidence is controversial. ERC is associated with reduction in mortality in cases of acute biliary pancreatitis with concomitant cholangitis [17, 24]. With persistent biliary obstruction but no cholangitis, is it not clear whether early ERC impacts mortality, but it does decrease likelihood of local (pancreatic) complications [25].

Chronic Pancreatitis

Chronic pancreatitis is associated with pancreatic structural changes, which may include pancreatic duct strictures, pancreatolithiasis, pseudocysts, and pancreatic fistulas. In symptomatic cases, endoscopic therapy may be appropriate as initial therapy and does relieve pain on short-term follow-up in the majority of patients [26, 27]. These patients may also benefit in the long term from surgical management of their disease; comprehensive management should be undertaken at specialty centers with readily available multimodal care.

Sphincter of Oddi Dysfunction

Sphincter of Oddi (SOD) dysfunction encompasses both sphincter stenosis and dyskinesis, which present similarly. Abnormal endoscopic manometric findings can clarify the likelihood of benefit from sphincterotomy. Manometric assessment is typically not needed for patients with type I SOD, which is defined by biliary pain, episodic liver test abnormalities, common bile duct dilation, and evidence of delayed biliary contrast drainage, as the majority of patients will benefit from sphincterotomy regardless of manometric findings. Manometry can be helpful in differentiating which patients with Biliary Type II SOD, who have biliary-type pain and only one to two of the aforementioned criteria, will benefit from sphincterotomy [23, 28, 29]. A recent RCT found no association between sphincterotomy and pain relief in patients with Type III SOD (biliary pain without associated findings). Further, manometry findings of pancreatic hypertension were not predictive of treatment success after sphincterotomy, so ERC with manometry is not indicated in most cases of Type III SOD [30].

Technique

Successful performance of ERCP requires an experienced endoscopist, an able assistant, essential equipment, and adequate anesthesia. The patient should be positioned in the prone or semi-prone position and all pressure points padded. A left lateral decubitus may be used. In women of child bearing age, a urine pregnancy test is obtained as fluoroscopic imaging is used. Regardless of pregnancy status, appropriate pelvic shielding should be used in this population. The type of anesthesia may be determined by team or local preference as well as patient considerations. A limited review of anesthetic approaches for ERCP finds no difference in serious cardiopulmonary complications with use of moderate sedation (benzodiazepine plus opioid), deep sedation (propofol), or general anesthesia. There is some evidence to support more rapid recovery with deep sedation using propofol than with moderate sedation [31].

Peri-procedural antibiotics are not administered routinely, but should be considered in patients undergoing the procedure for biliary obstruction if there is a reasonable chance that complete biliary decompression cannot be achieved. This is especially true in patients with primary sclerosing cholangitis, hilar strictures, or known multiple hepatic metastases.

Fig. 19.2. Duodenoscope.

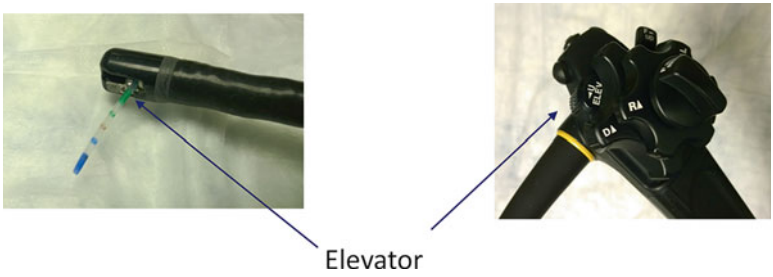

Fig. 19.3. Elevator mechanism.

Another patient group that benefits from prophylactic antibiotics is the post-liver transplant population. Antibiotics, when used, should cover biliary flora including gram-negative bacteria and enterococcus [32].

A duodenoscope, or side-viewing endoscope, is used to perform ERCP in patients with normal anatomy (Fig. 19.2). Standard suction and irrigation channels are present. An elevator at the tip of the scope enables articulation of instruments passed through the working channel into the field of view [33] (Fig. 19.3). Some duodenoscopes are large enough to accommodate a smaller choledochoscope within one of the channels in a "mother-daughter" configuration [34].

The esophagus is intubated blindly using a side-viewing endoscope. Full visualization of the esophagus will not be feasible. The safety of

passage is largely dependent on an experienced endoscopist. If notable resistance is met at any point, the duodenoscope should be removed and a forward-viewing scope used to delineate anatomy. A guidewire can be placed to safely pass the duodenoscope if needed. The duodenoscope is then placed in the "long scope" position along the greater curvature of the stomach. The pylorus is briefly viewed and the duodenal bulb is entered with the pylorus out of view. The fold between the duodenal bulb and second portion of the duodenum is negotiated and the scope then reduced to the "short scope" position. The resulting fluoroscopic view often resembles a "hockey stick" when the scope is fully reduced. The ampulla can be visualized on the medial aspect of the second part of the duodenum. Fine positional adjustments are made to keep the ampulla in view for cannulation. Difficulty visualizing the major papilla usually arises from inadequate scope reduction, patient positioning, or altered surgical anatomy. Cannulation of the selected ductal orifice can be performed with a sphincterotome or ERCP cannulation catheter. In many instances where previous sphincterotomy has been performed, cannulation can often be achieved using a biliary extraction balloon. A flexible wire is passed into the desired duct. The position of the wire alone on fluoroscopy can often be used to assess whether successful cannulation has been achieved. Ideally, contrast is not injected until wire cannulation has been achieved. Guidewire-assisted cannulation is superior to contrast-assisted cannulation in terms of increased cannulation success and decreased incidence of post-ERCP pancreatitis [35]. If difficulty is experienced cannulating the bile duct, alternative strategies can be used including double wire technique (placing a wire first in the pancreatic duct and leaving it in place), changing catheters or wires, and possibly performing pre-cut access sphincterotomy [36].

Sphincterotomy

Sphincterotomy is performed to enlarge access to the distal CBD or pancreatic duct for passage of catheters and instruments, stent placement, and stone extraction, and is usually performed using a "pull-type" sphincterotome. A sphincterotome is essentially a curved catheter with a parallel 2–3 cm electrosurgical wire affixed at the catheter tip and a point more proximal, appearing like a bow (catheter) and string (electrosurgical wire) [37]. The sphincterotome is inserted through the papilla such that the proximal one third of the wire remains visible outside the papilla. A biliary or pancreatic sphincterotomy can be performed. For

biliary sphincterotomy, the wire should be applied to the "roof" of the papilla at the 11 o'clock position. Pulsed electrosurgical current is applied while applying pressure upward toward 11 o'clock to create an incision approximately 5–15 mm in length [37]. Bleeding should be minimal, but can be managed using pure coagulation current gently applied with the wire. In addition, balloon tamponade can be used for hemostasis.

An alternative to sphincterotomy, balloon sphincteroplasty, has been described and compared with sphincterotomy in multiple randomized controlled trials and a meta-analysis. It is associated with decreased bleeding risk but increased incidence of post-ERCP pancreatitis [38, 39]. There is some evidence that combining sphincterotomy with dilation using a large (esophageal or pyloric) balloon may facilitate removal of large (>1 cm) stones, reducing the need for lithotripsy [40].

Stone Extraction

Gallstones in the common bile duct typically arise secondarily from passage of stones in the gallbladder through the cystic duct into the common bile duct, but choledocholiths can also form primarily in the intra- or extrahepatic bile ducts. Endoscopic management is similar, but may be more difficult with primary stones due to the fragile consistency of these stones [41]. The ampulla is cannulated as described previously, and a sphincterotomy is performed both to facilitate biliary access with stone extraction tools and to enable the removal of stones through the ampulla [42]. A cholangiogram should be performed to delineate ductal anatomy and the size and location of common duct stones. Under fluoroscopy, a guidewire can be passed into the duct beyond the location of the most proximal stone to facilitate placement of a retrieval basket or balloon for stone extraction [42]. Balloon extraction catheters are most commonly used, with retrieval baskets used for extraction of isolated, large stones [37].

Difficult Stones

Several options are available for stones that are difficult to remove. If the stone can be passed using a wire, a stent can be placed to bypass the area of obstruction. Methods to fragment large, impacted stones include mechanical lithotripsy, intraductal laser or electrohydraulic

lithotripsy, and extracorporeal shock wave lithotripsy [43]. Intraductal therapies are typically done under cholangioscopic vision to minimize risk of ductal injury [20]. Laser lithotripsy appears more effective in stone clearance than electrohydraulic or external shock wave lithotripsy, which have equivalent stone clearance rates [44–46].

Biliary Stent Placement

A biliary stent can be placed to create a drainage route across an area of obstruction such as a stricture or stone that cannot be removed, or to establish preferential drainage that reduces aberrant bile flow from an area of leakage (e.g., bile duct injury, cystic stump leak). Plastic or metal stents can be used, and stent selection should be informed by the disease process and the intended duration of stenting [47]. For short duration stenting, which is used for bile leak, initial management of benign biliary strictures, and to bypass irretrievable common bile duct stones, a large caliber (10 Fr) plastic stent is recommended [48]. Plastic stents do not incorporate into the bile duct epithelium and are easily retrieved endoscopically. They are prone to occlusion and migration and should be exchanged at least every 3 months [49]. Double pigtail plastic stents can often be left for longer periods between exchange or removal. When feasible, multiple adjacent stents can be placed to promote drainage and/or stricture resolution [50]. A sphincterotomy can facilitate large or multiple-stent placement [47]. Fully covered, self-expanding metal stents are increasingly used for benign biliary disease and have similar short-term outcome profiles [47, 51]. For this off-label indication (i.e., benign disease) fully covered metal stents have been removed several months after insertion [52]. Timing of removal should be dictated by indication for treatment (i.e., facilitating stone removal, management of benign stricture). In general, the shortest interval possible should be selected for planned removal or exchange of a fully covered metal biliary stent [53].

Stenting may also be indicated for palliation of malignant biliary strictures. Here, a partially covered or uncovered metal stent is traditionally placed to promote stent incorporation into the biliary epithelium, which is believed to minimize risk of stent migration. Uncovered stents are used for distal common bile duct malignant lesions, whereas depending on the anatomy, a partially covered stent may be needed for hilar malignant disease to avoid occlusion of the contralateral bile duct by the stent [54, 55]. Median patency of self-expanding metal stents ranges from 6 to 12 months [54, 55].

Pancreatic Stone Removal and Stent Placement

The techniques for management of pancreatolithiasis and pancreatic strictures are conceptually similar to those used for biliary stones and strictures, but may be more difficult due to the pancreatic duct's smaller caliber, increased tortuosity, and multiple side branches.

Stone removal can be beneficial in cases of symptomatic chronic pancreatitis. Small, mobile, downstream stones are most readily removed while larger stones will require intraluminal or extracorporeal shock wave lithotripsy prior to removal. Dilation of downstream strictures may be needed prior to stone removal. This can be accomplished using balloons or sequentially larger dilating catheters [56, 57]. Pancreatic sphincterotomy is typically performed prior to extracorporeal lithotripsy and attempted endoscopic stone removal. After performance of a biliary sphincterotomy, the common septum is divided using a sphincterotome or needle knife [58]. A pancreatic stent can be placed and used as a guide for sphincterotomy [59].

Pancreatic stents can be used to drain the main pancreatic duct in patients with chronic pancreatitis. Pancreatic stents are plastic and contain multiple side holes to drain secondary ducts. Typically, 3–5 Fr stents are used, although larger stents may be used in ducts that are dilated secondary to chronic pancreatitis. As in the biliary system, multiple stents can also be placed for refractory pancreatic strictures [60]. Fully covered metal stents are not indicated for pancreatic stricture disease given inadequate evidence and potentially increased risk of stent migration and stricture exacerbation [61, 62].

Stents can also be used to bridge pancreatic duct disruption or drain internal pancreatic fistulas or pancreatic pseudocysts that communicate with the main duct. Stents are placed over a guidewire, and a pusher (sphincterotome or catheter) is used to position the stent. The endoscope tip should be deflected away from the papillary orifice to bring out the distal pigtail. Pancreatic sphincterotomy is not needed unless multiple adjacent pancreatic stents are being placed [63].

An additional role for pancreatic stent placement is prophylaxis against post-ERCP pancreatitis in high-risk patients [64, 65]. Small (4–5 Fr) plastic stents without proximal flaps minimize trauma to the pancreatic duct and enable spontaneous passage [63].

ERCP in Patients with Surgically Altered Anatomy

In patients with altered anatomy due to roux-en-y gastrojejunostomy, Billroth II reconstruction, hepaticojejunostomy, or pancreaticoduodenectomy, ERCP can be technically challenging due to the length and tortuosity of bowel that needs to be traversed as well as the altered orientation of the ampulla [66]. It cannot be overemphasized that a clear endoscopic plan should be in mind prior to attempting ERCP in these patients. A contrast-enhanced CT scan is very useful to assess for any extrinsic periampullary anatomic issue such as a tumor or large duodenal diverticulum. Consideration should also be given to percutaneous radiologic interventions which may be less invasive than an endoscopic or surgically assisted endoscopic option.

Alternative endoscopic approaches are increasingly needed for roux-en-y anatomy, which is seen more frequently given the increased performance of roux-en-y gastric bypass for weight loss [67]. The use of a pediatric colonoscope or overtube-assisted enteroscopy using single- or double-balloon enteroscopy or spiral enteroscopy can facilitate arrival at the ampulla or hepaticojejunostomy; however, biliary cannulation using a forward-viewing scope and other therapeutic maneuvers can be very difficult, if not impossible [68]. With roux-en-y gastric bypass, in which the ampulla remains accessible via the excluded stomach, ERCP can be performed using a transgastric approach.

Transgastric ERCP

Transgastric access can be achieved either via surgical or radiographic means. In an outpatient setting where there is little urgency given the indication, a gastrostomy tube can be placed using image guidance and allowed to mature for 4–6 weeks. This tract can then be dilated with wire guidance to allow endoscopic access to the excluded stomach and ampulla (Fig. 19.4).

Should the need arise for more urgent intervention, typically seen with common bile duct stones, a surgical approach is preferred in reasonable-risk operative candidates. If the patient is a good surgical candidate, a laparoscopic or open technique can be used for transgastric access. In most patients with previous laparoscopic roux-en-y gastric bypass, laparoscopic transgastric access is usually feasible. Patients with previous open upper abdominal procedures may warrant an open or radiologically assisted approach. The goal for either open or laparoscopic transgastric

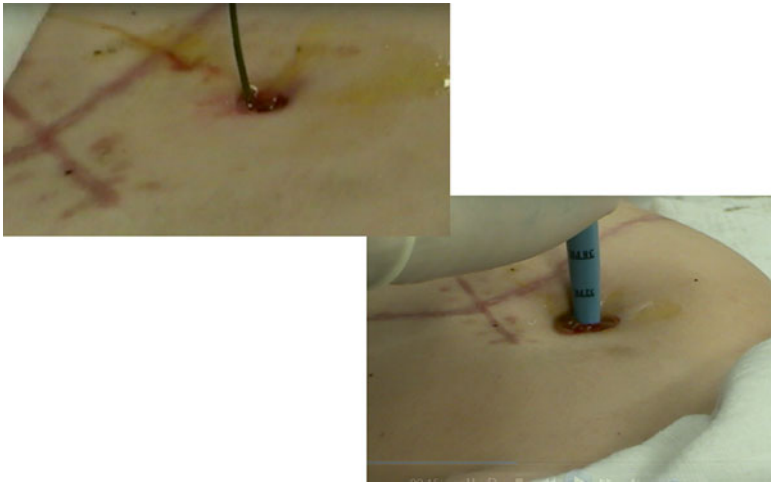

Fig. 19.4. Wire-guided dilation of transgastric tract.

access is the same: safe placement of a 15 mm laparoscopic port into the excluded stomach. Using a standard laparoscopic setup for upper gastrointestinal procedures, the excluded stomach is identified. Care is taken to carefully place a 5 mm port in the location of the eventual gastrostomy tube in the left upper abdomen also allowing easy laparoscopic access to the excluded stomach. The location of the gastrotomy should be on the greater curvature at least 7–10 cm proximal to the pylorus, which provides the most direct access to the distal stomach. Transabdominal stay sutures of 2-0 absorbable suture are placed at this location (Fig. 19.5) and a gastrotomy performed using either laparoscopic scissors or ultrasonic shears. Care is taken not to injure the posterior aspect the stomach or the pancreas. Then, the left upper quadrant 5 mm port is exchanged for a 15 mm port which is placed under laparoscopic visualization into the excluded stomach (Fig. 19.6) [69]. If the excluded stomach cannot be reached with the port, the tip of the port can be left in the peritoneal cavity. If using endoscopic air insufflation, the small bowel should be clamped to prevent bowel dilation; carbon dioxide endoscopic insufflation can be used without the need for clamping the small bowel distal to the pylorus. To maintain the sterile surgical field and create the nonsterile endoscopic field, an extremity drape is used to cover the entire operative field with the 15 mm port hub exiting the opening in the drape. This is then secured with a Kelly clamp, effectively keeping the field beneath it

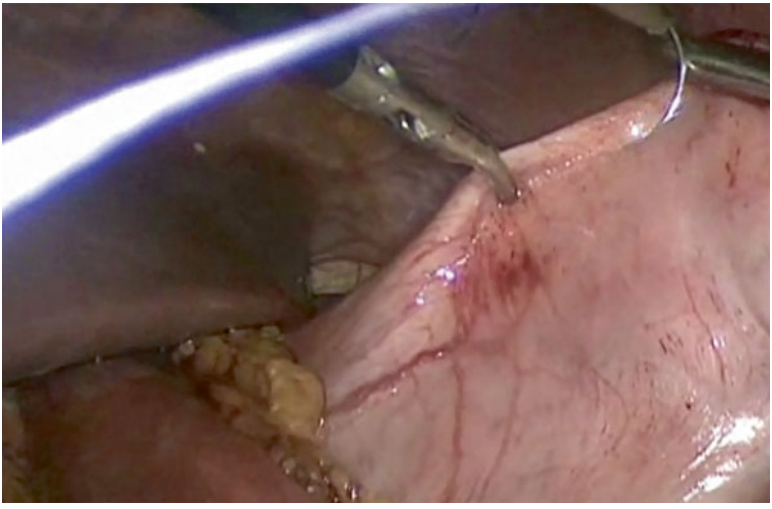

Fig. 19.5. Stay sutures on mid-body of stomach during transgastric ERCP.

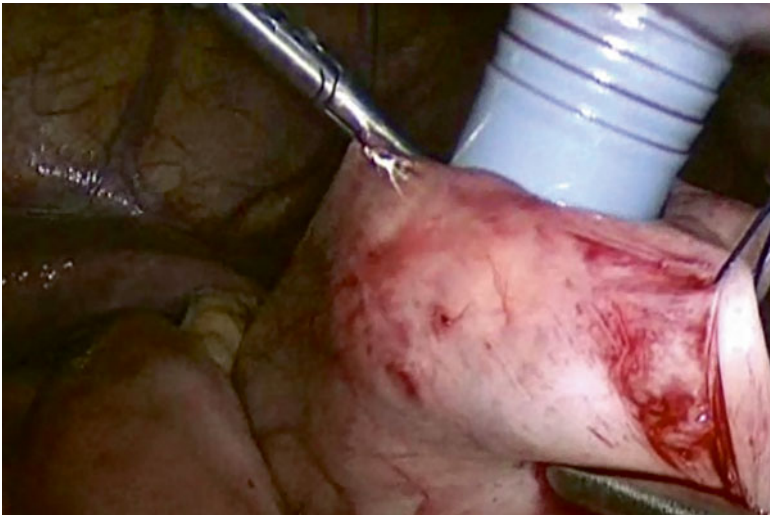

Fig. 19.6. 15 mm port placed into excluded stomach during transgastric ERCP.

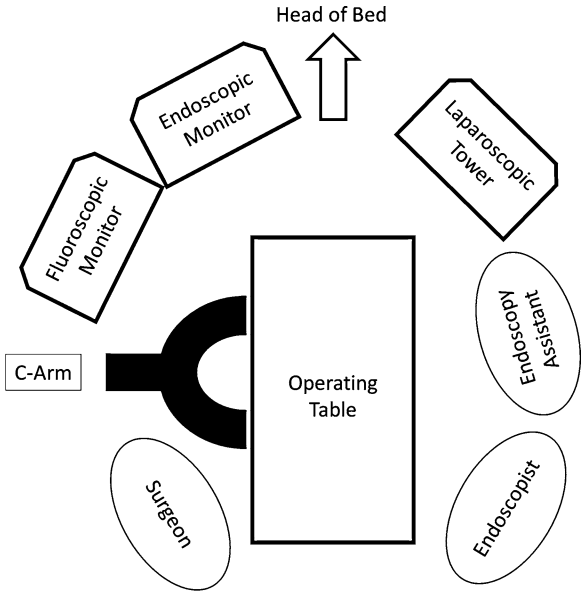

Fig. 19.7. Setup for transgastric ERCP.

sterile. The endoscope is then introduced through the port into the stomach. If the 15 mm port is not within the excluded stomach, some laparoscopic direction will be needed to guide the endoscope into the stomach taking care to eliminate looping within the peritoneal cavity. The ERCP is now performed after bringing the fluoroscopy c-arm into position. The general operating room setup is shown in Fig. 19.7. As the patient is usually supine, ERCP can be quite challenging. Tilting the operating table to the patient's left can facilitate passage of the scope into the duodenum. Fluoroscopy is useful to ensure that the scope is passing distally toward the pylorus and not looping within the excluded stomach. After completion of ERCP, the extremity drape and 15 mm port are removed together and a 10 mm port placed at the site. The abdomen is insufflated and the bowel clamp removed (if placed). Depending on the need for repeat endoscopic access, a standard laparoscopic gastrostomy tube can be placed (at least 20 F) or the gastrotomy can be closed in the usual manner [70]. Repeat endoscopic access can then be obtained by serially dilating the tract after maturation of 6 weeks. If an open approach is used, the gastric stay sutures are sutured to the 15 mm port and the port is brought out directly through the wound and covered with the extremity drape (Figs. 19.5, 19.6, and 19.7).

The procedure above allows general endoscopic access to the excluded stomach. Not only can this facilitate ERCP, but EUS and general endoscopy can be performed as well. The latter is especially useful in the acute setting after gastric bypass where an intraluminal bleed is suspected within the excluded stomach or the jejunojejunostomy.

If the patient is a poor surgical candidate, or there is acute need for biliary decompression, consideration should also be given to managing the patient's issue via percutaneous transhepatic cholangiography (PTC). This is especially true in the acute setting of cholangitis. Most experienced interventional radiologists are able to manage strictures, small common bile duct stones, and perform antegrade balloon sphincteroplasty. If a successful PTC catheter has been placed, an acute situation can then be converted to an elective one to allow better planning. In many instances, percutaneous therapeutics alone may be sufficient to manage underlying pathology.

Management of Complications

Complications occur after ERCP in approximately 4 % of patients, with most being mild. Severe complications occur in less than 0.5 % of cases, and the incidence of death after a complication of ERCP is <0.1 % [71]. The most common complication after ERCP is pancreatitis, which occurs in about 10 % of cases, with some series reporting rates as low as 1 % and some as high as 24 % [8, 72–74]. Post-ERCP pancreatitis is typically mild but can be severe. The wide range in reported incidence likely relates to variable patient populations as well as variable definitions of post-ERCP pancreatitis despite efforts to achieve a consensus definition [75, 76]. Risk factors for post-ERCP pancreatitis include previous history of post-ERCP pancreatitis (eightfold increased risk), biliary pain, suspected sphincter of Oddi dysfunction as the operative indication, more than ten cannulation attempts, cannulation of the main pancreatic duct, performance of pancreatogram, and pre-cut access sphincterotomy technique [72, 74]. Pancreatitis risk can be decreased by use of peri-procedure rectal administration of indomethacin or diclofenac and possibly with pancreatic stenting [77, 78].

Bleeding after ERCP occurs in 0.5–1.5 % of cases and is nearly always associated with sphincterotomy [71, 73, 79]. Bleeding risk can be minimized by ensuring normal coagulation parameters pre-procedure, making a controlled incision, limiting sphincterotomy length, and

coagulating any bleeding from cut edges [76]. Bleeding can usually be managed conservatively, although some cases require repeat endoscopy with thermocoagulation, balloon tamponade, or epinephrine injection. Placement of a fully covered metal stent to tamponade difficult-to-manage post-sphincterotomy bleeding has been described [80]. In rare circumstances, angiography can provide a useful means of bleeding control by empirically coiling the gastroduodenal artery; rarely is operative intervention required [76].

Perforation secondary to sphincterotomy may occur in less than 0.5 % of cases [71, 79, 81]. Perforation is typically retroperitoneal and may be successfully managed nonoperatively. Management usually consists of nothing by mouth, parenteral nutrition, antibiotics, and percutaneous drainage of associated fluid collections as needed. Typically after 2–3 weeks, an upper gastrointestinal series is obtained to assess for healing of the perforation and to determine initiation of enteral nutrition. Intraperitoneal perforations are usually scope-related and often require operative management [76].

Other complications occur in less than 1 % of cases and include sepsis, anesthetic complications, and general medical decompensation including cardiopulmonary or renal dysfunction [76].

References

1. McCune WS, Shorb PE, Moscovitz H. Endoscopic cannulation of the ampulla of vater: a preliminary report. Ann Surg. 1968;167(5):752–6.
2. Classen M, Demling L. Endoscopic sphincterotomy of the papilla of vater and extraction of stones from the choledochal duct (author's transl). Dtsch Med Wochenschr. 1974;99(11):496–7. doi:10.1055/s-0028-1107790.
3. Cotton PB, Blumgart LH, Davies GT, Pierce JW, Salmon PR, Burwood RJ, et al. Cannulation of papilla of vater via fiber-duodenoscope. Assessment of retrograde cholangiopancreatography in 60 patients. Lancet. 1972;1(7741):53–8.
4. Cotton PB, Beales JS. Clinical relevance of endoscopic retrograde cholangio-pancreatography. Gut. 1972;13(10):851.
5. Varadarajulu S, Kilgore ML, Wilcox CM, Eloubeidi MA. Relationship among hospital ERCP volume, length of stay, and technical outcomes. Gastrointest Endosc. 2006;64(3):338–47. doi:10.1016/j.gie.2005.05.016.
6. Cote GA, Imler TD, Xu H, Teal E, French DD, Imperiale TF, et al. Lower provider volume is associated with higher failure rates for endoscopic retrograde cholangiopancreatography. Med Care. 2013;51(12):1040–7. doi:10.1097/MLR.0b013e3182a502dc.
7. Kapral C, Duller C, Wewalka F, Kerstan E, Vogel W, Schreiber F. Case volume and outcome of endoscopic retrograde cholangiopancreatography: results of a nationwide

Austrian benchmarking project. Endoscopy. 2008;40(8):625–30. doi:10.1055/s-2008-1077461.
8. Kochar B, Akshintala VS, Afghani E, Elmunzer BJ, Kim KJ, Lennon AM, et al. Incidence, severity, and mortality of post-ERCP pancreatitis: a systematic review by using randomized, controlled trials. Gastrointest Endosc. 2014. doi:10.1016/j.gie.2014.06.045.
9. Cohen S, Bacon BR, Berlin JA, Fleischer D, Hecht GA, Loehrer Sr PJ, 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. doi:10.1067/mge.2002.129875.
10. Tanaka M. Intraductal papillary mucinous neoplasm of the pancreas: diagnosis and treatment. Pancreas. 2004;28(3):282–8.
11. Dasari BV, Tan CJ, Gurusamy KS, Martin DJ, Kirk G, McKie L, et al. Surgical versus endoscopic treatment of bile duct stones. Cochrane Database Syst Rev. 2013;12, CD003327. doi:10.1002/14651858.CD003327.pub4.
12. Ingraham AM, Cohen ME, Ko CY, Hall BL. A current profile and assessment of north american cholecystectomy: results from the American College of Surgeons National Surgical Quality Improvement Program. J Am Coll Surg. 2010;211(2):176–86. doi:10.1016/j.jamcollsurg.2010.04.003.
13. Rogers SJ, Cello JP, Horn JK, Siperstein AE, Schecter WP, Campbell AR, et al. Prospective randomized trial of LC+LCBDE vs ERCP/S+LC for common bile duct stone disease. Arch Surg. 2010;145(1):28–33. doi:10.1001/archsurg.2009.226.
14. Yachimski P, Poulose BK. ERCP vs laparoscopic common bile duct exploration for common bile duct stones: are the 2 techniques truly equivalent? Arch Surg. 2010;145(8):795, author reply 795–6. doi:10.1001/archsurg.2010.126.
15. Poulose BK, Speroff T, Holzman MD. Optimizing choledocholithiasis management: a cost-effectiveness analysis. Arch Surg. 2007;142(1):43–8, discussion 9. doi:10.1001/archsurg.142.1.43.
16. Poulose BK, Phillips S, Nealon W, Shelton J, Kummerow K, Penson D, et al. Choledocholithiasis management in rural America: health disparity or health opportunity? J Surg Res. 2011;170(2):214–9. doi:10.1016/j.jss.2011.03.040.
17. ASGE Standards of Practice Committee, Maple JT, Ben-Menachem T, Anderson MA, Appalaneni V, Banerjee S, et al. The role of endoscopy in the evaluation of suspected choledocholithiasis. Gastrointest Endosc. 2010;71(1):1–9. doi:10.1016/j.gie.2009.09.041.
18. Lee JG. Diagnosis and management of acute cholangitis. Nat Rev Gastroenterol Hepatol. 2009;6(9):533–41. doi:10.1038/nrgastro.2009.126.
19. Adler DG, Baron TH, Davila RE, Egan J, Hirota WK, Leighton JA, et al. ASGE guideline: the role of ERCP in diseases of the biliary tract and the pancreas. Gastrointest Endosc. 2005;62(1):1–8. doi:10.1016/j.gie.2005.04.015.
20. Monga A, Ramchandani M, Reddy DN. Per-oral cholangioscopy. J Interv Gastroenterol. 2011;1(2):70–7. doi:10.4161/jig.1.2.15352.
21. Vitale GC, Tran TC, Davis BR, Vitale M, Vitale D, Larson G. Endoscopic management of postcholecystectomy bile duct strictures. J Am Coll Surg. 2008;206(5):918–23, discussion 24–5. doi:10.1016/j.jamcollsurg.2008.01.064.
22. Wu YV, Linehan DC. Bile duct injuries in the era of laparoscopic cholecystectomies. Surg Clin North Am. 2010;90(4):787–802. doi:10.1016/j.suc.2010.04.019.

23. Rehman A, Affronti J, Rao S. Sphincter of Oddi dysfunction: an evidence-based review. Expert Rev Gastroenterol Hepatol. 2013;7(8):713–22. doi:10.1586/17474124.2013.849197.
24. Fan ST, Lai EC, Mok FP, Lo CM, Zheng SS, Wong J. Early treatment of acute biliary pancreatitis by endoscopic papillotomy. N Engl J Med. 1993;328(4):228–32. doi:10.1056/NEJM199301283280402.
25. Tse F, Yuan Y. Early routine endoscopic retrograde cholangiopancreatography strategy versus early conservative management strategy in acute gallstone pancreatitis. Cochrane Database Syst Rev. 2012;5, CD009779. doi:10.1002/14651858.CD009779.pub2.
26. Cahen DL, Gouma DJ, Nio Y, Rauws EA, Boermeester MA, Busch OR, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. N Engl J Med. 2007;356(7):676–84. doi:10.1056/NEJMoa060610.
27. Dite P, Ruzicka M, Zboril V, Novotny I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. Endoscopy. 2003;35(7):553–8. doi:10.1055/s-2003-40237.
28. Geenen JE, Hogan WJ, Dodds WJ, Toouli J, Venu RP. The efficacy of endoscopic sphincterotomy after cholecystectomy in patients with sphincter-of-Oddi dysfunction. N Engl J Med. 1989;320(2):82–7. doi:10.1056/NEJM198901123200203.
29. Toouli J, Roberts-Thomson IC, Kellow J, Dowsett J, Saccone GT, Evans P, et al. Manometry based randomised trial of endoscopic sphincterotomy for sphincter of Oddi dysfunction. Gut. 2000;46(1):98–102.
30. Cotton PB, Durkalski V, Romagnuolo J, Pauls Q, Fogel E, Tarnasky P, et al. Effect of endoscopic sphincterotomy for suspected sphincter of Oddi dysfunction on pain-related disability following cholecystectomy: the EPISOD randomized clinical trial. JAMA. 2014;311(20):2101–9. doi:10.1001/jama.2014.5220.
31. Garewal D, Waikar P. Propofol sedation for ERCP procedures: a dilemna? Observations from an anesthesia perspective. Diagn Ther Endosc. 2012;2012:639190. doi:10.1155/2012/639190.
32. ASGE Standards of Practice Committee, Banerjee S, Shen B, Baron TH, Nelson DB, Anderson MA, et al. Antibiotic prophylaxis for GI endoscopy. Gastrointest Endosc. 2008;67(6):791–8. doi:10.1016/j.gie.2008.02.068.
33. ASGE Technology Committee, Varadarajulu S, Banerjee S, Barth BA, Desilets DJ, Kaul V, et al. GI endoscopes. Gastrointest Endosc. 2011;74(1):1–6.e6. doi:10.1016/j.gie.2011.01.061.
34. ASGE Technology Committee, Shah RJ, Adler DG, Conway JD, Diehl DL, Farraye FA, et al. Cholangiopancreatoscopy. Gastrointest Endosc. 2008;68(3):411–21. doi:10.1016/j.gie.2008.02.033.
35. Tse F, Yuan Y, Moayyedi P, Leontiadis GI. Guidewire-assisted cannulation of the common bile duct for the prevention of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis. Cochrane Database Syst Rev. 2012;12, CD009662. doi:10.1002/14651858.CD009662.pub2.
36. Bourke MJ, Costamagna G, Freeman ML. Biliary cannulation during endoscopic retrograde cholangiopancreatography: core technique and recent innovations. Endoscopy. 2009;41(7):612–7. doi:10.1055/s-0029-1214859.

37. Binmoeller KF, Schafer TW. Endoscopic management of bile duct stones. J Clin Gastroenterol. 2001;32(2):106–18.
38. Disario JA, Freeman ML, Bjorkman DJ, Macmathuna P, Petersen BT, Jaffe PE, et al. Endoscopic balloon dilation compared with sphincterotomy for extraction of bile duct stones. Gastroenterology. 2004;127(5):1291–9.
39. Zhao HC, He L, Zhou DC, Geng XP, Pan FM. Meta-analysis comparison of endoscopic papillary balloon dilatation and endoscopic sphincteropapillotomy. World J Gastroenterol. 2013;19(24):3883–91. doi:10.3748/wjg.v19.i24.3883.
40. Madhoun MF, Wani S, Hong S, Tierney WM, Maple JT. Endoscopic papillary large balloon dilation reduces the need for mechanical lithotripsy in patients with large bile duct stones: a systematic review and meta-analysis. Diagn Ther Endosc. 2014;2014:309618. doi:10.1155/2014/309618.
41. Bernhoft RA, Pellegrini CA, Motson RW, Way LW. Composition and morphologic and clinical features of common duct stones. Am J Surg. 1984;148(1):77–85.
42. Vennes JA. Management of calculi in the common duct. Semin Liver Dis. 1983;3(2):162–71. doi:10.1055/s-2008-1040682.
43. ASGE Standards of Practice Committee, Maple JT, Ikenberry SO, Anderson MA, Appalaneni V, Decker GA, et al. The role of endoscopy in the management of choledocholithiasis. Gastrointest Endosc. 2011;74(4):731–44. doi:10.1016/j.gie.2011.04.012.
44. Neuhaus H, Zillinger C, Born P, Ott R, Allescher H, Rosch T, et al. Randomized study of intracorporeal laser lithotripsy versus extracorporeal shock-wave lithotripsy for difficult bile duct stones. Gastrointest Endosc. 1998;47(5):327–34.
45. Jakobs R, Adamek HE, Maier M, Kromer M, Benz C, Martin WR, et al. Fluoroscopically guided laser lithotripsy versus extracorporeal shock wave lithotripsy for retained bile duct stones: a prospective randomised study. Gut. 1997;40(5):678–82.
46. Adamek HE, Maier M, Jakobs R, Wessbecher FR, Neuhauser T, Riemann JF. Management of retained bile duct stones: a prospective open trial comparing extracorporeal and intracorporeal lithotripsy. Gastrointest Endosc. 1996;44(1):40–7.
47. Dumonceau JM, Tringali A, Blero D, Deviere J, Laugiers R, Heresbach D, et al. Biliary stenting: indications, choice of stents and results: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy. 2012;44(3):277–98. doi:10.1055/s-0031-1291633.
48. Mavrogiannis C, Liatsos C, Papanikolaou IS, Karagiannis S, Galanis P, Romanos A. Biliary stenting alone versus biliary stenting plus sphincterotomy for the treatment of post-laparoscopic cholecystectomy biliary leaks: a prospective randomized study. Eur J Gastroenterol Hepatol. 2006;18(4):405–9.
49. Perri V, Familiari P, Tringali A, Boskoski I, Costamagna G. Plastic biliary stents for benign biliary diseases. Gastrointest Endosc Clin N Am. 2011;21(3):405–33, viii. doi:10.1016/j.giec.2011.04.012.
50. Costamagna G, Tringali A, Mutignani M, Perri V, Spada C, Pandolfi M, et al. Endotherapy of postoperative biliary strictures with multiple stents: results after more than 10 years of follow-up. Gastrointest Endosc. 2010;72(3):551–7. doi:10.1016/j.gie.2010.04.052.

51. Bakhru MR, Kahaleh M. Expandable metal stents for benign biliary disease. Gastrointest Endosc Clin N Am. 2011;21(3):447–62, viii. doi:10.1016/j.giec.2011.04.007.
52. Kaffes AJ, Liu K. Fully covered self-expandable metal stents for treatment of benign biliary strictures. Gastrointest Endosc. 2013;78(1):13–21. doi:10.1016/j.gie.2013.02.019.
53. Vakil N. Expandable metal stents: principles and tissue responses. Gastrointest Endosc Clin N Am. 2011;21(3):351–7, vii. doi:10.1016/j.giec.2011.04.008.
54. Gerges C, Schumacher B, Terheggen G, Neuhaus H. Expandable metal stents for malignant hilar biliary obstruction. Gastrointest Endosc Clin N Am. 2011;21(3):481–97, ix. doi:10.1016/j.giec.2011.04.004.
55. Lee JH. Self-expandable metal stents for malignant distal biliary strictures. Gastrointest Endosc Clin N Am. 2011;21(3):463–80, viii–ix. doi:10.1016/j.giec.2011.04.009.
56. Siegel JH, Guelrud M. Endoscopic cholangiopancreatoplasty: hydrostatic balloon dilation in the bile duct and pancreas. Gastrointest Endosc. 1983;29(2):99–103.
57. Huibregtse K, Schneider B, Vrij AA, Tytgat GN. Endoscopic pancreatic drainage in chronic pancreatitis. Gastrointest Endosc. 1988;34(1):9–15.
58. Williamson RC. Pancreatic sphincteroplasty: indications and outcome. Ann R Coll Surg Engl. 1988;70(4):205–11.
59. Siegel JH, Cohen SA, Kasmin FE, Veerappan A. Stent-guided sphincterotomy. Gastrointest Endosc. 1994;40(5):567–72.
60. Costamagna G, Bulajic M, Tringali A, Pandolfi M, Gabbrielli A, Spada C, et al. Multiple stenting of refractory pancreatic duct strictures in severe chronic pancreatitis: long-term results. Endoscopy. 2006;38(3):254–9. doi:10.1055/s-2005-921069.
61. Sauer B, Talreja J, Ellen K, Ku J, Shami VM, Kahaleh M. Temporary placement of a fully covered self-expandable metal stent in the pancreatic duct for management of symptomatic refractory chronic pancreatitis: preliminary data (with videos). Gastrointest Endosc. 2008;68(6):1173–8. doi:10.1016/j.gie.2008.06.011.
62. Park do H, Kim MH, Moon SH, Lee SS, Seo DW, Lee SK. Feasibility and safety of placement of a newly designed, fully covered self-expandable metal stent for refractory benign pancreatic ductal strictures: a pilot study (with video). Gastrointest Endosc. 2008;68(6):1182–9. doi:10.1016/j.gie.2008.07.027.
63. Deviere J. Pancreatic stents. Gastrointest Endosc Clin N Am. 2011;21(3):499–510, ix. doi:10.1016/j.giec.2011.04.011.
64. Singh P, Das A, Isenberg G, Wong RC, Sivak Jr MV, Agrawal D, et al. Does prophylactic pancreatic stent placement reduce the risk of post-ERCP acute pancreatitis? A meta-analysis of controlled trials. Gastrointest Endosc. 2004;60(4):544–50.
65. Mazaki T, Masuda H, Takayama T. Prophylactic pancreatic stent placement and post-ERCP pancreatitis: a systematic review and meta-analysis. Endoscopy. 2010;42(10):842–53. doi:10.1055/s-0030-1255781.
66. Matsushita M, Shimatani M, Takaoka M, Okazaki K. Double-balloon enteroscopy for ERCP in patients with altered GI anatomy: front-viewing, a drawback for biliary cannulation? Gastrointest Endosc. 2009;70(3):601, author reply 601–2. doi:10.1016/j.gie.2008.12.244.

67. Hinojosa MW, Varela JE, Parikh D, Smith BR, Nguyen XM, Nguyen NT. National trends in use and outcome of laparoscopic adjustable gastric banding. Surg Obes Relat Dis. 2009;5(2):150–5. doi:10.1016/j.soard.2008.08.006.
68. 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. doi:10.1055/s-0034-1365698.
69. Ahmed AR, Husain S, Saad N, Patel NC, Waldman DL, O'Malley W. Accessing the common bile duct after Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2007;3(6):640–3. doi:10.1016/j.soard.2007.06.004.
70. Grover BT, Kothari SN. Biliary issues in the bariatric population. Surg Clin North Am. 2014;94(2):413–25. doi:10.1016/j.suc.2014.01.003.
71. Cotton PB, Garrow DA, Gallagher J, Romagnuolo J. Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. Gastrointest Endosc. 2009;70(1):80–8. doi:10.1016/j.gie.2008.10.039.
72. Testoni PA, Mariani A, Giussani A, Vailati C, Masci E, Macarri G, et al. Risk factors for post-ERCP pancreatitis in high- and low-volume centers and among expert and non-expert operators: a prospective multicenter study. Am J Gastroenterol. 2010;105(8):1753–61. doi:10.1038/ajg.2010.136.
73. Wang P, Li ZS, Liu F, Ren X, Lu NH, Fan ZN, et al. Risk factors for ERCP-related complications: a prospective multicenter study. Am J Gastroenterol. 2009;104(1):31–40. doi:10.1038/ajg.2008.5.
74. Cheng CL, Sherman S, Watkins JL, Barnett J, Freeman M, Geenen J, et al. Risk factors for post-ERCP pancreatitis: a prospective multicenter study. Am J Gastroenterol. 2006;101(1):139–47. doi:10.1111/j.1572-0241.2006.00380.x.
75. Testoni PA. Why the incidence of post-ERCP pancreatitis varies considerably? Factors affecting the diagnosis and the incidence of this complication. JOP. 2002;3(6):195–201.
76. Cotton PB, Lehman G, Vennes J, Geenen JE, Russell RC, Meyers WC, et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointest Endosc. 1991;37(3):383–93.
77. Elmunzer BJ, Scheiman JM, Lehman GA, Chak A, Mosler P, Higgins PD, et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. N Engl J Med. 2012;366(15):1414–22. doi:10.1056/NEJMoa1111103.
78. Puig I, Calvet X, Baylina M, Isava A, Sort P, Llao J, et al. How and when should NSAIDs be used for preventing post-ERCP pancreatitis? A systematic review and meta-analysis. PLoS One. 2014;9(3):e92922. doi:10.1371/journal.pone.0092922.
79. Williams EJ, Taylor S, Fairclough P, Hamlyn A, Logan RF, Martin D, et al. Risk factors for complication following ERCP; results of a large-scale, prospective multicenter study. Endoscopy. 2007;39(9):793–801. doi:10.1055/s-2007-966723.
80. Debenedet AT, Elta GH. Post-sphincterotomy bleeding: fully-covered metal stents for hemostasis. F1000Res. 2013;2:171. doi:10.12688/f1000research.2-171.v1.
81. Vandervoort J, Soetikno RM, Tham TC, Wong RC, Ferrari Jr AP, Montes H, et al. Risk factors for complications after performance of ERCP. Gastrointest Endosc. 2002;56(5):652–6. doi:10.1067/mge.2002.129086.

20. Advanced ERCP: Cholangioscopy and Through-the-Scope Imaging

Bradley R. Zagol and Jeffrey W. Hazey

Introduction

Gallstones and both benign and malignant strictures in the biliary and pancreatic tree were managed surgically for over a 100 years. Just over 40 years ago the development of endoscopic retrograde cholangiopancreatography (ERCP) allowed diagnosis of both biliary and pancreatic stones and strictures. ERCP evolved from a diagnostic procedure to a therapeutic procedure removing stones endoscopically, dilating biliary strictures, diagnosing biliary and pancreatic cancers, and managing operative complications associated with biliary injuries. ERCP has revolutionized the management of chronic pancreatitis, pancreatic pseudocysts, fluid collections, pancreatic strictures, and sphincter of Oddi dysfunction.

ERCP is a complex endoscopic procedure performed by gastroenterologist and a number of general surgeons. Therapeutic ERCP is performed by an even smaller number of specialists. The introduction of per oral cholangiography combined with ERCP adds an additional level of complexity to the procedure.

As the therapeutic aspects of ERCP developed attempts have been made to perform cholangioscopy, through a two-operator mother-daughter scope and now through a single-operator cholangioscopy, SpyGlass™ system (SpyGlass Direct Visualization System, Boston Scientific Corp, Natick, MA). Cholangioscopy allows for direct visualization of the biliary tree lumen. Direct visualization permits precisely directed biopsies of masses within the bile ducts and the introduction of lasers or electrohydraulic lithotripsy for the treatment of common bile duct stones. It also allows for introduction of emerging technologies, including narrowband

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imaging (NBI), autofluorescence, and ultrasound within the bile ducts. Mother-daughter and SpyGlass™ continue the evolution of therapeutic ERCP by increasing diagnostic and therapeutic interventions available to an endoscopist.

Instruments

The use of mother-daughter and SpyGlass™ requires special instrumentation. These systems require the use of a therapeutic duodenoscope with a 4.2 mm working channel. Initially, the systems required conversion to a long wire system, but today the systems are compatible with both short wire and long wire systems.

Reusable systems have a limited availability through Pentax™ and Olympus™. Pentax™ has three daughter scopes designed for per oral use FCP-8P, FCP-9P, and the FCP-8PT (newest version of the FCP-9P). The diameters of the scopes are 2.8 and 3.1 mm. All three scopes have a working length of 1900 mm. The working channel of FCP-8P is 0.75 mm. While the FCP-9P and the FCP-8PT both have accessory channels of 1.2 mm, the 2.8 mm cholangioscope accommodates a 0.025-in. guide wire. The 3.1 mm cholangioscope accommodates a 0.035-in. guide wire. All the ports can accommodate the use of biopsy forceps, electrohydraulic lithotripsy (EHL), or laser fibers [1] (Fig. 20.1).

The Olympus™ per oral systems includes the CHF-BP30 and the CHF-B160. These scopes have a diameter of 3.1 mm and 3.4 mm, respectively. Both of the scopes have a 1.2 mm working channel. The CHF-BP30 has a working length of 1870 mm. The CHF-B160 has a working length of 2000 mm. Again, the working channel can accommodate biopsy forceps, EHL, and laser fibers [1] (Figs. 20.2, 20.3, and 20.4).

Spyglass™ is a semi-reusable single-operator system with a 3.3 mm diameter cholangioscopy delivery system. The system is semi-reusable because the optical fiber is reusable but the catheter is disposable. There is a 1 mm optic channel for use with the SpyGlass™ Visualization Probe. The reusable visual probe is a fragile 0.9 mm probe with a working length of 231 mm. The SpyGlass™ probe is a 6000 pixel image bundle with 225 light transmission fibers. This provides a 70° field of view [4]. The SpyScope™ catheter is a disposable 10 Fr (3.3 mm) catheter with an optic port for the SpyGlass probe, a working or delivery port, and an irrigation port. The dedicated 1.2 mm accessory channel is used for biopsy forceps, EHL, or laser fibers.

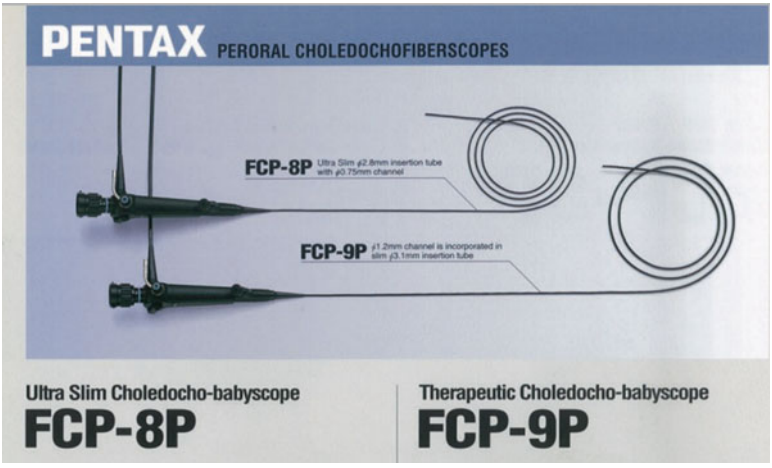

Fig. 20.1. Pentax FCP8-P Diagnostic Per Oral Choledocoscope and FCP-9P therapeutic Choledocoscope. Courtesy of Pentax Medical Company [2].

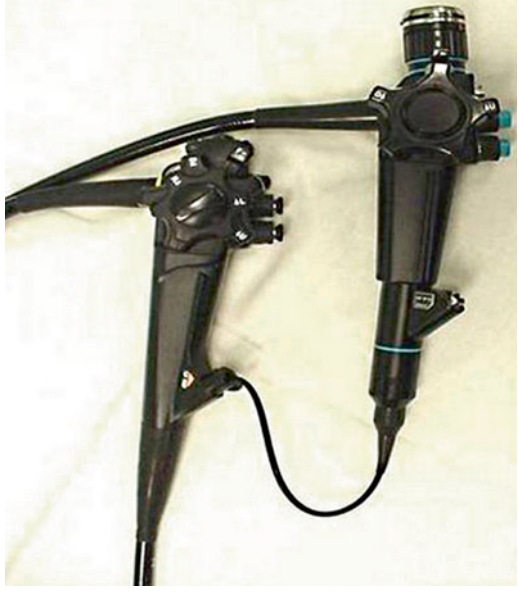

Fig. 20.2. Olympus choledocoscope with traditional duodenoscope. Courtesy Olympus, USA [3].

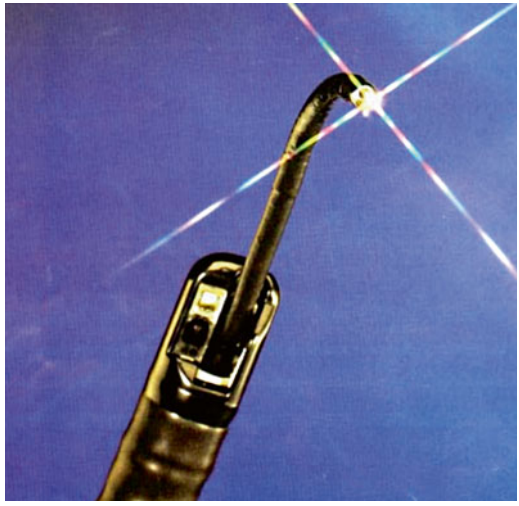

Fig. 20.3. Distal end of the Olympus Duodenoscope with a choledocoscope through the working channel. Courtesy Olympus, USA [3].

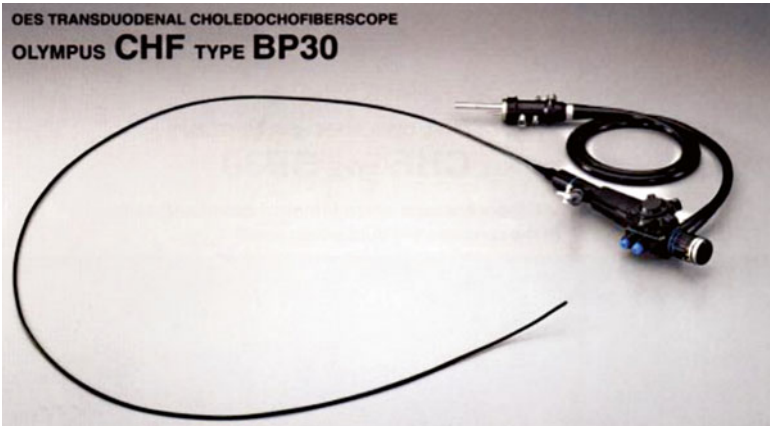

Fig. 20.4. Olympus Choledocoscope. Courtesy of Olympus, USA [3].

Additional instrumentation is required when performing per oral cholangioscopic evaluation. Reusable cholangioscopes require an endoscopic video adaptor, video monitor and irrigator. SpyGlass™ requires a video monitor, light source, video adaptor, and irrigation pump. In addition, SpyGlass™ requires the visualization probe and the SpyScope™ (Fig. 20.5).

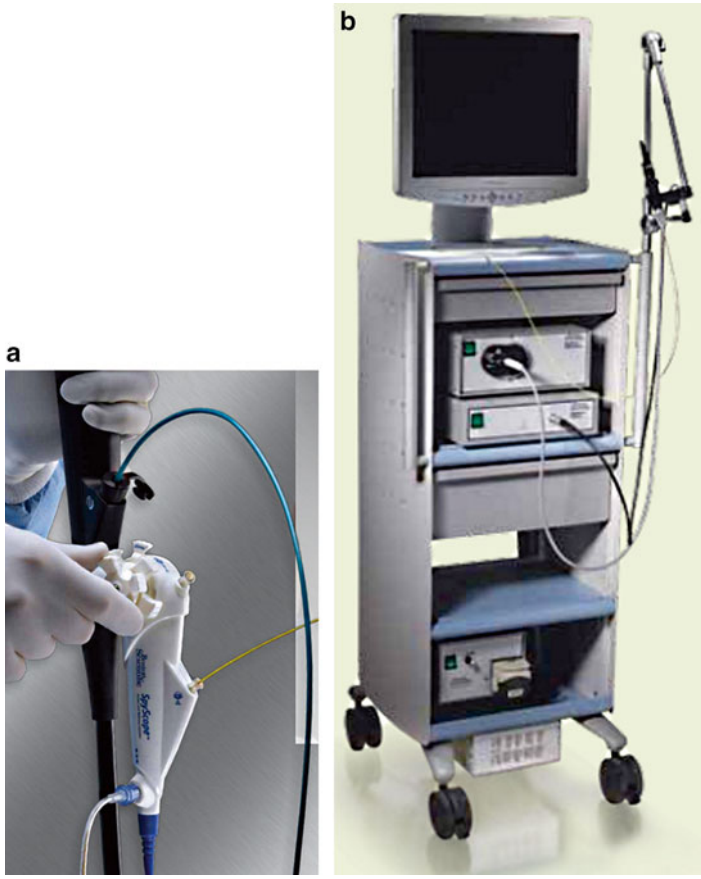

Fig. 20.5. Boston Scientific Single-operator Spyglass system (**a**) and the working tower (**b**). Courtesy of Boston Scientific Corporation [5].

Cholangioscopes (Table 20.1)

Both the Pentax™ and Olympus™ systems require an initial investment that is independent to the cost to perform ERCP. The average initial investment for all equipment for cholangiography ranges from $50,000 to $65,000 [1]. The cost for a cholangioscope, an additional video processor, light source, and video monitor to perform ERCP with cholangioscopy must be added to the cost to establish an ERCP practice.

Table 20.1. Cholangioscopes.

Company	Model	Diameter (mm)	Working channel (mm)	Length (cm)	Cost
Pentax	FCP-8P	2.8	0.75	190	~$25,000
Pentax	FCP-9P	3.1	1.2	190	~$25,000
Pentax	FCP-8PT	2.8	1.2	190	~$25,000
Olympus	CHF-BP30	3.1	1.2	187	~$21,000
Olympus	CHF-B160	3.4	1.2	200	Rental only
Boston Scientific	SpyGlass™ Probe	0.77	N/A	300	~$4,00
	SpyGlass™ Catheter	3.4	1.2/0.6/0.6	220	~$1000

Pentax™ scopes average approximately $24,885 for the FCP-8P, FCP-9P, and the FCP-8PT. It costs an additional $17,500 to purchase the video processors and light sources. Additional video monitor, cart, and irrigator raise the cost to approximately $55,000.

Olympus™ is selling the CHF-BP30 for $21,300 but the CHF-B160 is only available for rental. This would reduce the overall purchase cost because it would be procedure based cost. Nonetheless, it would require purchase of video processors, video monitor, and a light source. The estimated cost would exceed $60,000 for the purchase of the system.

The use of a "travel" cart into an ERCP suite would significantly reduce the cost of purchasing an entire system dedicated to ERCP with cholangiography. This would limit the cost to the specific instruments and daughter scope. Additional costs for disposable instruments remain with both systems.

Techniques of Use

Per oral cholangioscopy requires mastery of diagnostic and therapeutic ERCP. ERCP must be accomplished prior to cholangioscopy. The first step is to insert and position the duodenoscope. The next step is cannulation of the ampulla with a sphincterotome and wire. The bile ducts are then fluoroscopically evaluated to both confirm anatomy and evaluate intraluminal stones or strictures. A sphincterotomy is required

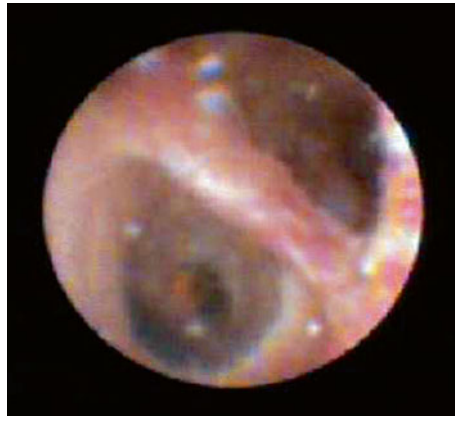

Fig. 20.6. Direct visualization of the biliary bifurcation using Boston Scientific Spyglass™. Courtesy of Boston Scientific Corporation [6].

to perform cholangioscopy. Using ERBE, the sphincter is typically cut to the first fold of the duodenum, approximately 5–10 mm. Placement of a cholangioscope may require removal of stones from the bile ducts or dilation of strictures. Dilation is performed using through the scope biliary dilating balloons. Following these maneuvers a cholangioscope can be inserted into the bile ducts.

The cholangioscope is inserted optionally over a guide wire through the working channel of the duodenoscope. Guide wire insertion reduces the risk to the daughter scope and reduces the use of the elevator. The cholangioscope is inserted into bile duct with unlocked dials. The cholangioscope is advanced under both fluoroscopic and direct visualization to the lesion of concern (Fig. 20.6).

Under direct observation, instrumentation can be inserted through the cholangioscope's working channel. Small caliber biopsy forceps can be passed through the cholangioscope and biopsies of lesions within the lumen of the bile ducts may be performed. Alternatively EHL probes or laser probes can be advanced through the scope. Then only under direct visualization larger stones, which are not amenable to extraction with balloons or baskets, can be broken and fragmented. The stone fragments can be removed with standard balloon and basket extraction.

An EHL electrode capable of producing sparks at the tip of the probe creates a high-amplitude hydraulic pressure waves for stone fragmentation [7]. EHL requires water emersion which is accomplished through

irrigation through the cholangioscope. The EHL probe should be placed within 2–3 mm of the surface of the target stone [1]. An alternative to EHL is the use of laser lithotripsy. The laser pulse is directed through a flexible quartz fiber to the surface of the stone. The laser energy generates a gaseous collection of ions and free electrons. The gaseous plasma rapidly expands and collapses creating a spherical shockwave to fragment common bile duct stones [8, 9] (Figs. 20.7, 20.8, and 20.9).

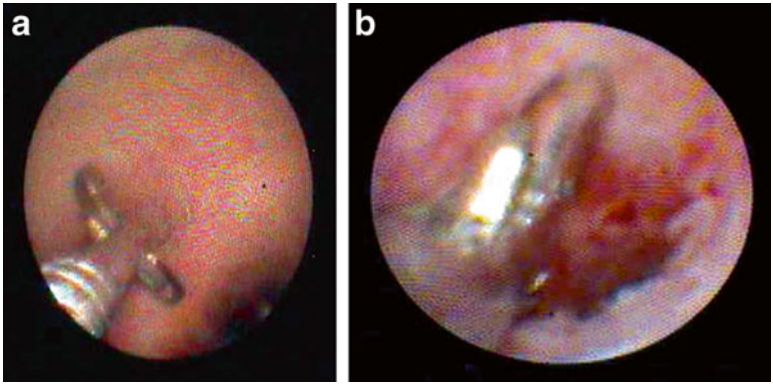

Fig. 20.7. Boston Scientific Spyglass™ through-the-scope single operator system with direct visualization of the biliary tree and use of the SpyBite™ Intraductal Biopsy. Courtesy of Boston Scientific Corporation [6].

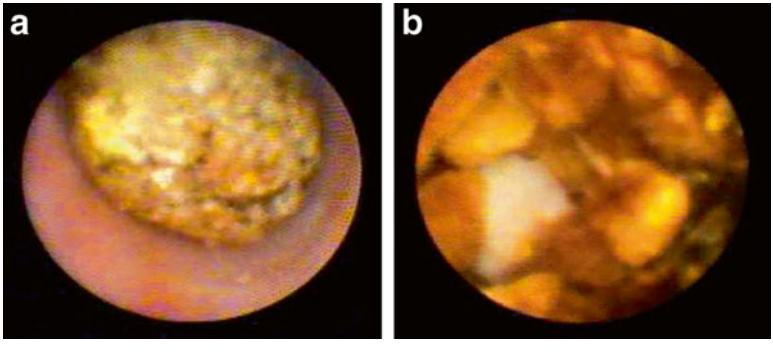

Fig. 20.8. Boston Scientific SpyGlass™ with electrohydraulic lithotripsy fracture of common bile duct stones. Courtesy of Boston Scientific Corporation [6].

Fig. 20.9. SpyScope™ with SpyGlass™ and SpyBite™. Courtesy of Boston Scientific Corporation [6].

Efficacy, Safety, and Limitations

Both Mother-daughter ERCP and SpyGlass™ have multiple evaluations for efficacy and safety. Mother-daughter ERCP required a significant equipment investment. It also required two skilled ERCP trained endoscopists to perform. Acceptance of mother-daughter ERCP has been limited due to the complexity and man power requirements. With the advent of SpyGlass™ by Boston Scientific as a single-operator cholangioscope, more wide spread acceptance of cholangioscopy has occurred. As a result, SpyGlass™ has become the most widely used cholangioscopic system on the market today. SpyGlass™ single operator system provides a platform that is easy and versatile. Chen et al. evaluated the SpyGlass™ system in a multi-center study evaluating the success rate, adequacy of sampling and sensitivity for bile duct malignancies. This study evaluated 297 patients, with an overall success rate of 89 %. In the procedures indicated for diagnosis for stricture, adequate

tissue samples were obtained in 88 % of the patients. Chen et al. showed a sensitivity of 78 % for the diagnosis of malignancy. For patients with common bile duct stones, they demonstrated a 92 % success rate in clearing or treating the stones. However, they showed a 7.5 % and 6.1 % serious procedure-related adverse event for diagnosis of malignancy and stones, respectively [10]. The most common complication associated with SpyGlass™ was post procedure cholangitis. The most severe complications were perforation of a large duodenal diverticulum at the ampulla in one patient and a bile duct perforation in one patient. The remaining complications included pancreatitis, aspiration, bacteremia, transient hypotension, and abdominal pain with distention. Of these complications only the duodenal perforation required surgical intervention.

Others have evaluated both mother-daughter and SpyGlass™ cholangiography for treatment of extrahepatic biliary stones. Multiple studies demonstrate a successful clearance rate from 83 to 100 % [11, 12]. Factors that decreased the duct clearance rate through the per oral route included surgically altered anatomy, downstream strictures, acute intrahepatic ductal angulation, and impacted stones [13–15].

In the applications for biliary and pancreatic malignancy, cholangioscopy showed a high rate of sensitivity for detecting cholangiocarcinoma; 100 % for polypoid type, 95 % for the stenotic type, and 100 % for the tumor vessel pattern. However, it was only 60 % sensitive for pancreatic cancer obstructing the bile ducts [1]. Chen et al. demonstrated a 71 % sensitivity and 100 % specificity for cholangiocarcinoma using SpyGlass™ [10].

Complications remain uncommon with per-oral cholangiography. The most common complications are cholangitis, hemobilia, and bile leak. A majority of the complications are associated with intra-ductal lithotripsy. Cholangitis occurs in 0–14 % of patients. The use of antibiotics in a prospective study failed to demonstrate a benefit in preventing cholangitis [16]. The hemobilia rate is estimated at 0–3 %. The bile leak rate associated with intraductal lithotripsy was 1 % [12]. The pancreatitis rate is similar to standard ERCP with a rate of 0–7 % [1].

The high efficacy rate of intraductal therapy with cholangiography, along with a relatively low increased complication rate over ERCP without cholangioscopy makes per oral cholangiography a vital resource as both a diagnostic and therapeutic tool.

ERCP Imaging

Narrowband Imaging

Currently Olympus produces cholangioscopes capable of performing NBI. NBI limits the light emitted by the endoscope to wavelengths of 415 and 540 nm. This is currently only available through the Olympus™ Mother-Daughter system. These wavelengths of light allows for enhanced visualization of superficial and deeper capillary lesions [17]. NBI light is composed of two specific wavelengths that are strongly absorbed by hemoglobin. The 415 nm light only penetrates the superficial layers of the mucosa. The 415 nm light is absorbed by capillary vessels in the surface of the mucosa and shows up brownish on the video image. This wavelength is particularly useful for detecting tumors, which are often highly vascular. The 540 nm light penetrates deeper than 415 nm light. It is absorbed by blood vessels located deeper within the mucosal layer, and appears cyan on the NBI image. This wavelength allows a better understanding of the vasculature of suspect lesions [18]. NBI within the bile ducts was studied by Itoi et al. and showed a statistically improved visualization of biliary lesions (57.4 % vs. 9.5 %) with the use of NBI. The studies also showed some limitations with NBI imaging due to presence of blood and bile within the biliary tree [19] (Fig. 20.10).

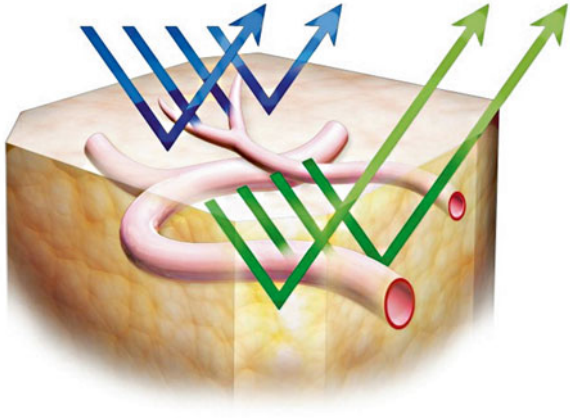

Fig. 20.10. Narrowband imaging using 415 and 540 nm light with different penetration into the underlying tissue. Courtesy of Olympus, USA [3].

Autofluorescence

There is limited evaluation of autofluorescence in the biliary tree. Autofluorescence uses blue light to excite cells of the mucosa. Then, red and green hypersensitive cameras are used to evaluate the mucosa. Normal mucosa is seen as green, whereas neoplastic tissues change to dark green or black because of the difference in autofluorescence. Itoi et al. evaluated the use of autofluorescence in the biliary tree [19]. While autofluorescence imaging increased the sensitivity of imaging in the biliary tree from 88 to 100 %, it decreased the specificity from 87.5 to 52.5 % for visualizing neoplastic tissue with in the biliary tree. The increased sensitivity with autofluorescence demonstrates that additional research should focus the use of autofluorescence within the biliary tree.

Confocal Endomicroscopy

Confocal endomicroscopy allows for real-time histological evaluation of the epithelium. Confocal endomicroscopy allows for the focusing of light through a confocal aperture. This allows for elimination of scattered light above and below the plane. When scanned together in the same plane it provides for a dynamic image [17]. Confocal Endomicroscopy is now possible within the biliary tree with the CholangioFlex (Mauna Kea Technologies) catheter. This is a through the scope, 0.94 mm catheter based system. It has linear surface field of view of 325 μm wide, an optical thickness of 30 μm, and a 50 μm optical penetration. This is an emerging technology that requires significant training to interpret the images. It has limited evaluation within the literature. Meining et al. studied confocal endomicroscopy in separate studies. He showed a statistically significant improvement in sensitivity, specificity, PPV, and NPV over traditional sampling of biliary stricture with the use of confocal endomicroscopy [20, 21]. This emerging technology shows promise to decrease the need for invasive procedures with ERCP with or without cholangiography (Figs. 20.11 and 20.12).

ERCP with Intraductal Ultrasound

High-frequency ultrasound probes that fit through the working channel of a duodenal scope have been around for several decades. Using a 12–30 MHz probe, intraductal ultrasound is able to diagnosis biliary

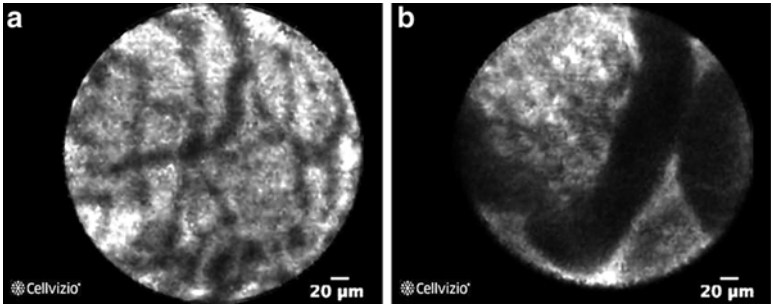

Fig. 20.11. Images demonstrating confocal microscopy within the biliary tree. (**a**) A healthy bile duct. (**b**) The image demonstrates a biliary malignancy. Courtesy Mauna Kea Tech [23].

malignancies within the common bile duct, common hepatic duct, and left and right hepatic ducts. Intraductal ultrasound can also differentiate between stones and air bubbles within the common bile duct [17]. Intraductal ultrasound probes are being fitted over 0.035 in. guide wires to eliminate the need for sphincterotomy [24].

Intraductal ultrasound is able to distinguish three layers of the bile duct wall: the mucosa, submucosa, and serosa. The ultrasound images are evaluated for disruptions in the interfaces between the bile duct layers. The heterogeneity of the internal echo pattern and irregularity of the outer border of the bile duct wall are evaluated during the ultrasound. In addition, a papillary source or a hypoechoic mass are diagnostic criteria for malignancies within the biliary tree [25–27].

Menzel et al. demonstrated that intraductal ultrasound has a higher accuracy for differentiating biliary strictures from benign verses malignant than endoscopic ultrasound alone (89 % vs. 76 %, $P<0.002$) [28]. Farrell et al. demonstrated that intraductal ultrasound had an accuracy of 92 %, sensitivity of 90 % and specificity of 93 % in detecting biliary malignancies [29]. Finally, Krishna et al. demonstrated a significant improvement in detecting the proximal extent of biliary tumor with the use of intraductal ultrasound [30, 31].

Conclusion

ERCP began as a diagnostic procedure for biliary strictures and stones. It has evolved into a therapeutic procedure for the removal and treatment of biliary stones and strictures. Cholangioscopy with mother-daughter and

Fig. 20.12. Confocal microscopy tower from Cellvizio. Courtesy Mauna Kea Tech [23].

SpyGlass™ further advanced the diagnostic and therapeutic abilities of ERCP. ERCP with cholangioscopy allows an endoscopist to diagnosis and treat a wider array of diseases than just a decade prior. ERCP with cholangioscopy has an excellent safety profile allowing for wide access to treatment. The increasing use of narrow band imaging, autofluorescence, and confocal endomicrosocpy will continue to enhance the diagnostic capabilities of ERCP. Recent advancements of intraductal ultrasonography will dramatically change the way ERCP can be used.

References

1. Shah RJ, Adler DG, Conway JD, Diehl DL, Farraye FA, Kantsevoy SV, et al. Cholangiopancreatoscopy. Gastrointest Endosc. 2008;68(3):411–21.
2. http://www.pentaxmedical.ca/Libraries/Product_Downloads/FCP-8P-9P_-_Choledocho-Babyscope.sflb.ashx
3. http://www.olympusamerica.com/msg_section/download_brochures/78_b_chfbp30.pdf
4. Boston Scientific Resource packet November 2010.
5. http://www.bostonscientific.com/content/dam/bostonscientific/endo/portfolio-group/spyglass/spyglass_detail_brochure.pdf
6. http://www.bostonscientific.com/global-endoscopy/product-image-download.html
7. Sievert CE, Silvis SE. Evaluation of electrohydraulic lithotripsy as a means of gallstone fragmentation in a canine model. Gastrointest Endosc. 1987;33:233–5.
8. Nishioka NS, Kelsey PB, Kibbi AG, et al. Laser lithotripsy: animal studies of safety and efficacy. Lasers Surg Med. 1988;8:357–62.
9. Hochberger J, Gruber E, Wirtz P, et al. Lithotripsy of gallstones by means of a quality-switched giant-pulse neodymium: yttrium-aluminum-garnet laser. Gastroenterology. 1991;101:1391–8.
10. Chen YK, Parsi MA, Binmoeller KF, et al. Single-operator cholangioscopy in patients requiring evaluation of bile duct disease or therapy of biliary stones. Gastrointest Endosc. 2011;74(4):805–14.
11. Piraka C, Shah RJ, Awadallah NS, et al. Transpapillary cholangioscopy-direct lithotripsy in patients with difficult bile duct stones. Clin Gastroenterol Hepatol. 2007;5:1333–8.
12. Arya N, Nelles SE, Haber GB, et al. Electrohydraulic lithotripsy in 11 patients: a safe and effective therapy for difficult bile duct stones. Am J Gastroenterol. 2004;99:2330–4.
13. Bonnel DH, Liguory CE, Cornud FE, et al. Common bile duct and intrahepatic stones: results of trans-hepatic, electrohydraulic lithotripsy in 50 patients. Radiology. 1991;180:345–8.
14. Yoshimoto H, Ikeda S, Tanaka M, et al. Choledochoscopic electrohydraulic lithotripsy and lithotomy for stone in the common bile duct, intrahepatic, and gallbladder. Ann Surg. 1989;210:576–82.

15. Jan UU, Chen MF, Wang CS, et al. Surgical treatment of hepatolithiasis: long-term results. Surgery. 1996;120:509–14.
16. Sheen-Chen SM, Chou FF. Postoperative choledochoscopy: is routine antibiotic prophylaxis necessary? A prospective randomized study. Surgery. 1994;115:170–5.
17. Kahaleh M, Lightdale CJ. Therapeutic and advanced ERCP. Gastrointest Endosc Clin N Am. 2012;22(3):454. 456–7.
18. http://www.olympus.co.uk/medical/en/medical_systems/applications/urology/bladder/narrow_band_imaging__nbi_/narrow_band_imaging__nbi_.html
19. Itoi T, Neuhaus H, Chen YK. Diagnostic value of image-enhanced video cholangiopancreatoscopy. Gastrointest Endosc Clin N Am. 2009;19:557–66.
20. Meining A, Shah RJ, Slivka A, Pleskow D, Chuttani R, Stevens PD, Becker V, Chen YK. Classification of probe-based confocal laser endomicroscopy findings in pancreaticobiliary strictures. Endoscopy. 2012;44(3):251–7.
21. Meining A, Frimberger E, Becker V, Von Delius S, Von Weyhern CH, Schmid RM, Prinz C. Detection of cholangiocarcinoma in vivo using miniprobe-based confocal fluorescence microscopy. Clin Gastroenterol Hepatol. 2008;6(9):1057–60.
22. http://www.synmed.co.uk/_discontinued/products_confocal_endomicroscopy_cholangioflex.htm
23. http://www.maunakeatech.com/en/content/cellvizio-solution
24. Ascher SM, Evans SR, Goldberg JA, et al. Intraoperative bile duct sonography during laparoscopic cholecystectomy: experience with a 12.5 MHz catheter-based US probe. Radiology. 1992;185:493–6.
25. Kuroiwa M, Tsukamoto Y, Naitoh Y, et al. New technique using intraductal ultrasonography for the diagnosis of bile duct cancer. J Ultrasound Med. 1994;13:189–95.
26. Fujita N, Utaka N, Kobayahi G. Analysis of layer structure of the gallbladder all delineated by endoscopic ultrasound using the pinning method. Dig Endosc. 1995;7:353–6.
27. Fujita N, Noda Y, Kobayashi G, et al. Staging of bile duct carcinoma by EUS and IDUS. Endoscopy. 1998;30 Suppl 1:a132–4.
28. Menzel J, Poremba C, Dietl KH, et al. Preoperative diagnosis of bile duct strictures—comparison of intraductal ultrasonography with conventional endosonography. Scand J Gastroenterol. 2000;35:77–82.
29. Farrell RJ, Agarwal B, Brandwein SL, et al. Intraductal US is a useful adjunct to ERCP for distinguishing malignant from benign biliary strictures. Gastrointest Endosc. 2002;56:681–7.
30. Krishna NB, Saripalli S, Safdar R, et al. Intraductal US in evaluation of biliary strictures without a mass lesion on CT scan or magnetic resonance imaging: significance of focal wall thickening and extrinsic compression at the stricture site. Gastrointest Endosc. 2007;66:90–6.
31. Kuroiwa M, Goto H, Hirooka Y, et al. Intraductal ultrasonography for the diagnosis of proximal invasion in extra hepatic bile duct cancer. J Gastroenterol Hepatol. 1998;13:715–9.
32. Tantau M, Pop T, et al. Intraductal ultrasonography for the assessment of preoperative biliary and pancreatic strictures. J Gastrointestin Liver Dis. 2008;17(2):217–22.

21. Interventional Endoscopic Ultrasound

Arthi Kumaravel and Tyler Stevens

Introduction

Endoscopic ultrasound (EUS) was developed as an adjunctive diagnostic modality to supplement cross-sectional imaging. EUS applications have expanded due to evolution in echoendoscope design, improved image resolution, and the development of fine needle aspiration (FNA) needles. This chapter will review current interventional EUS applications, including FNA, pseudocyst drainage, pancreatic necrosectomy, pancreaticobiliary access, celiac plexus interventions, cyst ablation, tumor injection, and vascular interventions.

Equipment

The two major types of echoendoscopes in common use are radial and linear (Fig. 21.1). The radial echoendoscope provides a circumferential image of structures in the plane perpendicular to the shaft of the scope. The advantage of the radial scope is that the images are similar to those obtained by computed tomography (CT), which may ease interpretation. The radial scope is not a therapeutic instrument because it does not have a working channel for passage of a needle or other devices. The linear echoendoscope is the therapeutic EUS "workhorse" and provides images of structures in the plane parallel to the shaft of the scope. The linear scope has a working channel, which allows the passage of needles in the plane of the endosonographic images for high precision tissue sampling and directed interventions. Additional specialized probes are available (e.g., catheter-based mini-probes, rigid

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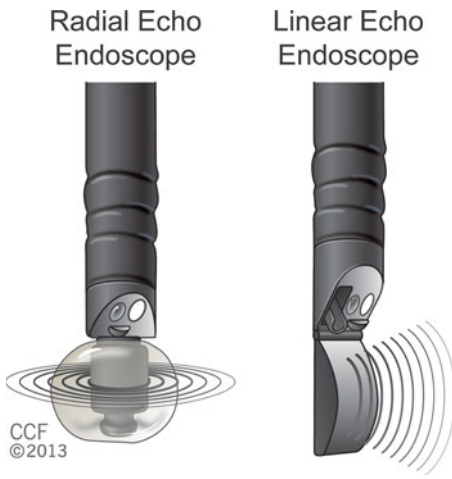

Fig. 21.1. Radial and linear echoendoscope depictions with plane of imaging. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography ©2015.

anal probe, transpapillary intraductal ultrasound). These radial probes have higher frequency capability allowing very fine mucosal detail, and specific diagnostic applications, such as assessing subepithelial lesions and superficial cancers, evaluating the colon proximal to rectum, assessing the anal sphincter, staging anal cancer, and assessing pancreaticobiliary ductal pathology. Because they are radial instruments without a working channel, these specialized probes cannot be used for therapeutic interventions.

EUS-Guided Fine Needle Aspiration (FNA)

EUS-guided FNA is the most commonly performed intervention and has almost completely replaced CT- and US-guided transcutaneous biopsy of pancreatic masses and other lesions in proximity to the upper GI tract. Common indications include upper GI mucosal and intramural lesions, solid and cystic pancreatic masses, and diagnosis of pathologic lymph nodes. Immunohistochemical stains and flow cytometry can be added to standard cytological interpretation to enhance the diagnosis of certain diseases like lymphoma and stromal tumors.

One limitation of EUS-FNA has been imperfect sensitivity for detecting cancer and other diseases resulting in false negative results and need for repeat procedures. A second limitation is that cytologic specimens (individual or aggregates of cells without preserved tissue architecture) are usually acquired, rather than core biopsies amenable to comprehensive histological analysis.

In recent years, clinical studies have attempted to define optimal FNA techniques and needle types that maximize cytological yield, or even achieve a core biopsy. Needle size may affect the sample, since smaller needles cause less bloody contamination and more easily actuate in torqued scope positions, whereas larger needles may obtain more cells. Studies comparing needle sizes (22 gauge versus 25 gauge) have shown varying results. Retrospective studies and a meta-analysis suggested a benefit of the 25 gauge (G) needle for detecting cancer [1, 2]. However, other studies showed no difference between these needle sizes in overall accuracy [3–8]. Twenty-five gauge needles may be more accurate for pancreatic head and uncinate lesions [4, 9]. The 19-G needle may enhance the diagnosis of cystic lesions since it drains material quickly and is less likely to become blocked with mucinous fluid.

The use of a stylet within the needle during puncture has not been shown to be beneficial [10–12]. The application of suction on the needle improved the diagnostic yield in pancreatic lesions [13, 14], but not in lymph nodes [15]. If a 25 G needle is used for FNA, then a "slow pull" of the stylet has been shown to be superior to suction [16].

The availability of an onsite cytopathologist or technician allows passes to be analyzed in real time to ensure cellular adequacy and minimize the number of passes. The optimal number of passes in the absence of onsite cytopathology is variable. Initially seven passes were recommended for pancreatic mass lesions and five passes for lymph nodes [17]. More recent studies have shown that three to four passes may be adequate [18, 19]. In some cases, core biopsies (with preserved cellular architecture) can be acquired using 19 G and "coring" needles (e.g., Cook Procore® and Trucut®) but the successful acquisition of tissue with these devices is variable.

EUS-FNA is generally safe and serious complications are rare. The overall complication rate reported is 2.5–3.4 % including bleeding (0.3 %), pain (0.85–1.2 %), infection (0.56 %), and pancreatitis (0.85–1.8 %) [20, 21].

EUS-Guided Drainage Procedures

Pancreatic Fluid Collection Drainage

Pancreatic fluid collections (PFCs) may occur as a result of acute or chronic pancreatitis, surgery, or trauma. Many of these collections are closely opposed to the stomach or duodenum, and may undergo drainage. Endoscopic drainage was previously done without the benefit of ultrasound guidance, by blindly puncturing the luminal bulge seen endoscopically using a needle knife cautery device. EUS has enhanced the safety and efficacy of endoscopic drainage because it visualizes intervening blood vessels that are common in patients with left-sided portal hypertension from prior pancreatitis, and because it allows drainage of PFCs that do not have an obvious luminal bulge. Studies of EUS-guided drainage have shown a higher technical success rate and lower complication rate than standard endoscopic drainage [22]. EUS-guided drainage has also mostly replaced surgical cystogastrostomy. A randomized control study has shown that EUS-guided drainage of pseudocysts is non-inferior to surgical drainage and associated with a shorter length of stay and lower cost [23]. Enlarging PFCs and those causing pain, obstruction (gastric or biliary), or infection require drainage. Endoscopic drainage should be timed based on the maturity of the PFC, since those with a thick, fibrous wall adhered to the gastrointestinal lumen are most safely drained.

The technical success rate of EUS-guided drainage in one of the largest single center series was 100 %, with a 5 % complication rate [24]. In a recent systematic analysis the technical and clinical success rates were reported as 97 % and 90 % respectively, with a complication rate of 17 % [25]. Reported complications include bleeding, infection, stent migration, and perforation. Most complications were managed conservatively or surgically with a mortality rate of 0.2 %. The success and complication rates of endoscopic drainage are influenced by the type of PFC. Pseudocysts arising in chronic pancreatitis respond better than those arising in acute pancreatitis. The newly revised Atlanta Classification defines different types of PFCs arising from acute pancreatitis based on location, timing following symptom onset, and the presence of solid necrotic debris. Most PFCs occurring more than 4 weeks after the onset of acute pancreatitis are actually walled off pancreatic necrosis (WOPN) rather than true acute pseudocysts. This distinction is vital for endoscopic management, since multiple sessions of aggressive

endoscopic debridement may be necessary for WOPN, whereas simple drainage may be sufficient for acute and chronic pseudocysts. EUS is advantageous because it is superior to CT scan for detecting solid material within a PFC, differentiating WOPN from acute pseudocyst.

Contraindications to endoscopic drainage include concern that the collection is a cystic neoplasm and the presence of uncorrected coagulopathy. If a cystic neoplasm is a possibility, initial EUS-FNA for diagnosis may be prudent prior to embarking on drainage. Techniques for EUS-guided drainage vary slightly between practitioners. The standard approach is the graded dilation technique. The PFC is first identified using a linear echoendoscope, and a suitable site chosen based on proximity from the lumen (preferably <1 cm) and absence of intervening blood vessels. Under fluoroscopy, the PFC is punctured using a 19-G FNA or access needle, contrast is injected to opacify the collection, and a guidewire passed through the needle and coiled within the cyst cavity. The tract is serially dilated over the guidewire using tapered and balloon dilating catheters, with or without electrocautery. After the initial intervention, the endoscopic cystogastrostomy should be maintained by placing stents. There is no consensus as to the type or number of stents. Plastic stents have lower migration rates but higher occlusion rates. Self-expandable metal stents have shown increased success rates in small case series but may increase the risk of stent migration, fluid leakage, and tissue injury from exposed metallic edges [26–29]. Newer lumen-apposing stents have been developed exclusively for drainage of pancreatic fluid collections (AXIOS™, Xlumena Inc., Mountain view, California, USA) with dedicated delivery systems (NAVIX™, Xlumena Inc., Mountain view, California, USA) [30–32].

In WOPNs and other debris filled collections that are symptomatic, endoscopic debridement should be considered. Infected WOPNs require intervention as they are associated with sepsis, multiorgan failure, and death. The recent guidelines advocate for a step-up approach starting with minimally invasive procedures such as percutaneous drainage and working up to surgical necrosectomy [33]. Delay in timing of surgical intervention improved mortality. A small randomized control trial has shown that death and major complications are lower in patients undergoing endoscopic transluminal necrosectomy compared to surgical necrosectomy [34]. Larger trials are underway to evaluate step-up endoscopic therapy versus step-up surgical therapy [35].

Endoscopic necrosectomy starts with standard EUS-guided cyst access, but involves more aggressive dilation (up to 18 or 20 mm) with subsequent passage of a standard upper scope through the endoscopic

cystogastrostomy into the cyst cavity for removal of necrotic debris using a variety of devices such as baskets, nets, and graspers. A covered self-expanding metal stent is deployed to secure the access to the cavity. Direct endoscopic necrosectomy is performed either in the same session or in the next session. The clinical success rate in a large US series was 91 % with a median of three procedures per patient and complications in 14 % of patients [36]. Complications included bleeding, perforation, pneumoperitoneum, sepsis, and failure of resolution.

Non-peripancreatic and Pelvic Fluid Collection Drainage

EUS-guided drainage of abscesses, inflammatory fluid collections, and hematomas in the subphrenic space, perihepatic space, paracolic gutters, perirectal spaces, and pelvis have been described. Endoscopic luminal drainage of such collections may be quite useful when percutaneous drainage is not technically feasible. The technical and clinical success rates reported in a systematic analysis of observational case series were 99 and 92 % [25]. The EUS-guided drainage technique is similar to that described above for PFCs. The reported complications are pneumoperitoneum, pneumomediastinum, stent migration, bleeding, and fluid leakage.

EUS-Guided Biliary Drainage

Percutaneous transhepatic cholangiography (PTHC) and surgical bypass have traditionally been offered when biliary cannulation fails during endoscopic retrograde cholangiopancreatography (ERCP). However, recent studies have shown that EUS-guided biliary drainage is as effective as PTHC and avoids the need for an external drainage catheter [37]. EUS-guided biliary drainage procedures encompass direct transluminal drainage (creation of a fistula maintained by a stent) and duct puncture with subsequent anterograde passage of a guidewire through the ampulla to achieve “rendezvous” access. Each technique is further subdivided into transgastric (via intrahepatic ducts) and transduodenal approaches (via common duct) as shown in Fig. 21.2. EUS-guided rendezvous procedures have fewer complications (e.g., bleeding, bile leak, pneumoperitoneum) compared with direct drainage and are usually attempted first, but are not always possible particularly if there

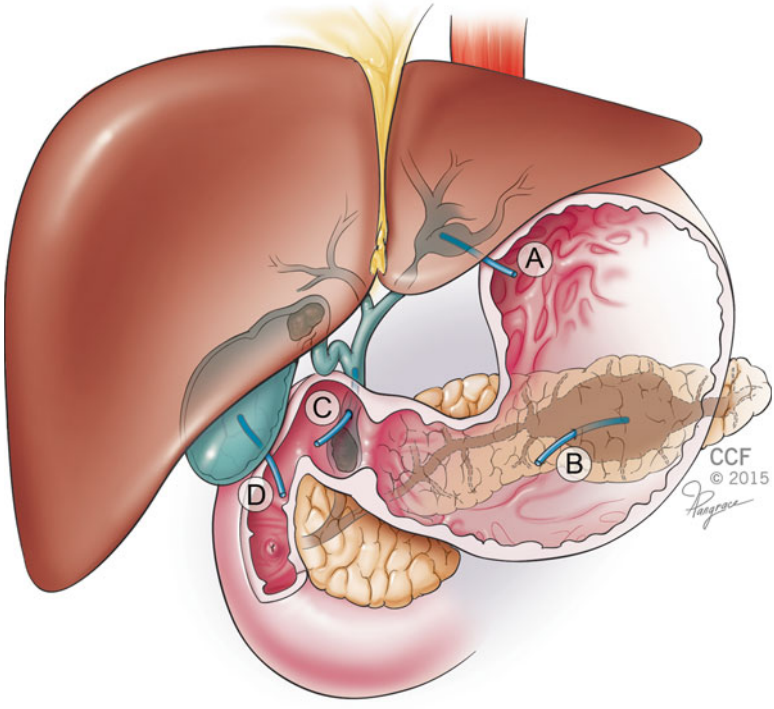

Fig. 21.2. Approaches for EUS-guided pancreatobiliary access. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography ©2015.

is concomitant duodenal obstruction preventing access to the ampulla. Studies have shown that the complication rate for direct transluminal stenting is 20 %, and the use of needle knife for tract dilation is an independent risk factor for complications [38].

In the EUS-guided rendezvous procedure, the dilated bile duct is punctured with a 19-gauge FNA needle, followed by passage of a guidewire. The wire is manipulated anterograde through the papilla. The echoendoscope is then removed over the guidewire. A duodenoscope is advanced alongside the guidewire to the second portion of the duodenum. The guidewire is grasped using a forceps or snare and pulled into the working channel of the endoscope, allowing subsequent transpapillary biliary access to complete the drainage. The initial site of EUS-guided puncture may be the intrahepatic ducts through the lesser curve

of the stomach or the common duct through the medial wall of the duodenal bulb. Though the transgastric route into the intrahepatic ducts was initially preferred because of the presumed decreased chance of bile leak, studies have shown that the intrahepatic route is associated with a higher complication rate (20 %), and the extrahepatic approach is preferred if both routes are accessible [39, 40].

In patients with tight biliary strictures that do not permit passage of the guidewire through the papilla or with altered anatomy or duodenal strictures that hinder access to the papilla, direct transluminal stenting may be considered. In this procedure, access to the bile duct is obtained using an FNA needle. The tract is dilated and a transmural stent is placed into the duct to facilitate direct enteric drainage of bile. The potential adverse events of direct transluminal drainage are similar to those of the rendezvous technique when a needle knife is not used for dilation [41]. The transgastric route has a higher complication rate than the transduodenal route [39, 40].

EUS-Guided Pancreatic Duct Drainage

In case of failed pancreatic duct cannulation during ERCP, EUS-guided pancreatic duct drainage has been used in a similar fashion as biliary duct drainage. The majority of pancreatic interventions have been for benign indications such as ductal stones or strictures from chronic pancreatitis, or in those with obstructed pancreaticojejunostomy after Whipple surgery.

The technique is similar as for biliary duct drainage and the possible access points are shown in Fig. 21.2. The pancreatic duct is visualized using a linear echoendoscope, accessed using an FNA needle, and a guidewire is advanced through the needle and if possible through the papilla for a rendezvous procedure. If the guidewire cannot be advanced past the papilla, then it is used for dilation and transmural stent placement. Pancreatic duct access is most commonly achieved via the transgastric route. Pancreatic duct drainage is more technically challenging than biliary duct drainage due to acute angulations between the scope and the pancreatic duct and fibrosis in the pancreas. The technical success rate reported in systematic analysis was 78 %, with a 20 % complication rate [25]. The complications described are pancreatitis, pancreatic leakage, bleeding, and perforation. A single large tertiary center experience concluded that EUS-guided pancreatic duct drainage may be done with good technical (74 %) and clinical (83 %) success rates and low complications (5.8 %) in large centers with experienced endoscopists [42].

EUS-Guided Gallbladder Drainage

EUS-guided gallbladder drainage may be considered for patients with acute cholecystitis that requires intervention but who are poor surgical candidates. Percutaneous gallbladder drainage has been traditionally offered to such patients as a bridge to surgery or as definitive treatment. EUS-guided drainage may have similar efficacy and complications as the percutaneous approach, and does not require an external drainage catheter [43]. Complications include bleeding, bile peritonitis, and stent migration. Newer lumen-apposing stents have been used for EUS-guided gallbladder drainage with good success to minimize stent migration and bile peritonitis [32, 44].

EUS-Guided Celiac Plexus Intervention

Celiac plexus blocks (CPB) and celiac plexus neurolysis (CPN) have long been performed for pain relief in patients with pancreatic cancer or chronic pancreatitis. EUS-guided celiac plexus interventions (Fig. 21.3) have been shown to be more effective than fluoroscopy or computed tomography directed percutaneous celiac plexus neurolysis in two small comparative trials [45, 46]. EUS-CPN is usually reserved for those with pancreatic or biliary cancer pain and involves injection of a neurolytic agent (most commonly 98 % dehydrated alcohol). EUS-CPB involves the injection of anesthetic agents with or without corticosteroids, has fewer complications, and is generally done for those with benign causes of pain like chronic pancreatitis. Meta-analyses suggest that EUS-CPN is durably effective in controlling cancer-related pain in 80 %, while EUS-CPB is only 50–60 % effective in temporarily controlling pain from chronic pancreatitis [47]. Early EUS-guided celiac plexus neurolysis in patients with inoperable pancreatic cancer had significantly lower pain scores with a trend towards lower narcotic usage. There was no effect on the survival or quality of life [48].

The linear echoendoscope is used to perform celiac plexus interventions. The origin of the celiac trunk from the aorta is identified along the lesser curve of the stomach. A 19 or 22 G FNA needle is advanced into the region cephalad of the celiac trunk. When the needle is in the target area 2 cc of saline is injected, and then aspirated to confirm that the needle is not within a blood vessel. After this “saline aspiration test,” the anesthetic agent/neurolytic agent is injected into the celiac plexus.

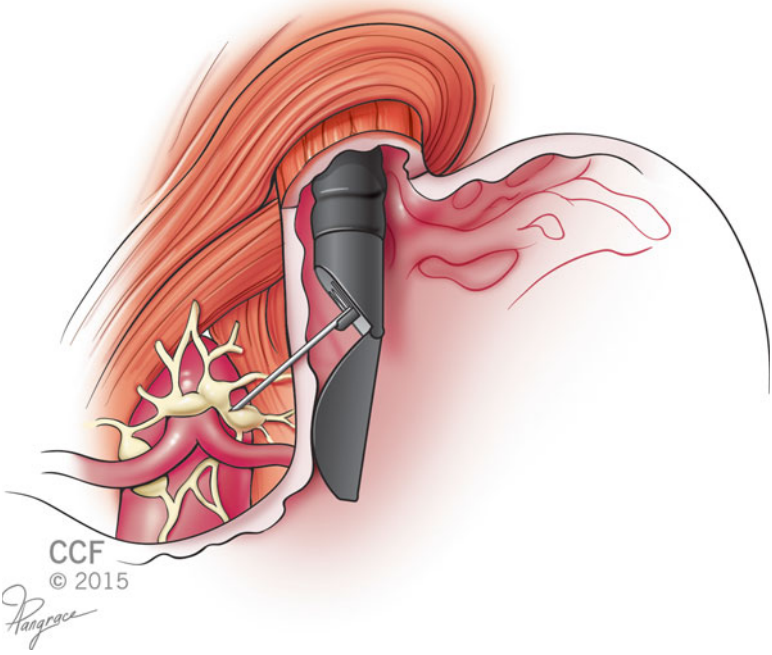

Fig. 21.3. EUS-guided Celiac plexus intervention. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography ©2015.

There are wide variations in the technique and agent used for celiac plexus interventions. An observational study suggested that bilateral injection in which the neurolytic agent was injected into either side of the celiac trunk was more effective than one central injection [47, 49]. Subsequent, randomized control trials in patients with pancreatic cancer and chronic pancreatitis pain comparing central injection versus bilateral injection have shown no difference in the number of patients with response, speed of onset, or duration of pain relief [50, 51]. A major advantage of EUS-guided over standard percutaneous fluoroscopy-guided or CT-guided celiac interventions is the ability of EUS to directly visualize and inject individual celiac ganglia. It has been shown that direct celiac ganglion injection is more effective than injection of the celiac plexus. Seventy-three percent of patients given direct celiac ganglion injection had pain relief compared to 45 % of those given a standard diffuse plexus injection. Complete pain relief was obtained in 50 %

with celiac ganglion injection compared to 18 % in the celiac plexus injection group [52]. The optimal type and amount of neurolytic agent has not been extensively studied. However, a common approach is to inject from 10 to 20 cc of a mixture of alcohol 98 % and 0.25 % bupivacaine. Celiac plexus blocks are performed using bupivacaine solution (0.25–0.75 %). Triamcinolone is commonly added to lengthen the duration of the block, but does not appear to add benefit [53]. The common adverse events reported with celiac plexus interventions are transient diarrhea, transient orthostatic hypotension, transient increase in pain, and abscess formation. Serious neurological complications such as lower extremity paresthesia and weakness have been reported with non-EUS-guided procedures [54], and there has been one case of permanent paralysis in a patient given EUS-guided neurolysis for pancreatic cancer pain [55]. Pooled analyses report an adverse event rate of 4.7 % for celiac plexus block and 27 % for celiac plexus neurolysis. However most of the adverse events were minor (<1 % major adverse event) and lasted less than 48 h [56].

EUS-Guided Cyst Ablation

Cystic lesions of the pancreas are often detected incidentally during cross-sectional imaging. Most of these lesions are branch-type IPMNs, which are generally indolent and benign, but may have premalignant potential. It can be difficult to definitively diagnose pancreatic cysts, even with high resolution imaging and EUS-guided FNA. The recently revised Sendai criteria provide expert consensus guidance on evaluating and monitoring these lesions, and advocate that most be followed with periodic imaging tests. Surgery is recommended for malignant cysts or cysts with high malignant potential. However surgery carries significant morbidity and mortality.

EUS-guided cyst ablation is an emerging technique that is performed for patients with premalignant cysts who are not good surgical candidates or in whom surveillance is cumbersome. Because evidence for efficacy and safety is still limited, this intervention is currently performed at limited centers throughout the United States and Japan in the confines of a research protocol. Cyst ablation is most effective in small, unilocular cysts and is contraindicated in cysts involving the main pancreatic duct due to risk of pancreatitis and cysts with potentially malignant features such as mural nodules. An FNA needle is used to puncture the cyst and fluid is aspirated until the cyst cavity is collapsed, with care

to leave the needle tip within the cavity. The aspirated fluid is sent for analysis and a volume of absolute alcohol equal to the amount of fluid aspirated from the cyst is injected into the collapsed cavity. Lavage is performed for 5 min by aspirating the fluid into the syringe and reinjection into the cavity.

In a randomized control trial comparing saline injection to alcohol, cyst resolution occurred in three patients after just one ethanol treatment and nine additional patients had cyst resolution after the second unblended ethanol treatment in both arms resulting in an overall cyst resolution rate of 33 %. Four patients of these patients underwent subsequent surgical resection. The one patient who underwent only saline injection demonstrated no epithelial ablation, whereas the patients who had undergone one to two sessions of ethanol ablation demonstrated 50–100 % epithelial ablation [57]. The observed complications after the first treatment were abdominal pain post-procedure (23.8 %), intracystic bleeding (2.4 %), and acute pancreatitis (2.4 %). An additional study found that the addition of paclitaxel into the cyst cavity improved the cyst resolution rate to 78 % [58]. Long-term follow-up on patients undergoing cyst ablation is not available and currently surveillance with imaging or EUS is still recommended for patients undergoing this procedure.

EUS-Guided Oncological Therapies

EUS-Guided Fiducial Placement

Stereotactic body radiotherapy (SBRT) concentrates high-dose radiation precisely to tumor tissue and minimizing damage to surrounding healthy structures. Traditionally this technology involved the use of frames or bony landmarks and was used only for intracranial lesions. With recent advances and development of the frameless image-guided system, it is possible to treat extracranial lesions with the implantation of radio-opaque markers called fiducials. Fiducials are gold seeds, which measure 3–5 mm in length and 0.8–1.2 mm in diameter, and serve as radiomarkers for real-time imaging. Patients with unresectable locally advanced pancreatic cancer can be treated with image-guided radiotherapy for loco regional control or down staging. The fiducials have been implanted surgically or percutaneously under radiologic guidance, but this method was invasive and difficult due to retroperitoneal nature of pancreatic cancer. Based on these challenges, EUS-guided

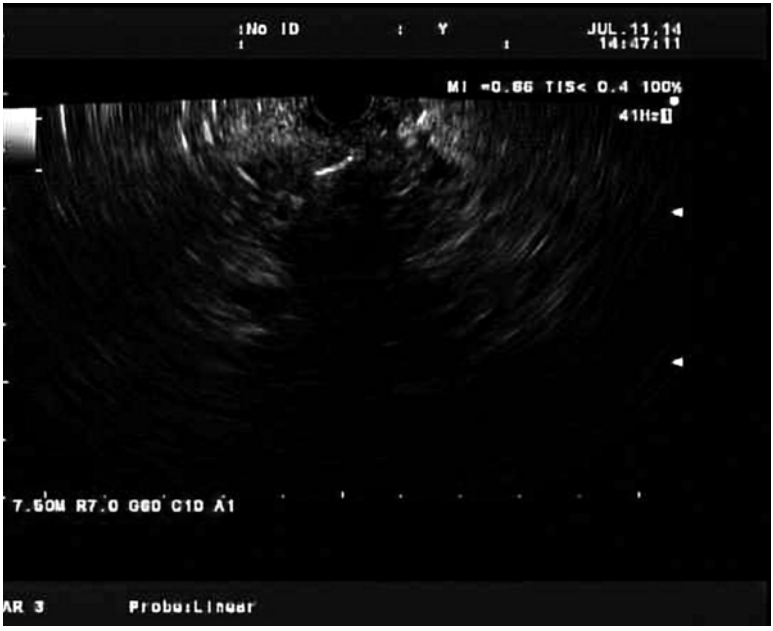

Fig. 21.4. EUS image of a pancreatic mass with a fiducial in place.

fiducial placement (Fig. 21.4) has been developed as a useful alternative [59]. Numerous studies have shown a high success rate (88–90 %) of EUS-guided placement with low migration rate and no migration related adverse events [60, 61]. Ideal fiducial geometry which is the spatial arrangement of fiducials which was believed to facilitate the best treatment planning and delivery is defined as placement of at least three fiducials, with an interfiducial angle of greater than 15° and a minimum interfiducial distance of 2 cm. Surgical placement of fiducials leads to more ideal geometry, but this was not clinically significant, as 90 % of patients with EUS-guided fiducial placement even if they did not have ideal geometry were able to be successfully tracked and treatment delivered [62].

Fiducials are backloaded into a 19-G FNA needle plugged with sterile bone wax and a stylet is used to push the fiducial into the tumor under direct sonographic visualization [61]. Reported complications include migration, bleeding, and acute pancreatitis. EUS-guided fiducial placement has also been used to aid in intraoperative localization of small pancreatic neuroendocrine tumors [63] and therapy of prostate cancer [64].

EUS-Guided Brachytherapy

Implantation of radioactive seeds has been used extensively in the therapy of prostate cancer. Intraoperative implantation of radioactive seeds has also been described for locally advanced pancreatic cancer in combination with systemic chemotherapy. Pilot studies have shown that it is feasible to implant ^{125}I seeds under EUS guidance. A significant improvement in survival was not observed; however, seed implantation improved pain control and stabilized disease in a few patients [65–68]. More data is needed regarding the long-term effects and benefits prior to routine use of interstitial brachytherapy.

EUS-Guided Cryothermal Ablation

Cryothermal ablation is performed using a device that combines bipolar radio frequency ablation (RFA) with cryogenic cooling to limit the thermal damage caused by RFA alone. This probe can be passed through a therapeutic linear echoendoscope and therapy delivered to the target lesion under real-time visualization. The power of the radiofrequency current and the pressure of the cryo gas are maintained at a constant level and the duration of delivery is varied based on the tumor size. In order to prevent unintended tissue damage, an automatic stop is built into the system based on detection of increased tissue desiccation, which stops therapy irrespective of programmed time. A pilot study was performed using this device in patients who failed neoadjuvant chemoradiation therapy for pancreatic cancer, and demonstrated the technical feasibility and safety of this procedure [69]. More data is needed to determine the oncologic efficacy of this device.

EUS-Guided Fine Needle Injection

EUS has been used to inject various agents into lesions in the pancreas and esophagus using the FNA technique with injection of the agent instead of aspiration of tissue. There is wide variation in the agents used and their success. The agents that have been described are allogenic mixed lymphocyte culture, TNFerade, ONYX-015, immature dendritic cells, and Onco VEX^{GMCSF} [70]. Most studies are still preliminary and more data is still required before routine use can be recommended.

EUS-Guided Vascular Interventions

EUS-Guided Treatment of Gastric Variceal Hemorrhage

Gastric varices are difficult to treat and injection of cyanoacrylate has been advocated for treatment of bleeding gastric varices. Initial studies have shown that EUS can be used to direct the injection of gastric varices, monitor successful obliteration, and reduce the re-bleeding rate [71]. Subsequent studies have compared EUS-guided cyanoacrylate injection and EUS-guided coil embolization and found both techniques to be equally effective but a high rate of distant emboli with cyanoacrylate use [72]. Even though these emboli were asymptomatic, this is a concerning finding. The simultaneous use of coil embolization followed by cyanoacrylate injection can theoretically reduce the incidence of emboli by forming a matrix for the glue [73]. Current evidence shows that EUS-guided therapy of gastric varices is effective and safe but a clear advantage over conventional therapy has not been demonstrated. Routine use has not been advocated as EUS use adds additional cost and expertise. Also, dealing with active bleeding using an EUS scope introduces technical challenges related to its oblique endoscopic view and smaller working channel [74].

EUS-Guided Therapy of Pseudoaneurysms

There are numerous case reports of managing a visceral artery pseudoaneurysm using EUS-guided therapy [75–78]. In patients who are not good operative candidates and angiography fails to reach the target vessel or the feeding stalk is unable to be demonstrated, EUS-guided therapy may be considered. There are reports of injecting cyanoacrylate and thrombin into the pseudoaneurysm until flow has been obliterated under the guidance of a linear echoendoscope. Even though EUS-guided therapy is not first-line therapy in these cases, this approach can be offered in certain instances where other options are not feasible.

EUS-Guided Gastroenterostomy

Gastric outlet obstruction is a frequent complication of gastric, duodenal, and pancreatic malignancies. Surgical bypass is used to palliate some of these patients. However, many patients are poor surgical

candidates and have significant morbidity and mortality related to surgery. Studies have shown that enteral stenting has better short-term outcome than surgery [79]. The long-term outcomes with enteral stents are not as good due to tumor ingrowth and stent migration. Several new devices and methods for EUS-guided gastroenterostomy have been described in porcine models [80, 81]. In one method using a novel lumen-apposing stent, the small bowel is distended with large amounts of water. The linear echoendoscope is positioned in the stomach and used to identify a bowel loop close to the stomach and punctured using a 19-G needle and an anchoring wire is placed into the small bowel and used to appose the stomach and small intestine. Access is gained again into the now anchored small bowel and using a dedicated stent deployment device the lumen-apposing stent is deployed and anchoring wire is removed [80]. In another technique, the small intestine was distended using a novel double-balloon enteric tube. Access to the small intestine was obtained using a 19-G FNA needle as previously described. The tract is dilated and novel bilaterally reflected lumen-apposing stent was deployed [81]. In both procedures the stent was removed in 4–5 weeks and the animal models showed patent anastomosis even after stent removal. No major complications have been described in the animal models. However, studies in human subjects are still needed before routine use.

Conclusions

EUS-guided therapeutic interventions are becoming increasingly popular less invasive alternatives to surgery and percutaneous therapies. There are numerous well-established interventions that are described here and more interventions that are on the horizon. This is a quickly evolving field with great potential.

References

1. 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.
2. Madhoun MF, Wani SB, Rastogi A, Early D, Gaddam S, Tierney WM, et al. The diagnostic accuracy of 22-gauge and 25-gauge needles in endoscopic ultrasound-guided fine needle aspiration of solid pancreatic lesions: a meta-analysis. Endoscopy. 2013;45(2):86–92.

3. Affolter KE, Schmidt RL, Matynia AP, Adler DG, Factor RE. Needle size has only a limited effect on outcomes in EUS-guided fine needle aspiration: a systematic review and meta-analysis. Dig Dis Sci. 2013;58(4):1026–34.
4. Camellini L, Carlinfante G, Azzolini F, Iori V, Cavina M, Sereni G, et al. A randomized clinical trial comparing 22G and 25G needles in endoscopic ultrasound-guided fine-needle aspiration of solid lesions. Endoscopy. 2011;43(8):709–15.
5. Vilmann P, Saftoiu A, Hollerbach S, Skov BG, Linnemann D, Popescu CF, et al. Multicenter randomized controlled trial comparing the performance of 22 gauge versus 25 gauge EUS-FNA needles in solid masses. Scand J Gastroenterol. 2013; 48(7):877–83.
6. Lee JK, Lee KT, Choi ER, Jang TH, Jang KT, Lee JK, et al. A prospective, randomized trial comparing 25-gauge and 22-gauge needles for endoscopic ultrasound-guided fine needle aspiration of pancreatic masses. Scand J Gastroenterol. 2013;48(6): 752–7.
7. Fabbri C, Polifemo AM, Luigiano C, Cennamo V, Baccarini P, Collina G, et al. Endoscopic ultrasound-guided fine needle aspiration with 22- and 25-gauge needles in solid pancreatic masses: a prospective comparative study with randomisation of needle sequence. Dig Liver Dis. 2011;43(8):647–52.
8. Siddiqui UD, Rossi F, Rosenthal LS, Padda MS, Murali-Dharan V, Aslanian HR. EUS-guided FNA of solid pancreatic masses: a prospective, randomized trial comparing 22-gauge and 25-gauge needles. Gastrointest Endosc. 2009;70(6): 1093–7.
9. Sakamoto H, Kitano M, Komaki T, Noda K, Chikugo T, Dote K, et al. Prospective comparative study of the EUS guided 25-gauge FNA needle with the 19-gauge Trucut needle and 22-gauge FNA needle in patients with solid pancreatic masses. J Gastroenterol Hepatol. 2009;24(3):384–90.
10. Wani S, Early D, Kunkel J, Leathersich A, Hovis CE, Hollander TG, et al. Diagnostic yield of malignancy during EUS-guided FNA of solid lesions with and without a stylet: a prospective, single blind, randomized, controlled trial. Gastrointest Endosc. 2012;76(2):328–35.
11. Rastogi A, Wani S, Gupta N, Singh V, Gaddam S, Reddymasu S, et al. A prospective, single-blind, randomized, controlled trial of EUS-guided FNA with and without a stylet. Gastrointest Endosc. 2011;74(1):58–64.
12. Sahai AV, Paquin SC, Gariepy G. A prospective comparison of endoscopic ultrasound-guided fine needle aspiration results obtained in the same lesion, with and without the needle stylet. Endoscopy. 2010;42(11):900–3.
13. Puri R, Vilmann P, Saftoiu 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.
14. Lee JK, Choi JH, Lee KH, Kim KM, Shin JU, Lee JK, et al. A prospective, comparative trial to optimize sampling techniques in EUS-guided FNA of solid pancreatic masses. Gastrointest Endosc. 2013;77(5):745–51.
15. Wallace MB, Kennedy T, Durkalski V, Eloubeidi MA, Etamad R, Matsuda K, et al. Randomized controlled trial of EUS-guided fine needle aspiration techniques for the detection of malignant lymphadenopathy. Gastrointest Endosc. 2001;54(4):441–7.

16. Nakai Y, Isayama H, Chang KJ, Yamamoto N, Hamada T, Uchino R, et al. Slow pull versus suction in endoscopic ultrasound-guided fine-needle aspiration of pancreatic solid masses. Dig Dis Sci. 2014;59(7):1578–85.
17. LeBlanc JK, Ciaccia D, Al-Assi MT, McGrath K, Imperiale T, Tao LC, et al. Optimal number of EUS-guided fine needle passes needed to obtain a correct diagnosis. Gastrointest Endosc. 2004;59(4):475–81.
18. Rong L, Kida M, Yamauchi H, Okuwaki K, Miyazawa S, Iwai T, et al. Factors affecting the diagnostic accuracy of endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) for upper gastrointestinal submucosal or extraluminal solid mass lesions. Dig Endosc. 2012;24(5):358–63.
19. Suzuki R, Irisawa A, Bhutani MS, Hikichi T, Takagi T, Sato A, et al. Prospective evaluation of the optimal number of 25-gauge needle passes for endoscopic ultrasound-guided fine-needle aspiration biopsy of solid pancreatic lesions in the absence of an onsite cytopathologist. Dig Endosc. 2012;24(6):452–6.
20. Katanuma A, Maguchi H, Yane K, Hashigo S, Kin T, Kaneko M, et al. Factors predictive of adverse events associated with endoscopic ultrasound-guided fine needle aspiration of pancreatic solid lesions. Dig Dis Sci. 2013;58(7):2093–9.
21. Eloubeidi MA, Tamhane A, Varadarajulu S, Wilcox CM. Frequency of major complications after EUS-guided FNA of solid pancreatic masses: a prospective evaluation. Gastrointest Endosc. 2006;63(4):622–9.
22. Varadarajulu S, Christein JD, Tamhane A, Drelichman ER, Wilcox CM. Prospective randomized trial comparing EUS and EGD for transmural drainage of pancreatic pseudocysts (with videos). Gastrointest Endosc. 2008;68(6):1102–11.
23. Varadarajulu S, Bang JY, Sutton BS, Trevino JM, Christein JD, Wilcox CM. Equal efficacy of endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage in a randomized trial. Gastroenterology. 2013;145(3):583–90.e1.
24. 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(10):1504–8.
25. Fabbri C, Luigiano C, Lisotti A, Cennamo V, Virgilio C, Caletti G, et al. Endoscopic ultrasound-guided treatments: are we getting evidence based—a systematic review. World J Gastroenterol. 2014;20(26):8424–48.
26. Penn DE, Draganov PV, Wagh MS, Forsmark CE, Gupte AR, Chauhan SS. Prospective evaluation of the use of fully covered self-expanding metal stents for EUS-guided transmural drainage of pancreatic pseudocysts. Gastrointest Endosc. 2012;76(3):679–84.
27. Nici AJ, Hussain SA, Kim SH, Mehta P. Unique usage of a partially covered metal stent for drainage of a pancreatic pseudocyst via endosonography-guided transcystgastrostomy. Dig Endosc. 2012;24(3):185–7.
28. Talreja JP, Shami VM, Ku J, Morris TD, Ellen K, Kahaleh M. Transenteric drainage of pancreatic-fluid collections with fully covered self-expanding metallic stents (with video). Gastrointest Endosc. 2008;68(6):1199–203.
29. Fabbri C, Luigiano C, Cennamo V, Polifemo AM, Barresi L, Jovine E, et al. Endoscopic ultrasound-guided transmural drainage of infected pancreatic fluid collec-

tions with placement of covered self-expanding metal stents: a case series. Endoscopy. 2012;44(4):429–33.
30. Binmoeller KF, Shah J. A novel lumen-apposing stent for transluminal drainage of nonadherent extraintestinal fluid collections. Endoscopy. 2011;43(4):337–42.
31. Gornals JB, De la Serna-Higuera C, Sanchez-Yague A, Loras C, Sanchez-Cantos AM, Perez-Miranda M. Endosonography-guided drainage of pancreatic fluid collections with a novel lumen-apposing stent. Surg Endosc. 2013;27(4):1428–34.
32. Itoi T, Binmoeller KF, Shah J, Sofuni A, Itokawa F, Kurihara T, et al. Clinical evaluation of a novel lumen-apposing metal stent for endosonography-guided pancreatic pseudocyst and gallbladder drainage (with videos). Gastrointest Endosc. 2012; 75(4):870–6.
33. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013;13(4 Suppl 2):e1–15.
34. Bakker OJ, van Santvoort HC, van Brunschot S, Geskus RB, Besselink MG, Bollen TL, et al. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. JAMA. 2012;307(10):1053–61.
35. van Brunschot S, van Grinsven J, Voermans RP, Bakker OJ, Besselink MG, Boermeester MA, et al. Transluminal endoscopic step-up approach versus minimally invasive surgical step-up approach in patients with infected necrotising pancreatitis (TENSION trial): design and rationale of a randomised controlled multicenter trial [ISRCTN09186711]. BMC Gastroenterol. 2013;13:161.
36. Gardner TB, Coelho-Prabhu N, Gordon SR, Gelrud A, Maple JT, Papachristou GI, et al. Direct endoscopic necrosectomy for the treatment of walled-off pancreatic necrosis: results from a multicenter U.S. series. Gastrointest Endosc. 2011;73(4): 718–26.
37. 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.
38. Park do H, 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.
39. 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.
40. Dhir V, Artifon EL, Gupta K, Vila JJ, Maselli R, Frazao M, et al. 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.
41. Khashab MA, Valeshabad AK, Modayil R, Widmer J, Saxena P, Idrees M, et al. EUS-guided biliary drainage by using a standardized approach for malignant biliary obstruction: rendezvous versus direct transluminal techniques (with videos). Gastrointest Endosc. 2013;78(5):734–41.

42. Fujii LL, Topazian MD, Abu Dayyeh BK, Baron TH, Chari ST, Farnell MB, et al. EUS-guided pancreatic duct intervention: outcomes of a single tertiary-care referral center experience. Gastrointest Endosc. 2013;78(6):854–864.e1.
43. Jang JW, Lee SS, Song TJ, Hyun YS, Park do H, Seo DW, et al. Endoscopic ultrasound-guided transmural and percutaneous transhepatic gallbladder drainage are comparable for acute cholecystitis. Gastroenterology. 2012;142(4):805–11.
44. de la Serna-Higuera C, Perez-Miranda M, Gil-Simon 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.
45. Santosh D, Lakhtakia S, Gupta R, Reddy DN, Rao GV, Tandan M, et al. Clinical trial: a randomized trial comparing fluoroscopy guided percutaneous technique vs. endoscopic ultrasound guided technique of coeliac plexus block for treatment of pain in chronic pancreatitis. Aliment Pharmacol Ther. 2009;29(9):979–84.
46. 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.
47. 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.
48. 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.
49. 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.
50. 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.
51. 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.
52. 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.
53. Stevens T, Costanzo A, Lopez R, Kapural L, Parsi MA, Vargo JJ. Adding triamcinolone to endoscopic ultrasound-guided celiac plexus blockade does not reduce pain in patients with chronic pancreatitis. Clin Gastroenterol Hepatol. 2012;10(2):186–91. 191.e1.
54. 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.
55. 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.

56. 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.
57. DeWitt J, McGreevy K, Schmidt CM, Brugge WR. EUS-guided ethanol versus saline solution lavage for pancreatic cysts: a randomized, double-blind study. Gastrointest Endosc. 2009;70(4):710–23.
58. Oh HC, Seo DW, Lee TY, Kim JY, Lee SS, Lee SK, et al. New treatment for cystic tumors of the pancreas: EUS-guided ethanol lavage with paclitaxel injection. Gastrointest Endosc. 2008;67(4):636–42.
59. Pishvaian AC, Collins B, Gagnon G, Ahlawat S, Haddad NG. EUS-guided fiducial placement for CyberKnife radiotherapy of mediastinal and abdominal malignancies. Gastrointest Endosc. 2006;64(3):412–7.
60. Park WG, Yan BM, Schellenberg D, Kim J, Chang DT, Koong A, et al. EUS-guided gold fiducial insertion for image-guided radiation therapy of pancreatic cancer: 50 successful cases without fluoroscopy. Gastrointest Endosc. 2010;71(3):513–8.
61. Sanders MK, Moser AJ, Khalid A, Fasanella KE, Zeh HJ, Burton S, et al. EUS-guided fiducial placement for stereotactic body radiotherapy in locally advanced and recurrent pancreatic cancer. Gastrointest Endosc. 2010;71(7):1178–84.
62. Majumder S, Berzin TM, Mahadevan A, Pawa R, Ellsmere J, Sepe PS, et al. Endoscopic ultrasound-guided pancreatic fiducial placement: how important is ideal fiducial geometry? Pancreas. 2013;42(4):692–5.
63. Law JK, Singh VK, Khashab MA, Hruban RH, Canto MI, Shin EJ, 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.
64. Yang J, Abdel-Wahab M, Ribeiro A. EUS-guided fiducial placement before targeted radiation therapy for prostate cancer. Gastrointest Endosc. 2009;70(3):579–83.
65. Sun S, Qingjie L, Qiyong G, Mengchun W, Bo Q, Hong X. EUS-guided interstitial brachytherapy of the pancreas: a feasibility study. Gastrointest Endosc. 2005;62(5):775–9.
66. Sun S, Xu H, Xin J, Liu J, Guo Q, Li S. Endoscopic ultrasound-guided interstitial brachytherapy of unresectable pancreatic cancer: results of a pilot trial. Endoscopy. 2006;38(4):399–403.
67. Jin Z, Du Y, Li Z, Jiang Y, Chen J, Liu Y. Endoscopic ultrasonography-guided interstitial implantation of iodine 125-seeds combined with chemotherapy in the treatment of unresectable pancreatic carcinoma: a prospective pilot study. Endoscopy. 2008;40(4):314–20.
68. Du Y, Jin Z, Meng H, Zou D, Chen J, Liu Y, et al. Long-term effect of gemcitabine-combined endoscopic ultrasonography-guided brachytherapy in pancreatic cancer. J Interv Gastroenterol. 2013;3(1):18–24.
69. Arcidiacono PG, Carrara S, Reni M, Petrone MC, Cappio S, Balzano G, et al. Feasibility and safety of EUS-guided cryothermal ablation in patients with locally advanced pancreatic cancer. Gastrointest Endosc. 2012;76(6):1142–51.
70. Chang KJ, Irisawa A. EUS 2008 Working Group. EUS 2008 Working Group document: evaluation of EUS-guided injection therapy for tumors. Gastrointest Endosc. 2009;69(2 Suppl):S54–8.

71. Lee YT, Chan FK, Ng EK, Leung VK, Law KB, Yung MY, et al. EUS-guided injection of cyanoacrylate for bleeding gastric varices. Gastrointest Endosc. 2000; 52(2):168–74.
72. Romero-Castro R, Ellrichmann M, Ortiz-Moyano C, Subtil-Inigo JC, Junquera-Florez F, Gornals JB, 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.
73. Binmoeller KF, Weilert F, Shah JN, Kim J. EUS-guided transesophageal treatment of gastric fundal varices with combined coiling and cyanoacrylate glue injection (with videos). Gastrointest Endosc. 2011;74(5):1019–25.
74. Levy MJ, Wong Kee Song LM. EUS-guided angiotherapy for gastric varices: coil, glue, and sticky issues. Gastrointest Endosc. 2013;78(5):722–5.
75. Gonzalez JM, Ezzedine S, Vitton V, Grimaud JC, Barthet M. Endoscopic ultrasound treatment of vascular complications in acute pancreatitis. Endoscopy. 2009;41(8): 721–4.
76. Roberts KJ, Jones RG, Forde C, Marudanayagam R. Endoscopic ultrasound-guided treatment of visceral artery pseudoaneurysm. HPB (Oxford). 2012;14(7):489–90.
77. Roach H, Roberts SA, Salter R, Williams IM, Wood AM. Endoscopic ultrasound-guided thrombin injection for the treatment of pancreatic pseudoaneurysm. Endoscopy. 2005;37(9):876–8.
78. Lameris R, du Plessis J, Nieuwoudt M, Scheepers A, van der Merwe SW. A visceral pseudoaneurysm: management by EUS-guided thrombin injection. Gastrointest Endosc. 2011;73(2):392–5.
79. Jeurnink SM, Steyerberg EW, van Hooft JE, van Eijck CH, Schwartz MP, Vleggaar FP, et al. Surgical gastrojejunostomy or endoscopic stent placement for the palliation of malignant gastric outlet obstruction (SUSTENT study): a multicenter randomized trial. Gastrointest Endosc. 2010;71(3):490–9.
80. Binmoeller KF, Shah JN. Endoscopic ultrasound-guided gastroenterostomy using novel tools designed for transluminal therapy: a porcine study. Endoscopy. 2012; 44(5):499–503.
81. Itoi T, Itokawa F, Uraoka T, Gotoda T, Horii J, Goto O, et al. Novel EUS-guided gastrojejunostomy technique using a new double-balloon enteric tube and lumen-apposing metal stent (with videos). Gastrointest Endosc. 2013;78(6):934–9.

Part IV
Hybrid Laparoscopic-Endoscopic Procedures

22. Hybrid Laparoscopic and Endoscopic Techniques: Upper Gastrointestinal Tract

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Introduction

Flexible endoscopic technology has rapidly evolved over the past decade allowing for continued expansion in the utilization of the scope. From a purely diagnostic instrument it has expanded to a therapeutic and indeed even a surgical platform used by both surgeons and gastroenterologists. Flexible endoscopy permits access to the gastrointestinal tract without transgressing the abdominal or chest walls; furthermore it allows for the performance of intra-abdominal and intrathoracic procedures by means of a scarless minimally invasive route. Although it is impossible to fully encompass the multitude of diagnostic and therapeutic procedures in one chapter, we aim to describe the most frequent uses of the scope as a diagnostic and interventional tool.

Esophageal Endoscopy

Upper endoscopy plays a vital role in the diagnosis and management of upper GI bleeding, esophageal malignancy, and numerous other conditions. Since gastroesophageal reflux disease (GERD) affects 10–20 % of the population in the western world, it is one of the most frequent conditions encountered by endoscopists. Upper endoscopy is frequently utilized in the assessment, and increasingly also in the management of GERD [1, 2].

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Table 22.1. Los Angeles classification of GERD.

Grade	Description
A	One (or more) mucosal break no longer than 5 mm that does not extend between the tops of 2 mucosal folds
B	One (or more) mucosal break more than 5 mm that does not extend between the tops of 2 mucosal folds
C	One (or more) mucosal break that is continuous between the tops of 2 or more mucosal folds but that involves less than 75 % of the circumference
D	One (or more) mucosal break that involves at least 75 % of the esophageal circumference

Table 22.2. The Savary-Miller classification of GERD.

Grade	Lesion
I	Single or isolated erosive lesion, oval or linear, but affecting only 1 longitudinal fold
II	Multiple erosive lesions, noncircumferential, affecting more than 1 longitudinal fold, with or without confluence
III	Circumferential erosive lesions
IV	Chronic lesions including ulcer(s), stricture(s), and/or short esophagus, alone or associated with lesions of grades I to III
V	Columnar epithelium in continuity with the Z line, noncircular, star-shaped, or circumferential, alone or associated with lesions grades I to IV

Esophageal ulcerations are a commonly encountered complication of GERD. The most commonly used endoscopic classification systems for esophageal erosions are the Los Angeles classification (Table 22.1) and the Savary-Miller classification (Table 22.2).

Both classification systems are based on the presence of esophageal mucosal breaks (erosions or ulcers). The Los Angeles classification was adopted in western countries due to its good intra- and interobserver agreement when tested among expert and inexperienced endoscopists. Studies have shown a correlation between the severity of the esophagitis as noted on endoscopy and the extent of esophageal acid exposure as determined by 24-h pH monitoring [3]. The extent of erosions and ulcerations may in fact be underappreciated on histologic examination of the biopsies alone, thus highlighting the importance of communication between endoscopists and pathologists [4].

Hill Grade Endoscopic Classification

The gastroesophageal flap valve is a musculomucosal fold created by the angle of entry of the esophagus into the stomach. It is typically seen to extend approximately 3–4 cm along the gastric lesser curve as viewed on a retroflexed endoscopic position. In 1996 Hill et al. described a grading system to standardize the reporting of the endoscopic appearance of the flap valve. The valve is scored from 1 to 4, corresponding to an increasingly patulous valve (Table 22.3) [5]. Curcic et al. have found that the GEJ opens wider during reflux in GERD patients and have demonstrated an alteration in the normal morphology of the GEJ flap valve likely resulting in compromise of the usual antireflux properties of the GEJ valve [6]. In a recent study, of 453 patients with symptoms of GERD, 82 underwent antireflux surgery for failure of medical treatment, complications of GERD, or for extraesophageal manifestations (e.g., asthma, cough, or aspiration). In this study, the proportion of patients who had surgery significantly increased with increasing alteration of the flap valve. For instance, none of the patients with grade 1 valves underwent surgery whereas 63.6 % of grade 4 had surgery. Multivariate logistic regression analysis showed that surgery rate was associated with a flap grade of 3 or higher (odds ratio [OR], 13.86; $p < 0.001$). Furthermore, flap valves grade 4 were associated with abnormal acid exposure, erosive esophagitis, and hiatal hernias highlighting the utility of Hill grade classification [7].

Table 22.3. Hill grade endoscopic classification of GEJ.

Grade	Description of the flap valve appearance
I	The ridge of tissue is closely approximated to the shaft of the retroflexed endoscope. It extends 3–4 cm along the lesser curve.
II	The ridge is slightly less well defined than in Grade I and it opens rarely with respiration and closes promptly.
III	The ridge is barely present, and there is often failure to close around the endoscope. It is nearly always accompanied by a hiatal hernia.
IV	There is no muscular ridge at all. The gastroesophageal area stays open all the time, and squamous epithelium can often be seen from the retroflexed position. A hiatus hernia is always present.

Barrett's Esophagus, Role of Endoscopy

Barrett's esophagus (BE) is defined as the replacement of the normal stratified squamous epithelium of distal esophagus by specialized columnar epithelium with prominent goblet cells otherwise known as intestinal metaplasia. The condition is thought to develop as a consequence of chronic gastroesophageal reflux disease and is a known risk factor for the development of esophageal adenocarcinoma.

Endoscopic Diagnosis

The detection and diagnosis of Barrett's by white light endoscopy alone has been shown to have a sensitivity of 80–90 % [8–10]. However, identification of intestinal metaplasia must be made by biopsy. The precise location of the proximal extent of the stomach (top of the rugal folds) can be difficult in the presence of columnar lined esophagus and more so in the setting of a hiatal hernia. To improve the diagnosis of Barrett's esophagus, the American Gastrointestinal Association (AGA) recommends the use of high-resolution endoscopy. When detected, the circumferential extent and maximum extent of the metaplasia should be systematically described in the endoscopic reports using descriptors such as the Prague classification of "C" for the circumferential extent in centimeters, and "M" for the maximum extent of the abnormality in centimeters.

Other techniques such as dye-based chromoendoscopy, optical chromoendoscopy, autofluorescence imaging, or confocal laser endomicroscopy have been used to improve the detection of early stage neoplasia but none of them have proved to be superior to high-resolution white light endoscopy [11].

The mucosal lining should be carefully inspected for evidence of abnormal nodularity. If present, this nodularity should be evaluated for evidence of clear malignant invasion such as central ulceration. Furthermore, the National Cancer Comprehensive Network recommends that endoscopic ultrasound should generally be considered for any nodules prior to attempted endoluminal resection although the sensitivity of this test has been called into question recently [12, 13].

Treatment of Dysplasia

Endoscopic Ablative Therapies

Endoscopic ablative therapies use thermal, photochemical, or radiofrequency energy to ablate the abnormal epithelium in Barrett's esophagus [14]. The most commonly used ablation technique is radiofrequency ablation (RFA).

The HALO system is the most widely used RFA system™. It consists of a balloon and/or probe to deliver radiofrequency energy to the affected mucosa. Endoscopy is first performed to identify the area in need of treatment and to make a precise measurement of its location. A sizing balloon is then inserted and inflated throughout the length of the esophagus. The treatment balloon is then selected based on the esophageal diameter as measured by compliance of the sizing balloon. The treatment balloon is then inserted, and the electrodes positioned across the Barrett's segment starting at the most proximal extent, or squamocolumnar junction, under direct endoscopic visualization. After the energy is delivered, the balloon is deflated and repositioned sequentially throughout the target area. The desiccated mucosa is scraped off and the process repeated. Multiple treatments are usually required (3.5 on average). These should be separated by approximately 3 months. Smaller areas of residual metaplasia can be treated with more targeted probe devices such as the HALO 90.

Endoscopic Resection (ER)

Endoscopic resection (ER) involves the excision of a segment of mucosa down to the submucosa, usually with saline-lift technique and a snare [14, 15]. This technique is more frequently used in the treatment of dysplasia associated with nodularity that cannot be ablated. As a first step, the circumference of the area to be resected may be marked using cautery to ensure an appropriate margin. Careful inspection of the lesions using high-resolution white light, narrow band imaging, or chromoendoscopy is required to elucidate the true margins of the lesion. The two most common types of ER include EMR (endoscopic mucosal resection) and ESD (endoscopic submucosal dissection). When there is a particularly large lesion or concern about submucosal invasion, a lifting solution may be injected submucosally to facilitate separation of the

layers by lifting the mucosal lesion away from the muscularis layer. These techniques provide large tissue specimens that can be examined by the pathologist to determine the character, extent of the lesion, and margins of resection and most importantly depth of invasion for both therapeutic and diagnostic purposes.

The most common EMR techniques involve the use of a single-channel therapeutic or standard diagnostic gastroscope fitted with a distal attachment dissection cap. The two most commonly used systems are the Duette Multi-Band Mucosectomy (DMBM, cook medical) and the Olympus EMR. The DMBM consists of two components: a banding device for creation of the pseudopolyp and a monopolar electrosurgical snare used in conjunction with an electrosurgical unit to remove the pseudopolyp using electrocautery. After the visualization of the selected area, aspiration is applied to the mucosa, and the band is deployed forming a pseudopolyp which is removed with the snare. The Olympus EMR kit utilizes a rimed distal attachment cap and an electrosurgical snare. Similarly to DMBM suction to the area of the lesion is applied, lifting the mucosa into the cap. The lesion is then immediately transected by the prepositioned snare at the rim of the cap.

For non-mucosal-based lesions such as GIST tumors, two new endoscopic techniques are currently in use: endoscopic submucosal excavation (ESE) (a technical variant of ESD which excavates deeper into MP) and submucosal tunneling endoscopic resection (STER) (which uses a mucosal incision proximal to the lesion as an entry site; a submucosal tunnel is created to the lesion which is dissected and then retrieved through the tunnel). This technique also allows a full-thickness resection of the esophageal wall if the tumor is compromising the serosa. While STER is gaining popularity since it preserves the integrity of the covering mucosa as a barrier against leakage, ESE is still being performed as a technically easier technique [16–18]. Although both ESE and STER have satisfactory therapeutic results, STER may be preferable to resect tumors >10 mm or when perforation is likely to happen [19].

GERD: Endoscopic Treatment

Although laparoscopic fundoplication remains the gold standard in the surgical management of GERD, a search is ongoing to develop a durable endoscopic treatment. Over the years numerous proposed endoscopic treatment methods have come and gone, failing to provide significant and durable relief from GERD symptoms or to effectively restore

normal physiology. Several endoscopic options have persisted and continue to be evaluated. The most commonly used systems include Stretta (Mederi Therapeutics, Norwalk, CT), EsophyX$_2$ (EndoGastric Solutions, Redmond, WA), and MUSE (Medigus, Omer, Israel).

Stretta

The Stretta system relies on the delivery of radiofrequency energy to the lower esophageal sphincter for the treatment of GERD. The system consists of a radiofrequency (RF) generator as well as a transoral catheter for the delivery of the RF energy. The transoral Stretta catheter system applies low power (5 W) RF energy during a series of 1-min treatment cycles. The therapy is thought to remodel the musculature of the lower esophageal sphincter (LES). These mechanisms act to restore the natural barrier function of the LES as well as to significantly reduce spontaneous regurgitation caused by transient inappropriate relaxations of the sphincter.

In a meta-analysis involving 18 studies, Stretta significantly reduced mean heartburn scores and produced significant improvements in quality of life as measured by GERD-HRQL scale. Furthermore, the total percent of time at pH <4 decreased from 10.29 to 6.51 posttreatment and DeMeester improved from 44.4 to 28.5 when comparing pre- and post-op treatment. Although this represents clear improvement in acid exposure, it is still far from normalization.

SAGES guidelines consider Stretta an appropriate therapeutic option for adult GERD patients who have declined laparoscopic fundoplication with heartburn or regurgitation symptoms for 6 months or more, who have been partially or completely responsive to antisecretory pharmacologic therapy.

EsophyX$_2$

The Transoral Incisionless Fundoplication (TIF) procedure, first performed in 2005, allows for the creation of a 2–3 cm, 270° anterior esophagogastric wrap using a transorally inserted device. Performed under general anesthesia, the device is used in conjunction with a flexible endoscope, which provides visualization during the procedure. The device deploys a series of H-shaped nonabsorbable polypropylene fasteners to create a full-thickness fundoplication. The latest generation of

the device (TIF 2.0) is able to form a longer 2–5 cm antireflux valve and more closely respects some of the basic surgical principle of antireflux procedures. The device however should not be used in the setting of hiatal hernias larger than 2 cm. Although there is a relative paucity of data regarding the latest generation of the device, a recent expert review suggests that TIF is an effective and safe treatment for mild to moderate GERD in carefully selected patients [20, 21]. Moreover, a recent multicenter randomized control trial comparing TIF plus placebo vs. sham surgery and PPI in patients with persistent regurgitation despite PPI therapy showed that TIF eliminated troublesome regurgitation in a higher proportion of patients (67 % vs. 45 % $p < 0.23$) with better control of esophageal pH for TIF (mean 9.3 % before and 6.3 % after; $p < 0.001$) vs. sham surgery (mean 8.6 % before and 8.9 % after) [22].

Endoscopic Anterior Fundoplication with the Medigus Ultrasonic Surgical Endostapler (MUSE)™

The device consists of a light source, control unit, and flexible surgical endostapler and is similar to an endoscope. The endostapler has a cartridge with five standard 4.8 mm titanium surgical staples. The distal tip has an ultrasonic transducer, a miniature video camera, a light source, and two fine screws. The control displays the information on a video monitor, including the bending angle and force, ultrasound signal level, screw position, and the gap between the distal tip and the cartridge. The procedure is performed under general anesthesia. The transoral stapler is advanced into the stomach through an overtube and retroflexed under direct video guidance. After identifying a stapling location, the tip of the device is flexed to press the gastric fundus against the esophagus. Next, the screws are deployed. In this step the tissues are compressed and the optical guidance is switched over to the ultrasonic range finder which automatically engages to display the tissue thickness. A tissue thickness of 1.4–1.6 mm allows for stapler firing. The objective is to mimic a partial anterior fundoplication.

Initial data shows that the procedure is feasible and safe with significant reduction in acid exposure obtained on short-term follow-up [23]. At this time however clinical data is quite limited.

Endoscopic Treatment of Achalasia

Peroral endoscopic myotomy (POEM) for the treatment of achalasia is perhaps the most successful adaptation of natural orifice translumenal endoscopic surgery (NOTES) to a traditional surgical procedure. POEM utilizes a flexible endoscope to perform a full or partial thickness esophageal myotomy leaving the overlying mucosal layer intact. The procedure begins with gaining access to the submucosal space via a mucosotomy. A "lifting" solution, consisting of saline and blue dye, is injected into the submucosa a few centimeters proximal to the expected beginning of the myotomy. A variety of dissection knives are available for the creation of the mucosotomy and are designed for use through the working channel of the scope. These include among others, the hook, triangle tip, and insulated tip knives (ITKnife2 Olympus). Recently, ERBE Hybrid knife has become available combining the abilities of electrocautery and hydrodissection. Once the mucosotomy has been performed, the endoscope is inserted into the submucosal plane. Sharp electrocautery dissection facilitated by repeated injection of the lifting solution is then performed along the deep submucosal layer. Great care must be taken during the dissection not to injure the thin overlying mucosa, which could result in a subsequent intra-tunnel or more widespread leak. The tunnel is extended for 2 cm past the gastroesophageal junction onto the gastric cardia. The gastroesophageal junction can be identified by observing the palisading vessels, the sudden widening of the submucosal space, and if needed, returning to the esophageal lumen to inspect the extent of dissection. Once the submucosal tunnel has been completed, the circular muscle fibers are selectively divided with cautery. Carbon dioxide insufflation must be used throughout the procedure.

Although some groups perform a full-thickness myotomy, our practice is to attempt to preserve the longitudinal muscle; splitting of the longitudinal muscle fibers is however frequently observed. The length of the myotomy can be tailored according to the preoperative manometry, intraoperative observation of the high pressure zone. The use of intraoperative adjunct devices such as the Endoflip^{R} (Endoluminal Functional Lumen Imaging Probe) Crospon™ (Crospon Inc., Carlsbad, California) to measure lower esophageal distensibility may play some role in tailoring the myotomy. After completion, intraluminal endoscopy confirms smooth passage through the gastroesophageal junction. The retroflexed view allows for the evaluation of the valve and blanched gastric mucosa

marking the distal extent of the dissection. The mucosotomy is closed using a series of endoscopic clips or an endoscopic suturing device. An increasing body of literature is becoming available, demonstrating that POEM is highly successful with over 90 % improvement in dysphagia while offering patients the advantage of a low impact endoscopic access.

The main long-term side effect is gastroesophageal reflux (GER) with an incidence ranging from 38 to 57 %, as measured by 24 h pH monitoring [24–28].

POEM is rapidly becoming a mainstream surgical option in the treatment of achalasia and other spastic esophageal disorders. Additional randomized trials and long-term outcomes are needed to establish the role of POEM among the other available therapeutic options for these patients.

Peroral Pyloromyotomy (POP)

Peroral endoscopic pyloromyotomy for gastroparesis represents the natural extension of the growing experience with endoscopic myotomy for achalasia and has proven to be feasible and safe, spanning the utilization of submucosal dissection techniques. The endoscopic pyloromyotomy technique utilizes the same fundamental technique used during a POEM procedure. The procedure begins with a submucosal injection, mucosotomy, and entry into the submucosal space several centimeters proximal to the pylorus on the gastric antrum. A submucosal tunnel is then created towards the pylorus taking great care not to injure the overlying gastric mucosa. Following the submucosal tunneling, the pylorus is then divided in a full-thickness fashion leaving the serosal layer, and overlying mucosal layer intact. Great care must be taken during the myotomy of the distal portion of the pylorus as the duodenal mucosa drapes over in a perpendicular fashion and can be inadvertently injured. Once the myotomy is completed, the mucosal incision is closed with endoscopic clips or sutures.

Case reports and early case series have shown good results in patients with delayed gastric emptying who post-POP have enjoyed normalization of gastric emptying in a majority of cases [29–32]. This technique may present a promising option for the management of foregut symptoms in a group of patients who represent a challenge for gastroenterologists and surgeons.

Endoscopic Suturing

Several endoscopic suturing devices have been previously developed. Currently, the most commonly used FDA-approved endoscopic suturing device is the OverStitch Endoscopic Suturing System (Apollo Endosurgery, Austin, Texas, USA). It is a single-use device that attaches directly to a dual-channel gastroscope (Olympus America, Center Valley, Pennsylvania, USA) and allows placement of sutures in an interrupted or running fashion. The device works by means of a curved needle holder which passes a needle mounted suture back and forth. It is able to approximate tissue from either side of a mucosal defect, fistula, or full-thickness perforation, allowing the deployment of both absorbable and nonabsorbable sutures under direct endoscopic visualization. Reports have been published describing the closure of numerous types of esophageal and gastric defects from closure of a PEG site, or gastrocutaneous fistulas, and the treatment of Boerhaave syndrome among others. Advances in therapeutic endoscopic techniques, including submucosal dissection and endoscopic resection increase the need for a reliable method of endoscopic suturing to close procedure-related defects or manage unintentional perforations [33, 34].

Furthermore, the endoscopic suturing device has also been used in support of bariatric surgery not only in the management of leaks but also in the management of dilated gastrojejunal stomal diameter following RYGB which is thought to be a risk factor for weight regain [35]. Two studies have shown good results with the use of the overstitch device to perform gastrojejunostomy stomal diameter reduction in the endoscopic management of weight regain after RYGB [36, 37].

Peritoneoscopy

Access to the peritoneum via a hollow viscus, typically the stomach, has been studied extensively as a part of the research into natural orifice surgical techniques. Various techniques have been described and demonstrated to be safe in accessing the peritoneal cavity in humans [38]. Obtaining access to the peritoneal cavity may be performed under laparoscopic guidance. A flexible endoscope is passed down to the stomach; a needle knife or other dissecting knife is then used to create a gastrotomy. A wire can then be passed into the peritoneal cavity through the gastrotomy under laparoscopic visualization and a wire-guided balloon can then be used to dilate the gastrotomy, thus permitting passage

of the flexible scope to the peritoneal cavity. The utilization of a balloon for the disruption of the gastric wall may allow for a less traumatic gastrotomy and may potentially reduce the risk of bleeding. Furthermore, the separation of the muscular layers through balloon dilation as opposed to cutting may preserve the tone of the gastric musculature surrounding the gastrotomy, which may act as a seal against gross seepage of gastric contents into the peritoneal cavity.

Another technique used to transgress the gastric wall is the tunneling method. This method involves performing a mucosotomy followed by creation of a submucosal tunnel before puncturing through the serosa. This creates a gastric mucosal flap that offers a protective tunneled space for offset entry into extraluminal anatomic cavities from the lumen and may decrease the risk of contamination by luminal contents [39].

Endoscopic Peritoneal Patch

Several small series have described the endoscopic treatment of a perforated gastric ulcers using omental patch. This technique has also been described for the closure of full-thickness defects following full-thickness endoscopic resections. In highly selected patients the endoscopic approach may offer a less invasive approach as compared to current methods.

The procedure utilizes a flexible endoscope to traverse the perforation or full-thickness defect. A tongue of omental fat is then grasped and retrieved into the stomach. This omental fat is then secured to the edges of the gastrotomy with either clips or endoscopic sutures.

Current commercially available instrumentation for the translumenal endoscopic approach requires about a 10 mm defect for passage of the endoscope to perform translumenal inspection, irrigation, and endoluminal omental patch closure of the defect. Smaller defects may also be repaired using an endoscopy-assisted laparoscopic repair as described by Binginer et al. [40].

Endoscopic PEG Salvage

Dislodgement of percutaneous endoscopic gastrotomy (PEG) tubes is a common surgical problem and may occasionally require urgent surgical intervention. When the dislodgement occurs in the early postoperative period, the possibility of an incomplete gastrocutaneous tract

formation and intra-abdominal leakage of gastric contents is high. Flexible endoscopy may facilitate PEG rescue and avoid some of the morbidity associated with current surgical techniques. Flexible endoscopic peritoneoscopy may allow for the evacuation of intra-abdominal fluid as well as the reestablishment of the PEG tube through the original gastrotomy tract. This may be performed by peritoneoscopy using a balloon to advance through the gastric defect. Once in the peritoneal cavity, the balloon is removed and a PEG guide wire is placed into the peritoneal cavity through the external PEG site and grasped using an endoscopic snare. The endoscope, snare, and guide wire are brought back into the stomach and out the mouth. The PEG tube re-insertion is then completed using the standard pull technique [41].

If the PEG tube cannot be reestablished, the gastrotomy defect may be closed using the previously described techniques of clipping or endoscopic suturing.

Cholecysto-duodenal or Gastric Drainage

Percutaneous cholecystostomy drainage is frequently used when a surgical cholecystectomy is not possible due to comorbidities, advance age, or malignances. An emerging endoscopic alternative to the percutaneous approach may be the creation of a cholecysto-duodenal or cholecysto-gastric fistula guided by endoscopic ultrasound. Endoscopic ultrasound is essential to evaluate the proximity of the gallbladder to the hallow viscus and avoid intervening vessels. The feasibility of the procedure which involves puncturing the gallbladder through the duodenal or gastric walls has been demonstrated in several case reports [42, 43]. Following the puncture the tract is dilated followed by insertion of a covered stent. Specialized covered stents utilizing a flared edge design to prevent stent migration are currently being investigated for this indication. Fluoroscopy is often used as an adjunct modality to confirm the localization of the anatomic structures and the absence of leakage to the peritoneal cavity [44].

Pancreatic Pseudocyst Drainage and Debridement

Pancreatic pseudocysts can be endoscopically managed with internal drainage by means of a cystogastrostomy. To perform the cystogastrostomy the pseudocyst is identified and punctured using endoscopic ultrasound guidance. If needed, the cyst cavity can be irrigated by means

of a nasocystic catheter. Double flanged stents (Axios™ Stent and Delivery System) are available and FDA approved for the creation of a cystogastrostomy. These stents allow for subsequent endoscopic debridement of the necrotic pancreatic tissue, and complex cyst contents through the stent by means of a basket, net, or snares.

Although initially laparoscopic drainage of pancreatic pseudocyst seemed to be more effective than the endoscopic treatment, a recent randomized trial showed no differences in terms of efficacy between both procedures. Moreover, hospital stay, postoperative physical and mental health of patients, and costs favored the endoscopic group [45, 46].

Endoscopic Gastric Band Removal

Placement of an adjustable gastric band (AGB) was once a very popular bariatric surgical technique. Although still in use, the popularity of this technique has decreased somewhat in favor of laparoscopic sleeve gastrectomy and laparoscopic gastric bypass. Some surgeons still choose to place AGB around a gastric bypass pouch in patients with inadequate weight loss or when the pouch has dilated over time. It is thought that up to 7 % of gastric bands placed during bariatric surgery may erode into the stomach requiring surgical intervention [47, 48].

Endoscopy may be useful for the diagnosis and removal of the band, using endoscopic forceps and snares inserted through the working channel, passed around the band and captured with biopsy forceps. When a purely endoscopic procedure is not feasible, laparoscopic assistance would allow access to the band through the stomach or through the Roux limb (Figs. 22.1, 22.2, 22.3, 22.4, and 22.5). Endoscopic guidance is

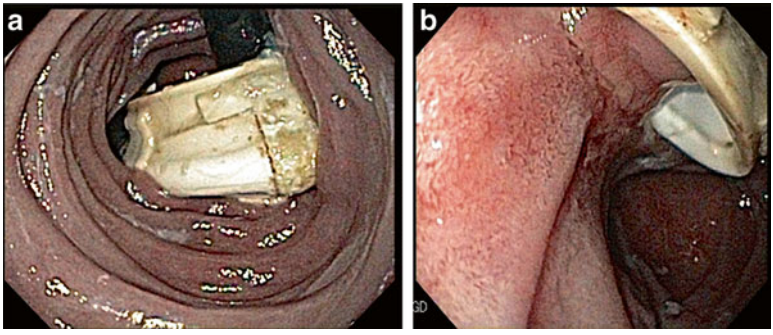

Fig. 22.1. (**a** and **b**) Endoscopic view of eroded gastric band.

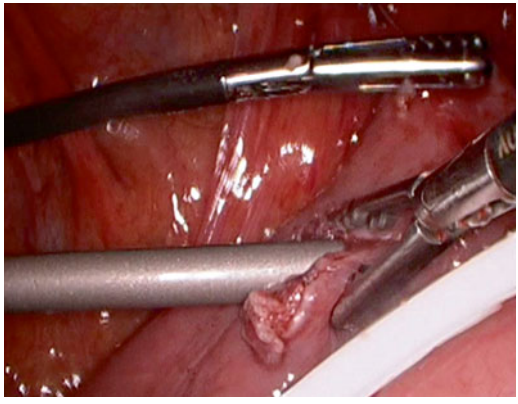

Fig. 22.2. Laparoscopic view of enterotomy.

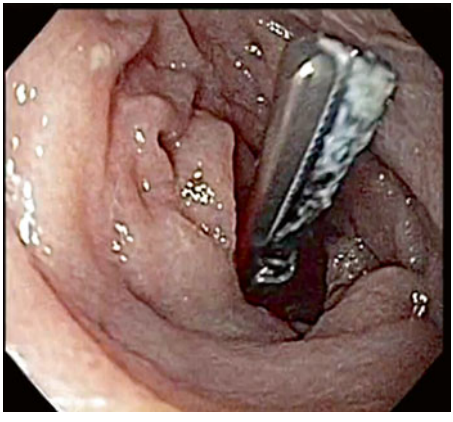

Fig. 22.3. Endoscopic view of laparoscopic ultrasonic device.

then used to direct a laparoscopic enterotomy to cut the band which may then be removed endoscopically or laparoscopically. This approach may reduce the risk of complications associated with dissection around the stomach, where tissue planes are disrupted and the consequences of damage to the gastric pouch can be devastating.

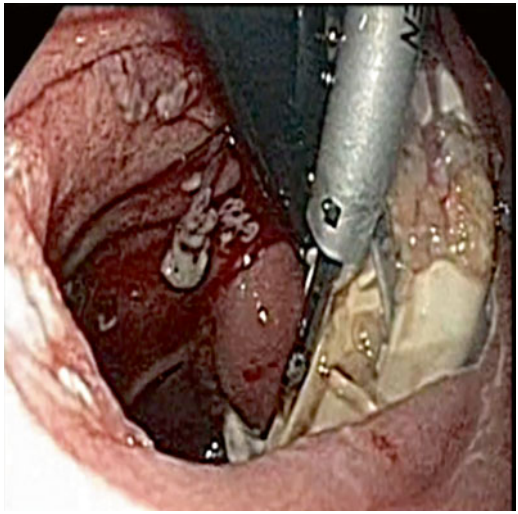

Fig. 22.4. Endoscopic visualization of laparoscopic device cutting the gastric band.

Fig. 22.5. Gastric band after endoscopic extraction.

Natural Orifice Translumenal Endoscopic Surgery (NOTES) Cholecystectomy

Cholecystectomy through a natural orifice represents perhaps a less invasive alternative to conventional laparoscopic cholecystectomy. The usual routes to perform the procedure are transvaginal (TV) and transgastric (TG). Although cholecystectomy using NOTES is technically feasible, it is usually performed in a hybrid manner with great variability in the utilized technique [49]. A 5-mm laparoscope is commonly placed at the umbilicus to safely access the peritoneal cavity, assist in dissection, and offer a "laparoscopic view" when orientation is necessary.

The workup is essential to detect possible contraindications for the procedure such as malignancy, severe cholecystitis, and choledocholithiasis. Information about the size of gallstones is crucial for the transgastric approach, since big specimens or gallstones greater than 1.5 cm could be stuck at the cricopharyngeus at the time of specimen retrieval. For a TV approach, gallstones larger than 3 cm may also result in difficulties in the extraction of the specimens increasing the chances of tearing the vaginotomy, representing a relative contraindication. In addition to the standard preoperative assessment, patients undergoing cholecystectomy through the transvaginal access should also have a negative gynecologic physical exam and a negative Papanicolaou test.

The main advantage of the transvaginal access is the anatomical orientation of the gall bladder, "aligned" with the vagina allowing for the utilization of rigid instruments with better transmission of the force and precision, compared to the technically demanding use of a flexible platform and retroflexion often required for a transgastric approach.

In a recent series of 102 patients who underwent transvaginal NOTES including 72 cholecystectomies, there was one major complication (bleeding from an omental vessel) and four minor complications (urinary retention, transient brachial plexus injury, dislodgement of an intrauterine device, and vaginal granulation tissue) [50].

Overall, a NOTES cholecystectomy approach appears to be safe when performed by appropriately trained surgeons and may be associated with a rapid return to normal activities and decreased postoperative pain [51].

Conclusions

Once utilized for diagnostics only, flexible endoscopy has recently emerged as potentially the next paradigm in minimally invasive surgical approaches. Flexible endoscopy permits access to the gastrointestinal tract while eliminating transabdominal incisional morbidity. Operations once performed through large debilitating incisions are now completed with staggeringly brief convalescence. While enthusiasm is growing quickly, the true positive impact of this technology on our field is only just beginning to take shape.

References

1. Dent J, El-Serag H, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2005;54:710–7.
2. DeMeester TR, Stein HJ. Surgical treatment of gastroesophageal reflux disease. In: Castell DO, editor. The esophagus. Boston: Little, Brown; 1992. p. 579.e626.
3. Rath HC, Timmer A, Kunkel C, et al. Comparison of interobserver agreement for different scoring systems for reflux esophagitis; impact of level of experience. Gastrointest Endosc. 2004;60:44–9.
4. Genta RM, Spechler SJ, Kielhorn AF. The Los Angeles and Savary-Miller systems for grading esophagitis: utilization and correlation with histology: poor correlation between endoscopic and histologic grading of esophagitis. Dis Esophagus. 2011;24(1):10–7. doi:10.1111/j.1442-2050.2010.01092.x.
5. Hill LD, Kozarek RA, Kraemer SJ, Aye RW, Mercer CD, Low DE, Pope II CE. The gastroesophageal flap valve, in vitro and in vivo observations. Gastrointest Endosc. 1996;44(5):541–7.
6. Curcic J, Roy S, Schwizer A, Kaufman E, Forras-Kaufman Z, Menne D, Hebbard GS, Treier R, Boesiger P, Steingoetter A, Fried M, Schwizer W, Pal A, Fox M. Abnormal structure and function of the esophagogastric junction and proximal stomach in gastroesophageal reflux disease. Am J Gastroenterol. 2014;109(5):658–67. doi:10.1038/ajg.2014.25. Epub 2014 Mar 4.
7. Kayaoglu HA. Correlation of the gastroesophageal flap valve grade with the surgery rate in patients with gastroesophageal reflux disease. Surg Endosc. 2013;27(3):801–7. doi:10.1007/s00464-012-2515-x.
8. Fawcett DW. The esophagus and stomach. In: Bloom W, Fawcett DW, editors. A textbook of histology. 11th ed. Philadelphia: Saunders Company; 1986. p. 619.
9. SL K, 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.
10. Spechler SJ, Sharma P, Souza RF, Inadomi JM, Shaheen NJ. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. Gastroenterology. 2011;140:1084.

11. Boerwinkel DF, Swager A, Curvers WL, Bergman JJ. The clinical consequences of advanced imaging techniques in Barrett's esophagus. Gastroenterology. 2014;146(3):622–629.e4. doi:10.1053/j.gastro.2014.01.007.
12. Bergeron EJ, Lin J, Chang AC, Orringer MB, Reddy RM. Endoscopic ultrasound is inadequate to determine which T1/T2 esophageal tumors are candidates for endoluminal therapies. J Thorac Cardiovasc Surg. 2014;147(2):765–71, Discussion 771–3. doi:10.1016/j.jtcvs.2013.10.003. Epub 2013 Dec 4.
13. Hammoud GM, Hammad H, Ibdah JA. Endoscopic assessment and management of early esophageal adenocarcinoma. World J Gastrointest Oncol. 2014;6(8):275–88. doi:10.4251/wjgo.v6.i8.27.
14. Pech O, May A, Gossner L, et al. Management of pre-malignant and malignant lesions by endoscopic resection. Best Pract Res Clin Gastroenterol. 2004;18:61.
15. van den Boogert J, van Hillegersberg R, Siersema PD, et al. Endoscopic ablation therapy for Barrett's esophagus with high-grade dysplasia: a review. Am J Gastroenterol. 1999;94:1153.
16. Gong W, Xiong Y, Zhi F, Liu S, Wang A, Jiang B. Preliminary experience of endoscopic submucosal tunnel dissection for upper gastrointestinal submucosal tumors. Endoscopy. 2012;44:231–5.
17. Liu BR, Song JT, Kong LJ, Pei FH, Wang XH, Du YJ. Tunneling endoscopic muscularis dissection for subepithelial tumors originating from the muscularis propria of the esophagus and gastric cardia. Surg Endosc. 2013;27:4354–9.
18. Khashab MA, Saxena P, Valeshabad AK, Chavez YH, Zhang F, Akshintala V, Aguila G, Inoue H, Pasricha PJ, Neuhaus H, Kalloo AN. Novel technique for submucosal tunneling and endoscopic resection of submucosal tumors (with video). Gastrointest Endosc. 2013;77(4):646–8. doi:10.1016/j.gie.2012.11.011. Epub 2013 Jan 23.
19. Lu J, Jiao T, Zheng M, Lu X. Endoscopic resection of submucosal tumors in muscularis propria: the choice between direct excavation and tunneling resection. Surg Endosc. 2014;28(12):3401–7. doi:10.1007/s00464-014-3610-y.
20. Auyang ED, Carter P, Rauth T, Fanelli RD, SAGES Guidelines Committee. Endoluminal treatments for gastroesophageal reflux disease (GERD). Surg Endosc. 2013;27:2658–72.
21. Reavis KM, Perry KA. Transoral incisionless fundoplication for the treatment of gastroesophageal reflux disease. Expert Rev Med Devices. 2014;11(4):341–50. doi:10.1586/17434440.2014.925394.
22. Hunter JG, Kahrilas PJ, Bell RC, Wilson EB, Trad KS, Dolan JP, Perry KA, Oelschlager BK, Soper NJ, Snyder BE, Burch MA, Melvin WS, Reavis K, Turgeon DG, Hungness ES, Diggs BS. Efficacy of transoral fundoplication vs omeprazole for treatment of regurgitation in a randomized controlled trial. Gastroenterology. 2014. doi:10.1053/j.gastro.2014.10.009. pii: S0016-5085(14)01208-6.
23. Zacherl J, Roy-Shapira A, Bonavina L, Bapaye A, Kiesslich R, Schoppmann SF, Horgan S. Endoscopic anterior fundoplication with the Medigus Ultrasonic Surgical Endostapler (MUSETM) for gastroesophageal reflux disease: 6-month results from a multi-center prospective trial. Surg Endosc. 2014. doi:10.1007/s00464-014-3731-3.

24. Inoue H, Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, Satodate H, Odaka N, Itoh H, Kudo S. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42(4):265–71. doi:10.1055/s-0029-1244080. Epub 2010 Mar 30.
25. Sharata AM, Dunst CM, Pescarus R, Shlomovitz E, Wille AJ, Reavis KM, Lee L. Swanström peroral endoscopic myotomy (POEM) for esophageal primary motility disorders: analysis of 100 consecutive patients. J Gastrointest Surg. 2014. doi:10.1007/s11605-014-2610-5.
26. 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;256:659–67.
27. Bhayani NH, Kurian AA, Dunst CM, Sharata AM, Rieder E, Swanstrom LL. A comparative study on comprehensive, objective outcomes of laparoscopic heller myotomy with per-oral endoscopic myotomy (POEM) for achalasia. Ann Surg. 2014;259:1098–103.
28. Familiari P, Gigante G, Marchese M, Boskoski I, Bove V, Tringali A, Perri V, Onder G, Costamagna G. EndoFLIP system for the intraoperative evaluation of peroral endoscopic myotomy. United European Gastroenterol J. 2014;2(2):77–83.
29. Kawai M, Peretta S, Burckhardt O, Dallemagne B, Marescaux J, Tanigawa N. Endoscopic pyloromyotomy: a new concept of minimally invasive surgery for pyloric stenosis. Endoscopy. 2012;44(2):169–73. doi:10.1055/s-0031-1291475.
30. Chung H, Dallemagne B, Perretta S, Lee SK, Shin SK, Park JC, et al. Endoscopic pyloromyotomy for postesophagectomy gastric outlet obstruction. Endoscopy. 2014;46(Suppl 1 UCTN):E345–6. doi:10.1055/s-0034-1377599.
31. Chaves DM, de Moura EGH, Mestieri LHM, Artifon EL, Sakai P. Endoscopic pyloromyotomy via a gastric submucosal tunnel dissection for the treatment of gastroparesis after surgical vagal lesion. Gastrointest Endosc. 2014;80(1):164. doi:10.1016/j.gie.2014.03.045.
32. Shlomovitz E, Pescarus R, Cassera MA, Sharata AM, Reavis KM, Dunst CM, Swanström LL. Early human experience with per-oral endoscopic pyloromyotomy (POP). Surg Endosc. 2014. doi:10.1007/s00464-014-3720-6.
33. Law R, Martin JA. Endoscopic stitching: techniques and indications. Curr Opin Gastroenterol. 2014;30(5):457–62. doi:10.1097/MOG.0000000000000112.
34. Bonin EA, Moran E, Gostout CJ, McConico AL, Zielinski M, Bingener J. Natural orifice transluminal endoscopic surgery for patients with perforated peptic ulcer. Surg Endosc. 2012;26(6):1534–8. doi:10.1007/s00464-011-2063-9.
35. Abu Dayyeh BK, Lautz DB, Thompson CC. Gastrojejunal stoma diameter predicts weight regain after Roux-en-Y gastric bypass. Clin Gastroenterol Hepatol. 2011;9:228–33.
36. Jirapinyo P, Slattery J, Ryan M, Dayyeh B, Lautz D, Thompson C. Evaluation of an endoscopic suturing device for transoral outlet reduction in patients with weight regain following Roux-en-Y gastric bypass. Endoscopy. 2013;45(07):532–6. doi:10.1055/s-0032-1326638.
37. Thompson CC, Chand B, Chen YK, et al. Endoscopic suturing for transoral outlet reduction increases weight loss after Roux-en-Y gastric bypass surgery. Gastroenterology. 2013;145:129.e123–137.e123.

38. Nau P, Ellison EC, Muscarella P, 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(4):1004–11. doi:10.1007/s00464-010-1369-3.
39. Schomisch SJ, Furlan JP, Andrews JM, Trunzo JA, Ponsky JL, Marks JM. Comparison of anterior transgastric access techniques for natural orifice translumenal endoscopic surgery. Surg Endosc. 2011;25(12):3906–11. doi:10.1007/s00464-011-1818-7.
40. Bingener J, Loomis EA, Gostout CJ, Zielinski MD, Buttar NS, Wong Kee Song LM, Rajan E. Feasibility of NOTES omental plug repair of perforated peptic ulcers: results from a clinical pilot trial. Surg Endosc. 2013;27(6):2201–8. doi:10.1007/s00464-012-2740-3.
41. Marks JM, Ponsky JL, Pearl JP, McGee MF. PEG "Rescue": a practical NOTES technique. Surg Endosc. 2007;21(5):816–9. doi:10.1007/s00464-007-9361-2.
42. Kwan V, Eisendrath P, Antaki F, Le Moine O, Devière J. EUS-guided cholecystenterostomy: a new technique (with videos). Gastrointest Endosc. 2007;66(3):582–6. doi:10.1016/j.gie.2007.02.065.
43. Song TJ, Park DH, Eum JB, Moon S-H, Lee SS, Seo DW, et al. EUS-guided cholecystoenterostomy with single-step placement of a 7F double-pigtail plastic stent in patients who are unsuitable for cholecystectomy: a pilot study (with video). Gastrointest Endosc. 2010;71(3):634–40. doi:10.1016/j.gie.2009.11.024.
44. 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. doi:10.1016/j.gie.2012.09.021.
45. Aljarabah M, Ammori BJ. Laparoscopic and endoscopic approaches for drainage of pancreatic pseudocysts: a systematic review of published series. Surg Endosc. 2007;21(11):1936–44. doi:10.1007/s00464-007-9515-2.
46. Varadarajulu S, Bang JY, Sutton BS, Trevino JM, Christein JD, Wilcox CM. Equal efficacy of endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage in a randomized trial. Gastroenterology. 2013;145(3):583–590.e1. doi:10.1053/j.gastro.2013.05.046.
47. De Palma GD, Formato A, Pilone V, et al. Endoscopic management of intragastric penetrated adjustable gastric band for morbid obesity. World J Gastroenterol. 2006;12:4098–100.
48. Neto MP, Ramos AC, Campos JM, et al. Endoscopic removal of eroded adjustable gastric band: lessons learned after 5 years and 78 cases. Surg Obes Relat Dis. 2010;6:423–7.
49. Auyang ED, Santos BF, Enter DH, Hungness ES, Soper NJ. Natural orifice translumenal endoscopic surgery (NOTES): a technical review. Surg Endosc. 2011;25:3135–48. doi:10.1007/s00464-011-1718-x.
50. Wood SG, Panait L, Duffy AJ, et al. Complications of transvaginal natural orifice transluminal endoscopic surgery: a series of 102 patients. Ann Surg. 2014;259:744.
51. Sodergren MH, Markar S, Pucher PH, Badran IA, Jiao LR, Darzi A. Safety of transvaginal hybrid NOTES cholecystectomy: a systematic review and meta-analysis. Surg Endosc. 2015. doi:10.1007/s00464-014-3915-x.

23. Hybrid Laparoscopic and Endoscopic Techniques: Colon and Rectum

Amanda V. Hayman and Mark H. Whiteford

Introduction

The advent of minimally invasive surgical techniques has revolutionized the field of colon and rectal surgery. Complex pelvic dissections and reoperations are increasingly being performed with robotic or laparoscopic techniques for a wide range of indications, including cancer. Studies have proven that a minimally invasive approach can be performed safely, with equal oncologic outcomes, and with significant benefits to the patient, such as reduced pain, shorter time back to work, and fewer intra-abdominal adhesions [1]. As the colorectal surgeon's laparoscopic techniques have improved and expanded, the expansion of endoscopic indications has become another essential intraoperative tool for both diagnostic and therapeutic means.

While it is always good to know how to get out of trouble, it is often considered better to know how to stay out of trouble. Unfortunately, complications are inherent in the practice of surgery and much of our training is focused on learning how to best manage these complications. The learning curve and safe adoption of advanced laparoscopic and endoscopic colorectal procedures may have been slow and progressive over the past two decades, but those early adopters have demonstrated that these advanced procedures can be performed with significantly reduced pain and perioperative convalescence with no loss in efficacy when compared to open surgery. In that spirit, advanced laparoscopic and endoscopic skills are now being adopted to manage procedural complications with the goal of avoiding major reoperative interventions and the inherent multiple morbidities known to accompany them.

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Surgery on the colon and rectum is associated with a high rate of perioperative morbidity. For example, clinically significant leaks are associated with 3–10 % of colorectal anastomoses, and increases the more distal the anastomosis [2]. Further, advanced therapeutic colonoscopy also carries a substantially higher risk of complications than that of diagnostic colonoscopy. The incidence of endoscopic perforations increases with the magnitude of the intervention. Perforation following diagnostic colonoscopy occurs in 0.06–0.12 % of cases, while perforation following endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) occurs in 0–1.1 % and 0–12 % of cases, respectively [3, 4].

Surgical and endoscopic complications can present either early or late in the perioperative period and may include perforation, anastomotic leak, enteric fistulae, hemorrhage (intralumenal or extralumenal), wound infection, bowel obstruction, or anastomotic stricture. Traditionally, many of these complications required re-exploration, at the cost of a high morbidity. The advent of interventional radiology and therapeutic endoscopy offers less invasive measures for managing these complications or allows the surgeon preoperatively to convert an operative emergency into an elective situation. Therapeutic endoscopy can also be used intraoperatively in the setting of technical misadventures to prophylaxis against postoperative complications.

The use of flexible endoscopy in the management of gastrointestinal complications requires a team approach. At the center of this team are skilled advanced therapeutic or surgical endoscopists who have developed technical skills such as balloon dilation, endolumenal stent placement, EMR, and ESD. The endoscopist is supported by an endoscopy suite and nursing team properly equipped to perform these procedures and transportable to the operating room where they can complement the minimally invasive surgeon. At a minimum, necessary endoscopic equipment includes high-definition endoscopes, carbon dioxide insufflations, EMR/ESD dissecting equipment and cap, through-the-scope clips, over-the-scope clips, and an assortment of dilating balloons and stents. A dedicated, experienced endoscopy nursing team is necessary to facilitate and assist in these complex procedures as well as have a working knowledge of and the facility to troubleshoot this often novel equipment. An otherwise very experienced and capable OR nursing team adept at laparoscopy will not necessarily have the required endoscopic skills to assist the surgeon. Successful creation of such a team will take time, patience, and a lot of trial and error.

Combined Laparoendoscopic Management of Colorectal Polyps

Many surgeons have found themselves in the unfortunate position of being unable to locate an endoscopically unresectable polyp intraoperatively. Even if the polyp in question had been preoperatively localized by tattooing, the tattoo can sometimes be difficult to detect laparoscopically. This can be due to an inadequate volume of ink being used, injection sites within the mesenteric side of the polyp, or the presence of a large amount of intra-abdominal fat obscuring the bowel wall. Lastly, there are few definitive intralumenal landmarks, so what is thought to be a "hepatic flexure" polyp by an endoscopist may in fact turn out to be in the descending colon, which dramatically alters the intraoperative plan and resection site. Intraoperative endoscopy is an imperative skill for localizing the "elusive polyp." Fortunately, many institutions utilize carbon dioxide insufflation, a gas which is much more readily absorbed than air. This facilitates intraoperative use by minimizing bowel distension, which can make the laparoscopic portion of the operation much more challenging.

Another use of hybrid endoscopy-laparoscopy is in the management of endoscopically unresectable cecal polyps. If there is minimal concern for malignancy, the least invasive procedure is a laparoscopic partial cecectomy, including the appendix. However, as the appendiceal orifice is near to the ileocecal valve (ICV), the surgeon must be aware to not narrow the valve when firing the stapler. One way to assess this is to perform intraoperative colonoscopy; this allows confirmation of the exact polyp location to minimize the extent of bowel resection and to confirm the ICV is patent.

Lastly, some surgeons and endoscopists have used a team approach for resection of large colonic polyps, using either endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR) techniques with a laparoscopist assisting with extralumenal retraction, or to assist in oversewing the polyp site should a full-thickness defect be suspected or created.

Intraoperative Endoscopic Anastomotic Evaluation

Most colorectal surgeons immediately survey their completed circular staple lines after end-to-end rectal anastomoses for rectosigmoid resections with either rigid proctoscopy or flexible sigmoidoscopy.

While occluding the proximal bowel, gentle insufflation of the anastomoses when submerged in saline can dilate the staple line to assess for air bubbles, which would indicate a leak. If a leak is detected, this is usually addressed with an extralumenal approach via reinforcing sutures or resection and recreation of a fresh anastomosis. Direct intralumenal visualization can also reveal staple line bleeding, which can be immediately managed with lavage, epinephrine injection, and/or clips. However, there are also many postoperative opportunities for endoscopic management of anastomotic problems.

Endoscopic Management of Colorectal Complications

The most common clinical situations that arise include inadvertent or suspected perforation during an endoscopic procedure, acute anastomotic leaks, enterocutaneous fistula, anastomotic stricture, and occluded anastomoses. This last event is a rare sequela of creation of an anastomosis distal to a diverting ostomy. Endoscopic management of lower GI bleeding will be covered elsewhere. There are several endolumenal techniques available to the surgical endoscopist. Tools for fixing holes include fibrin glue, through-the-scope clips (TTSC), and over-the-scope clips (OTSC). Tools for managing strictures and occlusions include pneumatic balloon dilation and stents. Some novel endoscopic suturing devices are also in development and early clinical use.

Colorectal Perforations and Leaks

Traditionally, endoscopic perforations, anastomotic leaks, and perianastomotic abscesses mandated re-exploration, at the cost of high morbidity. The advent of interventional radiology and therapeutic endoscopy offers less invasive measures for managing these complications or preoperatively to convert an operative emergency into an elective situation.

Even in well-trained, experienced hands, up to 10 % of colorectal anastomoses will be complicated by a leak [2]. The treatment of anastomotic leak is based on the clinical presentation, anatomic location, and timing. Some leaks are contained and present as deep organ space abscess. These are usually managed by percutaneous drainage of the

cavity only. More significant leaks often present with peritonitis and usually require abdominal exploration. A delayed manifestation of anastomotic leak may present as an enteric fistula, whether to small bowel, large bowel, vagina, urethra, or skin.

Through-the-Scope Clips

Through-the-scope clips (TTSC) are commonplace in the endoscopy suite due to their relative simplicity of use and their usefulness in decreasing the incidence of post-procedure bleeding and perforation. As the name implies, TTSCs are small hinged clips that can be placed down the working channel of an endoscope and extended just beyond the tip. The operator can then open and close the clip, and in some cases rotate the clip to facilitate proper orientation towards the target. Once the target pathology has been properly grasped, the clip can then be deployed in a locked and closed position. When multiple clips are needed, the recommended technique is to begin applying clips starting furthest away from the scope and progress back towards the operator. In most cases, the clips will slough off over time. TTSC's depth of grasping is usually only that of the mucosa and submucosa. For this reason the approved indications are for control of and prevention of bleeding and to reinforce or close over a mucosal defect following endoscopic polypectomy [5]. Off-label indications such as closures of full-thickness defects less than 1 cm have also been described [6].

Over-the-Scope Clip

Over-the-scope clips are much more robust endoscopic closure devices usually reserved for closing 1–2 cm full-thickness defects or the internal opening of enteric fistulas. Because of the increased size needed to close these larger defects, the clips come loaded in the open position on a clear cylindrical cap designed to fit over the tip of the endoscope. They come in a kit which includes a ratcheted firing mechanism secured to the handle of the colonoscope which is connected to the dissecting cap/clip by a string threaded through the working channel. There is also an available dual grasping forcep tool that is likewise placed down the working channel and is used to oppose the two sides of the defect and pull them up into the dissection cap prior to clip application. The clip is spring-loaded and, when deployed, clamps down on

the two sides of the approximated bowel wall in a full-thickness fashion. These are often used in conjunction with through-the-scope clips to complete a defect closure [7].

Endo-SPONGE®

Negative pressure sponges have revolutionized management of open surgical wounds. This concept has been miniaturized and married to endoscopy to allow endoscopic placement of a negative pressure sponge. This device has been commercially available in Europe and numerous case series have reported more rapid healing of colorectal anastomotic leaks. The described technique is very involved and labor-intensive. The majority of patients are managed with a diverting ostomy. The technique involves endoscopic access of the anastomotic sinus for irrigation, debridement, and dimension measurement. An appropriately sized sponge is then deployed into the sinus through an overtube and subsequently connected to a machine that provides constant negative pressure. Sponges are changed out every 3–5 days. After initial inpatient management, selected patients can be managed in the outpatient setting. Up to a dozen Endo-SPONGE® sessions are required for sinus healing. One series reported more rapid healing when initiation of Endo-SPONGE® management occurred within 6 weeks of leak detection when compared to those patients whose sponge management started after this time [8].

Self-expanding Endoscopic Stents

Clinical data for the use of self-expanding stents to manage colorectal leaks is fairly limited. This technique is extrapolated from clinical experience gained in managing esophageal perforations and anastomotic leaks with covered stents. Ideal candidates would include left-sided leaks or fistulae that are more easily accessible via colonoscopy and do not have the large diameter of the right colon. For this indication, plastic covered stents, usually designed for esophageal purposes, are preferred. Because they have a high stent migration rate, fixation with endoscopic suture or through-the-scope clips may help reduce migration rates. Stents should be removed after 4–8 weeks in an effort to reduce the risk of stent perforation and to minimize the discomfort frequently associated with long-term indwelling distal colonic stents.

Enterocutaneous Fistulae

Enterocutaneous fistulae are often the result of anastomotic leaks or surgical misadventure, commonly associated with reoperative abdominal surgery, trauma, and inflammatory bowel disease. It is a complication dreaded by all surgeons and occurs more commonly in malnourished patients. Enterocutaneous fistulae are associated with ongoing wound and sepsis issues. Because they have a low and prolonged spontaneous closure rate, they result in significant time and resource utilization.

The principles in the management of enterocutaneous fistulae are well established. Initial management is focused on volume and electrolyte replacement along with early recognition and control of sepsis. Wound management and skin protection is critical and is facilitated by early and continued involvement of wound ostomy continence nurses. Total parenteral nutrition is often necessary as bowel rest is utilized to help reduce a high output fistula to low output and facilitate spontaneous closure. Eventually fistula imaging is necessary to define the anatomy and devise a long-term management strategy. Definitive surgery is usually deferred 3–6 months or longer to allow resolution of the sepsis and inflammatory processes and to allow restoration of a normal nutritional state. The prospect of a complex, revisional reoperation must be considered. Due to high morbidity rates, surgeons and patients alike are desirable of a minimally invasive option.

Endoscopic attempts to close enterocutaneous fistulae are an appealing option for these challenging patients. Endoscopic interventions can often be performed much sooner than major surgery, are substantially less morbid, and are often repeatable. Fibrin glue has been described in the management of fistulae with small (<7 mm) endoscopically accessible primary openings [9]. This technique involves endoscopic localization followed by tract debridement using a cytology brush or argon plasma coagulation. Two to four milliliters of fibrin glue is then administered through a dual lumen applicator tube threaded down the working channel of the endoscope. There are limited data on outcomes of this therapy, although several small case series demonstrated 50–90 % healing rates usually following 3–5 treatments. Higher failure rates are associated with high output fistulas, fistula diameter greater than 7 mm, distal obstruction, and fistulae in communication with abscess cavities [9].

Over-the-scope endoscopic clips have also been described in the management of colocutaneous fistulae. The described technique again

involves endoscopic localization of the internal opening followed by fistula tract debridement endoscopically using a cytology brush or argon plasma coagulation. The edges of the fistula are then reapproximated using the bilateral tissue grasping forceps, and the tissue then incorporated up into the suction followed by clip deployment. A post-procedure fistulogram is performed to confirm adequacy of closure and need for additional defect closure. Experience using over-the-scope clips is slowly increasing. To date, most OTSC series are small with fewer than three dozen patients, have heterogeneous patient populations, but show relatively high procedural success and moderate to high clinical success rates, with low periprocedural morbidity. Long-term follow-up, however, is limited [7].

Strictures

Colonic anastomoses can have a stricture rate up to 30 % [10] which can be due to inflammation, ischemia, post-anastomotic leak, prolonged disuse (as in the case of proximal fecal diversion), or other technical reasons. Endoscopic balloon dilation can be used to restore continuity and avoid a difficult reoperative anastomotic revision. Mild asymptomatic strictures need not be dilated. Symptomatic, short segment (less than 1 cm length) anastomotic strictures without extensive fibrosis are readily amenable to endoscopic dilation. Long segment and densely fibrotic strictures are much less amenable to successful and durable endoscopic dilation and may be more suitable for traditional surgical management techniques. Indications for and the technique of endoscopic balloon dilation are reviewed in detail in prior chapters.

Occasionally, such as in the case of an occlusive, thin web-like bridge of tissue which forms across an anastomosis after a low anterior resection, tandem endoscopy, i.e., one endoscopist approaching transanally and the other through the distal limb of a loop ostomy, can be used to safely maneuver an anastomotic stricture with the use of needle tip cautery, wires, and balloons. Lower endoscopy has been selectively used to successfully dilate inflammatory or fibrotic strictures in the setting of Crohn's disease, either in the colon or in the distal ileum. This approach is best suited for short and/or multiple strictures in conjunction with maximal medical therapy, or for patients who are poor candidates for or resistant to surgical resection, whether due to hostile abdomens or the risk of short gut syndrome.

Postoperative Hemorrhage

Another common postoperative complication is hemorrhage, frequently as a result of staple line bleeding. This can be managed intraluminally, by one or more of the following endoscopic techniques which are detailed in previous chapters of this text: endoscopic lavage (ice-cold saline), injection of epinephrine or lidocaine, through-the-scope clips, or argon plasma coagulation.

Conclusion

As technology advances, combining therapeutic endoscopic experience with laparoscopic skills has allowed the surgical endoscopist to offer patients safer, less invasive colorectal procedures. Once these skills have been honed in the elective setting and a capable, experienced endoscopic team has been established, the surgeon can also use many of these same techniques in more urgent settings after a complication has occurred.

References

1. The Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med. 2004;350:2050–9. May 13, 2004.
2. Vignali A, Fazio VW, Lavery IC, Milsom JW, Church JM, Hull TL, et al. Factors associated with the occurrence of leaks in stapled rectal anastomoses: a review of 1,014 patients. J Am Coll Surg. 1997;185(2):105–13. PMID:9249076.
3. Kedia P, Waye JD. Colon polypectomy: a review of routine and advanced techniques. J Clin Gastroenterol. 2013;47(8):657–65.
4. Repici A, Hassan C, De Paula PD, Pagano N, Arezzo A, Zullo A, et al. Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review. Endoscopy. 2012;44:137–47.
5. Raju GS. Endoscopic clip closure of gastrointestinal perforations, fistulae, and leaks. Dig Endosc. 2014;26 Suppl 1:95–104. doi:10.1111/den.12191. Epub 2013 Nov 8. PMID: 24373001.
6. Trecca A, Gaj F, Gagliardi G. Our experience with endoscopic repair of large colonoscopic perforations and review of the literature. Tech Coloproctol. 2008;12(4):315–21.
7. Weiland T, Fehlker M, Gottwald T, Schurr MO. Performance of the OTSC System in the endoscopic closure of iatrogenic gastrointestinal perforations: a systematic review.

Surg Endosc. 2013;27(7):2258–74. doi:10.1007/s00464-012-2754-x. Epub 2013 Jan 24. Review. PMID:23340813.

8. Strangio G, Zullo A, Ferrara EC, Anderloni A, Carlino A, Jovani M, et al. Endosponge therapy for management of anastomotic leakages after colorectal surgery: a case series and review of literature. Dig Liver Dis. 2015. doi:10.1016/j.dld.2015.02.007. pii: S1590-8658(15)00218-2. [Epub ahead of print] PMID: 25769505.
9. Willingham FF, Buscaglia JM. Endoscopic management of gastrointestinal leaks and fistulae. Clin Gastroenterol Hepatol. 2015. doi:10.1016/j.cgh.2015.02.010. pii: S1542-3565(15)00148-2. [Epub ahead of print] PMID:25697628.
10. Hiranyakas A, Da Silva G, Denoya P, Shawki S, Wexner SD. Colorectal anastomotic stricture: is it associated with inadequate colonic mobilization? Tech Coloproctol. 2013;17(4):371–5. doi:10.1007/s10151-012-0929-z. Epub 2012 Nov 15.

Part V
Endoluminal Bariatrics

24. Primary Endoscopic Treatments for Morbid Obesity

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Introduction

The World Health Organization (WHO) estimates that, in 2014, there will be approximately 500 million obese individuals, with over 1.4 billion people classified as overweight. In the United States alone, it is predicted that by 2015 the prevalence of obesity will rise to 41 % in the adult population, while 75 % of Americans will be considered overweight [1]. With these alarming epidemiologic trends, it is no question that obesity is a rapidly growing national and global epidemic. Furthermore, healthcare systems will have to absorb the significant costs of managing the comorbidities that inevitably follow obesity, such as coronary artery disease and peripheral vascular disease, diabetes, nonalcoholic steatohepatosis and cirrhosis, obstructive sleep apnea, pulmonary hypertension, hypercoagulability, and many others. This issue has become so prevalent that the WHO has nicknamed the epidemic "Globesity" [2].

Although recently there has been significant emphasis placed on preventative medicine and education, it has been shown that within the obese population conservative management options, such as diet and exercise, have limited efficacy in treating the disease. Instead, the role of bariatric surgery has become increasingly important in the treatment algorithm of obesity. Laparoscopic sleeve gastrectomy, gastric banding, and Roux-en-Y gastric bypass (RNYGB) are well documented as effective treatment options. Patients who undergo a Roux-en-Y gastric bypass, reportedly the most successful of these surgical modalities, lose and maintain an average of 70 % of their excess weight 1 year following

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surgery and experience significant improvement in presurgical comorbid conditions such as diabetes and hyperlipidemia. However, RNYGB is not without complications: bleeding, anastomotic leak, and internal hernias are significant sources of morbidity for this procedure. Furthermore, an estimated 15–20 % of patients "fail" RNYGB, which is defined as either less than 50 % weight loss after a year or actual weight gain surpassing presurgical weight, placing the patient at even greater risk for developing or worsening their cardiopulmonary risk factors [3].

The role of endoscopy has emerged as a less invasive and potentially cost-effective modality for the primary treatment of obesity. Within the last 10 years, a wide variety of endoscopic procedures and devices have been marketed claiming to function as bridging, revisional, or primary bariatric procedures. This chapter will focus on the role of endoscopy as a primary tool in bariatric surgery.

Endolumenal Malabsorptive Procedures

Striving to duplicate the weight loss and immediate metabolic effects seen with Roux-en-Y gastric bypass, endolumenal procedures are currently being investigated. The ability to achieve these goals without an operation, particularly in high-risk patients or as a bridge to bariatric surgery, has been the primary goal of the endoscopic malabsorptive techniques. These procedures are designed to bypass the absorptive surface of the proximal portion of the small bowel, particularly the biliary and pancreatic secretions. This leads to improved glucose homeostasis prior to any significant weight loss, as seen with gastric bypass surgery. The secondary goal of achieving significant % excess weight loss (%EWL) is also a strong consideration for the success of these treatments.

Duodenal-Jejunal Bypass Sleeve

EndoBarrier

The EndoBarrier gastrointestinal liner (GI Dynamics, Lexington, MA, USA) is an endoscopically placed malabsorptive barrier device that prevents absorption of nutrients and mixture of biliary and pancreatic secretions. It is 60 cm in length and extends into the proximal jejunum (Fig. 24.1). The device is placed under a combination of endoscopic and

Fig. 24.1. EndoBarrier sleeve. Courtesy of GI Dynamics, Inc.

fluoroscopic guidance with an over-the-wire system. In the first step, the sleeve is deployed into the proximal jejunum followed by anchor deployment in the proximal duodenum to anchor the device in place and prevent migration. The anchor has self-deploying barbs that attach to the duodenal mucosa to prevent movement. Positioning is confirmed using fluoroscopy, to ensure the sleeve is patent [4, 5]. The pilot study for this device was performed in 2008 by Rodriguez-Grunert et al. and included 12 patients with an endpoint of 12 weeks. The primary outcome measures were to identify adverse events with secondary measures focused on percent excess weight loss and changes in comorbidities. There was successful deployment of the device in all 12 cases and 10 out of 12 patients completed a 12-week course, with two patients requiring early retrieval secondary to intractable abdominal pain, nausea, and vomiting. The percent excess weight loss was 23.6 %. Additionally, 4 of the 12 patients with diabetes had significant decreases in hemoglobin A1C at the completion of the trial [6]. Complications included a partial pharyngeal tear and esophageal tear at the time of device removal. All patients had inflammation at the duodenal bulb at the site of anchoring noted during removal.

A second multicenter prospective randomized control trial was performed by Tarnoff et al. comparing the duodenal-jejunal bypass sleeve with a low-fat diet to a low-fat diet alone for 12 weeks. In 25 patients who underwent placement of the EndoBarrier system compared with diet alone controls ($n=14$), the excess weight loss was 22.1 % vs. 5.3 %, respectively. In terms of improvement or resolution of comorbid conditions, 4 patients had type 2 diabetes; 1 in the control group and 3 in the device group. Within 1 week, all 4 patients had improvement of hemoglobin A1C levels and by 12 weeks, 1 patient in the device group had resolution of diabetes. Of note, 5 of 25 patients (20 %) required premature device removal secondary to bleeding ($n=3$), migration ($n=1$), and obstruction ($n=1$) [7].

In a more recent multicenter randomized control trial, the EndoBarrier device was studied for preoperative bariatric surgery patients. A total of 41 patients were enrolled, with 30 patients randomized to the device group and 11 randomized to a diet control group. Twenty-six devices were successfully implanted for 12 weeks, with 4 device failures due to dislocation of anchor ($n=1$), obstruction ($n=1$), migration ($n=1$), and intractable epigastric pain ($n=1$). After 12 weeks, mean excess weight loss was 19 % for the device group and 6.9 % for the diet group. Type 2 diabetes was present in 8 patients pre-procedure and improved, as seen with lower hemoglobin A1C and decreased medication requirements, at the completion of the study in 7 out of 8 patients [8].

Major adverse events from the duodenal-jejunal bypass sleeve included sleeve migration, obstruction, bleeding, and inflammation at the anchor site, nausea, vomiting, and intractable abdominal pain. In all studies, these complications occurred in 10–20 % of cases, requiring early removal of the device. Early device removal secondary to intractable symptoms appears to be the major obstacle for this device. The EndoBarrier has demonstrated significant weight loss at 12 weeks with improvement of comorbidities, including diabetes as seen with decreases in hemoglobin A1C, lower glucose levels, and decreasing requirements of glycemic control medications. Innovations in device design and decreased complication rates could make this device a viable option as a bridge for weight loss and improvement in comorbidities prior to bariatric surgery.

As of 2015, the most recent study involving the Endobarrier: EndoTrial clinical trial by GI Dynamics has enrolled 200+ patients and results are pending.

ValenTx Sleeve

The ValenTx endolumenal bypass device (ValenTx, Inc., Carpinteria CA, USA) attempts to mimic the Roux-en-Y gastric bypass by having both restrictive and malabsorptive properties. It is an endoscopically implantable sleeve placed at the GE junction and extends into the proximal to mid-jejunum. The sleeve is 120 cm in length and allows for food to bypass the stomach and duodenum, causing similar malabsorption to the Roux-en-Y gastric bypass [9]. This is a hybrid procedure, with the sleeve placed endoscopically and the device sutured to the GE junction endoscopically under laparoscopic visualization [10]. The first single-center prospective human trial with this device enrolled 22 patients, with 17 patients completing the 12-week trial. Patients completing the trial had an average of 39.7 % EWL with premature device removal of 23 %, with 5 patients requiring device removal, all due to odynophagia. No major complications occurred either during the placement or removal of the device. In terms of comorbidities, 7 of the patients were diabetic and had significant reduction in hemoglobin A1C and did not require medication while the sleeve was in place. Further, 2 patients had resolution of their hypertension and 3 patients had normalization of their lipid profile while the device was in place [11]. The ValenTx sleeve continues to undergo clinical trials and has not been approved by the Food and Drug Administration (FDA) yet. The >20 % early retrieval rate for odynophagia requires improvement prior to widespread use of this device.

Endoluminal Restrictive Procedures

Endoluminal restrictive procedures are designed to mimic restrictive laparoscopic procedures, such as gastric banding, vertical banded gastroplasty, and sleeve gastrectomy. These procedures decrease the amount of food that is able to be consumed at one time, by restricting stomach size. The endoscopic devices used include intragastric balloons, endolumenal suturing, endolumenal stapling, and transoral restrictive implant system.

Intragastric Balloon Placement

Intragastric balloon devices were one of the first endoscopic devices to be introduced into the field of obesity surgery, and they have remained the most frequently utilized modality in endoscopic bariatric

surgery. Introduced in 1982, intragastric balloons (such as the Garren-Edwards, Ballobes, Taylor, and Wilson-Cook balloons, De Castrol) have undergone many revisions since their original inception, as they were ineffective due to their low volume capacity. Another significant complaint was that the balloon material was not durable. Furthermore, reported complications such as erosion into the gastric mucosa and gastric outlet syndrome made their safety profile less than desirable. Since then, several modifications have been made to provide both effective and relatively safe devices. Of the several commercially available designs, the Bioenteric Intragastric Balloon has been the most widely researched, although other alternatives have become increasingly accepted as well, such as MedSil, the Heliosphere Bag, Obalon system, and the Gastric Balloon.

The balloons are designed to fill a volume ranging between 400 and 800 mL, depending on the brand of balloon being used. They are placed in the endoscopy suite under conscious sedation, which can be managed either by the endoscopist or with the help of a general anesthesiologist [12]. In most cases, the procedure is considered outpatient, with occasional patients remaining in the hospital overnight. Once deployed, the balloons are filled with saline or air, thereby reducing the effective gastric volume, which in turn causes early satiety. Most balloons are removed after 6 months. All patients are typically sent home on a proton pump inhibitor in order to prevent reflux symptoms after the procedure.

Although the main function of the intragastric balloon is to act as a space-occupying device that facilitates weight loss, numerous articles have recently focused on the hormonal changes associated with this procedure. Specifically, changes in the production of leptin and ghrelin, key hormones involved in the regulation of adipocyte function and metabolism respectively, have been studied after intragastric balloon placement. Leptin is produced by adipocytes, and its function has been linked to promoting inflammatory and hypercoagulable states, as well as contributing to increasing cardiovascular risk in obese patients. As such, one of the important goals of post-bariatric surgery is not simply weight loss but specifically decreasing body fat percentage and leptin production. In a recent article examining hormonal trends after MedSil intragastric balloon placements, Buzga et al. reported statistically significant increases in Ghrelin and decreased amounts of Leptin at 1, 3, and 6 months after the procedure, which correlated with previous studies conducted on the same subject [13]. Ghrelin, on the other hand, was found to be increased above baseline on all three of these follow-up periods. Furthermore, FGF21, a hormone known at high levels to be associated

with obesity, and A1C levels were also found to be significantly decreased on follow-up after intragastric balloon placement [13]. Alternative theories propose that the balloon induces a stretch response in the stomach that causes CCK release inducing delayed gastric emptying, which in turn causes early satiety and weight loss.

Efficacy

In comparison to diet and exercise, intragastric balloon devices are by far more effective in treating obesity. In a double-blind, crossover study performed by Genco et al. in 2006, the effectiveness of BioEnterics Intragastric Balloon (BIB) placement was compared to patients who only underwent strict dietary and exercise regimens. The authors demonstrated that BIB placement had a statistically significant increase in weight reduction over conservative management. The same authors also conducted one of the most comprehensive retrospective reviews on the subject and studied over 2000 patients who had received intragastric balloons. In these results, patients had lost approximately 34 % of their initial weight at 6-month follow-up [2].

However, whether that weight loss can actually be maintained as a viable permanent option for obese patients is another question. In a recent review of its safety and efficacy parameters, de Castro et al. conducted a prospective cohort analysis of 91 patients who underwent intragastric balloon placement for obesity treatment. The authors noted that while over 70 % of their patients exhibited significant weight loss (11+/− 7 % of pre-procedure weight) at the time of the balloon removal, the percent of these patients able to maintain this weight loss decreased significantly at 6 and 12 months after the balloon retrieval. They concluded that while the balloon offered good initial weight loss, its effectiveness was limited by its temporary nature [12].

Because of its potential for only temporary weight loss, many advocate repeated balloon placement in order to maximize its effectiveness. In a study conducted by Alfredo et al., patients who had undergone intragastric balloon placement were followed for a 6-year period after removal in order to ascertain long-term results. Patients who had gained more than 50 % of their previous weight loss after the first balloon placements were automatically considered eligible for a second round. All patients had at least two intragastric balloon placements, and a significant portion had up to three, sometimes four procedures. With this protocol, patients were able to maintain relatively stable weight loss profiles, although weight cycling between placements was noted [14].

Safety Profile

The popularity of the intragastric balloon is due to both its effectiveness as a minimally invasive adjunct to obesity surgery and its safety profile. In fact, because of its relatively easy deployment, repeated intragastric balloon placement has been advocated by many. Unlike Roux-en-Y gastric sleeve procedures, intragastric balloon placement can occur as many times as needed, which may be a better option in an obese patient who is not deemed a safe surgical candidate.

While the mortality rate following intragastric balloon placement is reported as less than 1 %, the procedure is not without its complications [15]. De Castro et al. reported that approximately half of their study patients experienced emesis after the procedure; epigastric pain, nausea, and reflux symptoms were the next most common side effects, which is why a proton pump inhibitor is routinely prescribed to patients following balloon placement. Removal of the balloon after 6 months was usually uncomplicated, except for 13 % of patients who required earlier removal secondary to protracted nausea and vomiting. Other rare complications included gastrointestinal bleeding, which was only noted in two patients [12]. Of note, Alfredo et al. found that these symptoms were more prominent after the second or third balloon placement, highlighting that epigastric pain, nausea, and vomiting were present for approximately 4 days post-procedure after the second balloon insertion in comparison to 2.5 days after the initial procedure [14].

Air filled balloons, such as Heliosphere, have demonstrated a reduction in post-procedure nausea and emesis, and for that reason, are typically better tolerated. An important complication with Heliosphere balloons is spontaneous deflation. This is especially important during retrieval, as it renders removal of the device from the gastric cardia very difficult. If deflation occurs, forceps or snares may be needed for successful removal of the balloon, and more invasive procedures such as laparoscopy have been reported in extreme cases [12]. A recent case report by Drozdowski et al. documents a patient who underwent intragastric balloon placement with a Heliosphere balloon and presented 2 months later with symptoms of a bowel obstruction. An emergent exploratory laparotomy was performed, revealing a deflated intragastric balloon that had eroded into the wall of the small intestine [16]. Because these balloons are air filled, it is postulated that the deflation may have occurred 3–4 days prior to this patient's presentation to the emergency room but was not clinically noticeable, thus delaying the diagnosis. De Castro et al. compared the safety profiles between the BIB and

Heliosphere balloons and found that there was no significant difference in their efficacies. Heliosphere balloons had a slightly higher incidence of balloon migration, requiring rigid endoscopy or surgery for removal. On the other hand, a higher incidence of post-procedure nausea and vomiting occurred after BIB placement [12].

The Orbera intragastric balloon (Allergan Inc., Irvine, CA, USA) has adopted a method which seeks to prevent subclinical deflation; this balloon is filled with methylene-blue dye during initial placement. If it leaks, the dye is absorbed and excreted in the urine, turning it blue and alerting the patient of its deflation [4]. In contradistinction to balloon dynamics over time, the long-term effects on gastric shape, potential accommodation and long-standing dilation of the stomach, and how this may impact gastric emptying, satiety, and overall gastric physiology are yet to be determined.

Endo Cinch Suturing System

The Endo Cinch Suturing System (C.R. Bard, Murray Hill, NJ, USA) is the first endoscopic suturing device used in the treatment of obesity. It was originally designed for the treatment of gastroesophageal reflux disease and revisions of gastric pouch for failed gastric bypass surgery. Interest has transitioned its use toward primary intervention in morbid obesity. A metal capsule is placed on the end of an endoscope and suction applied to the gastric wall bringing it into the device. Polypropylene sutures are then used repeatedly to create a sleeve. The vertical gastroplasty is created by approximating the anterior and posterior stomach with full-thickness plications and excluding the fundus of the stomach. Modifications to the system, known as the Restore suturing system, have been developed to enable the device to be reloaded without removing the endoscope. The largest study of this device to date was performed in 2008 by Fogel et al., who reported 64 patients underwent the procedure and were followed for 1 year. The average %EWL was 58.1 ± 19.9, and for patients with a lower starting BMI, the %EWL was greater [17]. There were no serious procedural complications. An additional pilot study, entitled the TRIM (transoral gastric volume reduction) trial, was performed with 18 patients and reported a 12-month %EWL of 27.7 ± 21.9. Interestingly, at 12-month follow-up, all patients underwent upper endoscopy which demonstrated loss of plications in 13 patients (72 %), raising concern of the durability of this procedure for primary management of morbid obesity [18]. Although it appears to be

safe and a viable option, additional studies are needed to determine the long-term efficacy of this procedure as a primary therapy for the treatment of obesity.

TOGa System

The TOGa system (Transoral gastroplasty system; Satiety, Palo Alto, CA, USA) is an endoscopic stapling device that is used to create a gastric sleeve starting at the angle of His to the midportion of the stomach. It is performed along the lesser curvature and the goal is to mimic a sleeve gastrectomy without resection. The TOGa stapler is a flexible 18 cm stapler passed over a guidewire and the endoscope is placed through the device, which is then retroflexed in order to visualize the procedure. Suction is used to oppose the anterior and posterior gastric walls, they are clamped, and then divided with the full-thickness stapling device. The process is repeated to achieve desired luminal size and a length of 8–9 cm. The first multicenter trial enrolled 21 patients with an average BMI of 43.3 (35–53 kg/m^2). There were no serious complications, but the most common periprocedural side effects were nausea, vomiting, abdominal pain, and transient dysphagia. At the 6-month endoscopic evaluation, all patients had intact partial or full stapled sleeves; staple line gaps were noted in a majority of patients (13/21). Posttreatment %EWL 16.2 % at 1 month, 22.6 % at 3 months, and 24.4 % at 6 months [19]. A subsequent European trial published in 2011 included 67 patients, of which 53 patients had follow-up at 12 months. Excess BMI loss was 33.9, 42.6, 44.9 % at 3, 6, and 12 months, respectively. Further, significant decreases in hemoglobin A1C (7.0–5.7 %) and triglycerides (142.8–98 mg/dL) were found. Two complications were noted in this trial and included respiratory insufficiency and asymptomatic pneumoperitoneum [20]. Further studies of this device with longer follow-ups and randomized control trials are needed to delineate the efficacy and long-term durability of this procedure.

Transoral Endoscopic Restrictive Implant System

The transoral endoscopic restrictive implant (TERIS) system (BaroSense, Redwood City, CA, USA) endoscopically implants a prosthesis at the gastric cardia creating a small gastric pouch. The procedure entails creating five gastric plications, placing five silicone anchors,

followed by deployment of the prosthesis and securing it to the anchors. The gastric plications are created starting at approximately 3 cm distal to the GE junction using an endoscopic circular stapler through an endoscopic overtube. The silicone anchor is then placed through a hole in the plication and this is repeated until all five anchors are in place. The implant is brought into place and locked into position via the anchors. This creates a restrictive gastric pouch, similar to the pouch created in the laparoscopic adjustable gastric band [10]. In a phase 1 trial of the system, 13 patients were studied. 12 of 13 patients had the device successfully implanted. In short-term follow-up (3 months), the %EWL was 12.3 % at 1 month and 22.2 % at 3 months [21]. An additional randomized, uncontrolled single-group phase I study was performed by Biertho et al. This trial studied 20 patients and demonstrated %EWL at 3 and 6 months was 21 % and 26 %, respectively [22]. Further investigations into safety, efficacy, long-term outcomes, and comparison to control group are necessary to determine the long-term use of this system.

Neural Modulation Therapies

Gastric Electrical Stimulation Therapy

One of the theories for the underlying cause of morbid obesity is the dysregulation of peripheral and central neural pathways that control hunger and food intake. The development of gastric electrical stimulators for weight loss relies on the activation of gastric motor afferent fibers and its effects on the central neural activities [5]. Multiple gastric stimulators have been developed and trialed in both animal models and human trials. Results have been variable. The multicenter European LOSS (Laparoscopic Obesity Stimulation Survey) reported 25–40 % EWL in the treatment group [23]. However, these results have not been duplicated. The nonrandomized DIGEST (Dual-lead Implantable Gastric Electrical Stimulation Trial) trial enrolled 30 patients and reported a 23 % EWL at 16 months. The follow-up study, the randomized US O-01 trial, with 103 patients, did not show significant weight loss with the gastric stimulators [24].

The first method of stimulation is the Transcend Gastric Stimulator (Medtronic, Minneapolis, MN, USA). The theory behind this device is that it decreases food intake by acting on the vagal afferent pathways [25]. This is a laparoscopically placed device that has electrodes sutured to the surface

of the lesser curvature of the stomach and an implantable pacemaker-like device in the subcutaneous tissue. The device provides a low level of electrical stimulation that provides a sense of satiety. The procedure is done through 4–6 ports and takes approximately 1 h to perform.

The second gastric stimulator is the Tantalus system (MetaCure, Orangeburg, NY, USA) which utilizes three pairs of electrodes; one in the fundus to sense food intake and two pairs in the antrum to stimulate slow waves. The electrodes are only stimulated after a food bolus and by increasing antral contraction, satiety that is mediated by gastric distension. In a study performed by Bohdjalian et al., 12 patients had the Tantalus system implanted. Results at 20 weeks demonstrated a body weight loss from 129 ± 6 kg to 120 ± 5 kg. Additionally, 9 of the 12 patients were followed up at 52 weeks and weight decreased to 112 ± 4 kg. Further, the weight loss was also associated with an improvement in hypertension [26].

Complications of the gastric stimulators include intragastric lead perforations and lead dislodgement. This occurred in up to 20–25 % in one study [27]. Other side effects of the devices include nausea, bloating, and abdominal pain. In 2005, Medtronic reported that a double-blind study with 200 patients failed to achieve desired study endpoints; the device currently is not FDA approved in the USA [25].

Gastric Electrical Stimulation may provide modest weight loss benefit to morbidly obese patients; however studies have failed to demonstrate consistent results. New generations of stimulators are in development that would require endoscopic placement, eliminating the need for laparoscopic placement. These new devices have not undergone human trials yet [23]. To date, none of these devices are currently FDA approved in the USA for treatment of morbid obesity.

Satiety Devices

Fullsense

A proximal gastric endolumenal device currently under evaluation using stimulation of neuro-hormonal feedback mechanisms without restriction or requirement of food to induce weight loss is the Full Sense Device (Sentinel Group, Grand Rapids, MI, USA) which consists of a conical component which presses against the gastric cardia, and a cylindrical stent that is placed just above the gastroesophageal junction. The upward pressure produced by the conical component on the top of the

stomach generates a sense of satiety. An initial human trial of the device generated a mean of 74.9 % excess body weight loss 27 weeks after placement of the device. The current configuration is deployed endoscopically. Clinical availability is anticipated soon in Europe with pending approval from the Food and Drug Administration (FDA) prior to release in the United States.

Transpyloric Shuttle

Another device also designed to induce satiety by inducing delayed gastric emptying is the Transpyloric Shuttle (Baronova Inc., Goleta, CA, USA). This endoscopically deployed device was recently evaluated in clinical trial NCT01386905, A Study of the TransPyloric Shuttle (TPS) for Weight Reduction in Obese Subjects (ENDObesity Study) which followed patients for 12 weeks with encouraging results.

Conclusion

There are multiple endoscopic devices that have been developed in attempts to find an effective primary endoscopic bariatric procedure. The goals of these therapies include primary intervention for bariatric patients, bridging to bariatric surgery, early treatment for patients who do not qualify for bariatric surgery, to improve comorbid conditions including diabetes, and for revisions post bariatric surgery. There are multiple devices and procedures, restrictive and malabsorptive techniques that have been trialed. The restrictive procedures, including intragastric balloons, endoscopic suturing, and endoscopic stapling, all have potential, but studies remain limited and effect size is modest. Further investigation into all of these devices is warranted. Malabsorptive procedures including the duodenal-jejunal bypass sleeve and the ValenTx endoluminal sleeve are designed to mimic the restrictive and malabsorptive results of Roux-en-Y gastric bypass. Satiety sensation devices include FullSense and Transpyloric Shuttle and potentially provide appetite suppression regardless of food ingestion. Although results in terms of percent excess weight loss and improvement in comorbidities, especially diabetes, are promising, complication rates remain high and weight loss results do not appear to be long term. Further studies and device alterations to reduce complication rates are needed prior to widespread implementation of these devices. Currently, no primary endoscopic bariatric treatment is FDA approved in the USA.

References

1. The World Health Organization. Obesity and overweight fact sheet. 2015. http://www.who.int/mediacentre/factsheets/fs311/en/. Accessed 2 Sept 2015.
2. Genco A et al. Bioenterics intragastric balloon (BIB): the Italian Experience with 2515 patients. Obes Surg. 2005;15:1161–4.
3. Thompson CC, Slattery J, Bundga ME, Lautz DB. Peroral endoscopic reduction of dilated gastrojejunal anastomosis after Roux-en-Y gastric bypass: a possible new option for patients with weight regain. Surg Endosc. 2006;20:1744–8.
4. Majumder S, Birk J. A review of the current status of endoluminal therapy as a primary approach to obesity management. Surg Endosc. 2013;27:2305–11.
5. Narula VK, Mikami DJ, Hazey JW. Endoscopic consideration in morbid obesity. Principles of flexible endoscopy for surgeons. New York: Springer Science + Business Media; 2013. p. 139–55.
6. Rodriguez-Grunert L, Galvao Neto MP, Alamo M, et al. First human experience with endoscopically delivered and retrieved duodenal-jejunal bypass sleeve. Surg Obes Relat Dis. 2008;4:55–9.
7. Tarnoff M, Rodriguez L, Escalona A, et al. Open label, prospective, randomized controlled trial of an endoscopic duodenal-jejunal bypass sleeve versus low calorie diet for pre-operative weight loss in bariatric surgery. Surg Endosc. 2009;23:650–6.
8. Schouten R, Rijs CS, Bouvy ND, et al. A multicenter, randomized efficacy study of the EndoBarrier gastrointestinal liner for presurgical weight loss prior to bariatric surgery. Ann Surg. 2010;251:236–43.
9. ValenTx Endo Bypass System: initial trial. 2009. www.valentx.com/news-1.php. Accessed 1 Aug 2014.
10. Ryou M, Ryan MB, Thompson CC. Current status of endoluminal bariatric procedures for primary and revision indications. Gastrointestinal Endoscopy Clin N Am. 2011;21:315–33.
11. Sandler BJ, Rumbaut R, Swain CP, et al. Human experience with an endoluminal, endoscopic, gastrojejunal bypass sleeve. Surg Endosc. 2011;25:3028–33.
12. De-Castrol ML et al. Safety and effectiveness of gastric balloons associated with hypocaloric diet for the treatment of obesity. Rev Esp Enferm Dig. 2013;105(9):529–36.
13. Buzga M et al. Effects of the intragastric balloon MedSil on weight loss, fat tissue, lipid metabolism, and hormones involved in energy balance. Obes Surg. 2014;24:909–15.
14. Alfredo G et al. Long-term multiple intragastric balloon treatment—a new strategy to treat morbid obese patients refusing surgery: prospective 6-year follow-up study. Surg Obes Relat Dis. 2014;10:307–12.
15. Vargas AM, Fernandez NC, Ortega Serrano J. Preoperative weight loss in patients with indication of bariatric surgery: which is the best method? Nutr Hosp. 2011;26(6):1227–30.
16. Drozdowski R et al. Small bowel necrosis as a consequence of spontaneous deflation and migration of an air-filled intragastric balloon—a potentially life-threatening complication. Wideochir Inne Tech Maloinwazyjne. 2014;9(2):292–6.

17. Fogel R, De Fogel J, Bonilla Y, De La Fuente R. Clinical experience of transoral suturing for an endoluminal vertical gastroplasty: 1 year follow up of 64 patients. Gastrointest Endosc. 2011;68(1):51–8.
18. Brethauer SA, Chand B, Schauer PR, et al. Transoral gastric volume reduction as intervention for weight management: 12 month follow up of TRIM trial. Surg Obes Relat Dis. 2012;8(3):296–303.
19. Deviere J, Ojeda Valdes G, Cuevas Herrera L, et al. Safety, feasibility, and weight loss after transoral gastroplasty: first human multicenter study. Surg Endosc. 2008; 22(3):589–98.
20. Familiari P, Costamagna G, Blero D, Le Moine O, Perri V, Boskoski I, et al. Transoral gastroplasty for morbid obesity; a multicenter trial with 1 year outcome. Gatrointestinal Endosc. 2011;74(6):1248–58.
21. De Jong K, Mathus-Vligen EM, Veldhuyzen EA, et al. Short-term safety and efficacy of the trans-oral endoscopic restrictive implant system for the treatment of obesity. Gastrointest Endosc. 2010;72:497–504.
22. Biertho L, Hould FS, Lebel S, Biron S. Transoral endoscopic restrictive implant system: a new endoscopic technique for the treatment of obesity. Surg Obes Relat Dis. 2010;4:203–5.
23. Cigaina V. Long-term follow up of gastric stimulation for obesity: the Mestre 8 year experience. Obes Surg. 2004;14 Suppl 1:S14–22.
24. Shikora SA. “What are the yanks doing?” The U.S experience implantable gastric stimulation for the treatment of obesity—update on ongoing clinical trials. Obes Surg. 2004;14 Suppl 1:S40–8.
25. Hasler WL. Methods of gastric electrical stimulation and pacing: a review of their benefits and mechanisms of action in gastroparesis and obesity. Neurogastroenterol Motil. 2009;21:229–43.
26. Bohdjalian A, Prager G, Aviv R, et al. One year experience with Tantalus: a new surgical approach to treat morbid obesity. Obes Surg. 2006;16:627–34.
27. D’Argent J. Gastric electrical stimulation as therapy for morbid obesity: preliminary results from a French study. Obes Surg. 2002;12 Suppl 1:21S–5.

25. Endoscopic Revisional Procedures After Bariatric Surgery

Dvir Froylich and Stacy Brethauer

Introduction

Obesity is a global epidemic [1] that is most effectively treated with bariatric surgery [2–5]. The number of bariatric procedures performed annually in the United States is estimated at 113,000 per year [6] and 340,000 worldwide [7]. Roux-en-Y gastric bypass (RYGB) is one of the most effective weight loss procedures, resulting in an average excess weight loss (EWL) of approximately 70 % at the first year [8]. Over the last decade, RYGB has been the most commonly performed procedure in the United States and worldwide [7]. Although the majority of patients have durable success after RYGB, 10–20 % of RYGB patients will loss less than 50 % of their excess weight at 1 year [2] or will experience significant weight regain (>15 % from nadir) [9–11]. Given the increasing number of procedures performed each year, the number of patients with suboptimal weight loss after RYGB will increase, presenting a major challenge for the bariatric team to handle. It has also been shown that recurrence of diabetes and other comorbidities after RYGB is associated with weight regain [12].

The etiology of weight regain after bariatric procedure is thought to be multifactorial. It's likely that combinations of genetic, physiologic, behavioral, and anatomic factors are the reasons for weight regain. Anatomical changes, like enlargement of the pouch size and stoma diameter of the gastrojejunostomy after RYGB, are speculated to be contributors to the loss of mechanical restriction after RYGB [13–16].

In some series, long-term weight loss was more likely to be achieved with a small size pouch [11]. The diameter of the gastrojejunostomy has also correlated with weight regain after RYGB [16]. Reoperation on a

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pouch or a dilated gastrojejunostomy requires a technically difficult surgical dissection with considerable risk of morbidity and mortality that reach 8–20 % [17–19] and 0.7–2.9 % respectively [17, 20, 21]. Given this high risk-to-benefit ratio, less invasive interventions have been developed to address this problem. Endolumenal techniques for reducing pouch size and stoma diameter have the potential to improve restriction with a lower morbidity and to arrest weight gain or achieve some degree of weight loss and comorbidity improvement.

Endoscopic Procedures for Weight Regain

Sclerotherapy

Sclerotherapy is a common treatment for bleeding esophageal varices. It was shown that 10 % of patients who were injected with sodium morrhuate developed esophageal stricture [22]. This could potentially be beneficial for the reduction of the gastrojejunostomy diameter for weight regain patients. Endoscopic sclerotherapy of the gastrojejunostomy with sodium morrhuate for weight regain after RYGB has been initially described in 2003 by Spaulding [23]. The technique was used for narrowing the diameter of the gastrojejunostomy in 20 patients by injecting an average of 6 cc of sodium morrhuate with an average of 1.3 treatments per patient. Gastrojejunostomy diameter was reduced to 9–10 mm after injection and at 6-month follow-up, 75 % of patients lost an average of 6.7 kg. Spaulding et al. [24] also published 12-month follow-up sclerotherapy results in 32 patients with dilated anastomosis. Their study showed that nearly 90 % of the injected patients either lost weight or maintained their weight after 1 year. The remaining 10 % continued to gain weight. Various retrospective trials reported weight loss of 5–23 kg after sclerotherapy that occurred in 30–64 % of patients during a follow-up period of 12–18 months [25–27]. Another study evaluated 231 patients after sclerotherapy found 4.5 kg average weight loss, which represented 18 % of average weight regained after RYGB. This study identified predictors of response to sclerotherapy. The greater the amount of weight regain from the nadir and the more sclerotherapy sessions performed predicted better response [28]. The diameter of the gastrojejunal anastomosis, although claimed to be a predictor of weight regain after RYGB [13, 16], was not a predictor of treatment response to sclerotherapy in this study [28].

Sclerotherapy of the gastrojejunal anastomosis after RYGB is considered a safe and inexpensive procedure with few complications including epigastric and throat pain. Rarely an anastomotic stricture can develop which requires endoscopic balloon dilation. Because of its simplicity, it could be performed without the need of special equipment for several times with relatively modest weight loss at a short-term follow-up. Further data is required to support the long-term efficacy of this approach.

Endoscopic Suturing for Stoma Size and Pouch Volume Reduction

Bard EndoCinch™ Suturing System (C.R. Bard, Inc., Murray Hill, NJ)

The EndoCinch™ was developed by Dr. Paul Swain for the endoscopic treatment of gastroesophageal reflux disease (GERD). The device involves placing suture through gastric tissue that is suctioned into a chamber and then endoscopically pushing a needle through the tissue. The two suture strands of the plication are then secured in place with a plug and ring anchor system (Fig. 25.1). Since EndoCinch™ is not a full-thickness tissue grasper, mucosal ablation with electrocautery is often applied during the procedure to enhance tissue approximation. The EndoCinch™ was used for stoma reduction size and not for pouch reduction. Endolumenal suturing for bariatric revision was first described by Thompson in 2004 [29]. In the same year Schweitzer reported a successful endoscopic stoma and pouch plication in four patients [30]. Since then, several devices for suturing and plication have shown various degrees of efficacy in the management of weight regain after RYGB. There is currently very limited evidence supporting the durability of endoscopic revisions after RYGB.

The RESTORe Trial

RESTORe was a prospective, multicenter, randomized, sham-controlled trial evaluating the effectiveness of transoral outlet reduction (TORe) procedure for inadequate weight loss or weight regain after

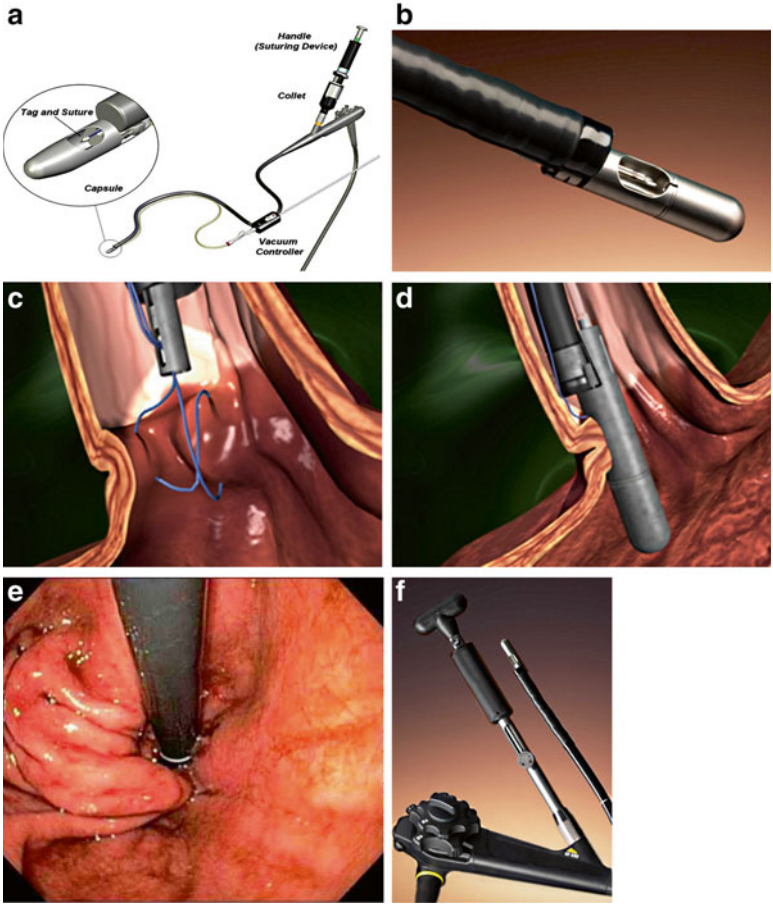

Fig. 25.1. The EndoCinch™ Suturing System. Copyright: C. R. Bard, Inc. Murray Hill, NJ, with permission.

RYGB [31]. This study used the Bard EndoCinch™ suturing system (C.R. Bard, Inc., Murray Hill, NJ). Seventy-seven patients with inadequate weight loss or weight regain and a dilated stoma (>2 cm) after RYGB were randomly assigned to undergo EndoCinch™ gastrojejunostomy diameter reduction versus a sham procedure. Successful stoma diameter reduction to less than 10 mm was achieved in 90 % of patients. After a 6-month follow-up 96 % of patients in the EndoCinch™ group achieved weight loss or weight stabilization, compared with 78 % in the

sham group ($P<0.001$). The authors concluded that this procedure is effective for arresting weight gain and achieving additional weight loss in a subset of patients. This study also found pre-procedure characteristics that were positive independent predictors for 6-month weight loss. Those factors included larger weight gains from nadir and increased percentage EWL at nadir. Negative predictors were greater pre-RYGB weight, increased waist circumference, and later weight gain after RYGB. While some of the results from this study were encouraging, the effects were not durable and further studies with this device were not pursued. EndoCinch™ is no longer commercially available.

StomaphyX™ (EndoGastric Solutions, Redmond, WA)

StomaphyX™ was an endoscopic plication device that use polypropylene H-fastener and can create full-thickness, serosa to serosa approximation (Fig. 25.2). The device used suction to draw tissue through an opening near the distal end of the device. A circular pleat of tissue is created 1 cm proximal to the anastomosis and a series of plications are performed circumferentially and proximally to narrow the pouch lumen. The first trial with the StomaphyX™ was conducted in 2010 by Mikami et al. [32]. They included 39 patients with at least 10 % regain of their

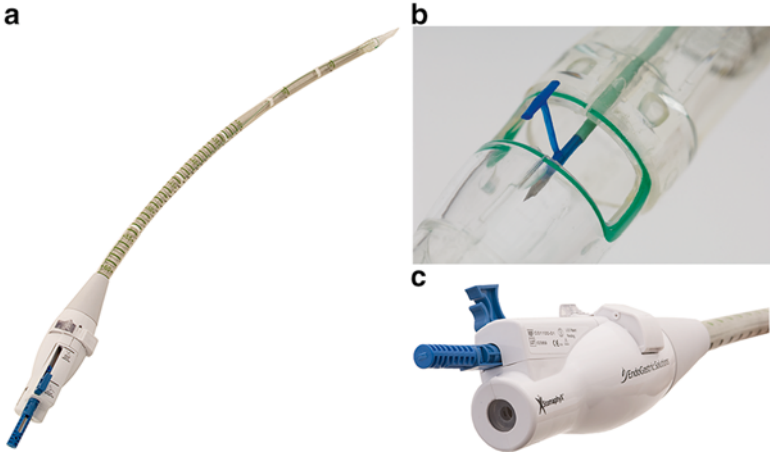

Fig. 25.2. StomaphyX™. Copyright: © 2014 EndoGastric Solutions, Inc. Redmond, WA, with permission.

lowest nadir weight at least 2 years after RYGB. Eighty-seven percent of patients experienced sore throat for less than 2 days, and 77 % of patients had epigastric pain that lasted a few days. Weight loss at 1 month in 34 patients was 5.4 kg (10.6 % EWL), and in 6 patients followed up to 1 year, weight loss was 10.0 kg (19.5 % EWL). Another study published in 2010 by Leitman et al. [33] included 64 patients who had either inadequate weight loss (7), dumping syndrome (42), or gastroesophageal reflux disease (15) after RYGB. An average of 23H-fasteners per case were placed starting just above the gastrojejunostomy and proceeding within the gastric pouch up to just below the gastroesophageal junction. Stoma diameter was reduced from 22 mm to 9 mm, and the length of the gastric pouch was reduced by 33 %. An average weight loss in this cohort was 7.3 kg (range 0–31 kg), and 79 % of patients did not regain weight during the follow-up period (3–12 months). Forty-two patients who underwent the procedure for dumping syndrome, symptoms were improved in all patients and completely resolved in 30 (71 %). In 80 % of patients with gastroesophageal reflux disease, symptoms improved, and in 20 %, there was complete symptom resolution. All but two of the patients were discharged on the day of the procedure, and one patient was observed for bleeding, which did not require transfusion. StomaphyX™ has been also used to revise pouches after failed vertical banded gastroplasty [34]. With a median follow-up of 4 months, patients lost an average of 10 kg. This study suggested promising results for the use of StomaphyX™ revision procedure. A recent randomized trial, however, evaluated the safety and effectiveness of the StomaphyX™ for revisional surgery in RYGB patients and reached disappointing results in the assessment of 12-month weight loss [35]. This trial was conducted on 90 patients that previously lost 60 % or more of EBW and reached a BMI of 35 or less after surgery followed by at least 20 % increase of the pre-RYGB excess weight. Patients were randomized to StomaphyX™ or sham procedure using 2:1 randomization. The primary efficacy end point was decrease of $\geq$15 % excess BMI loss and BMI < 35. At 12-month assessment end points achieved by 22.2 % after StomaphyX™ vs. 3.4 % after sham procedure. Adverse events were mostly mild (77.5 %). Only one serious adverse event was related to the procedure (gastric perforation, requiring laparoscopic exploration and repair). StomaphyX™ did not result in satisfactory weight reduction in this trial.

This device had several limitations and is no longer available for use. Although StomaphyX™ is capable of creating full-thickness plication,

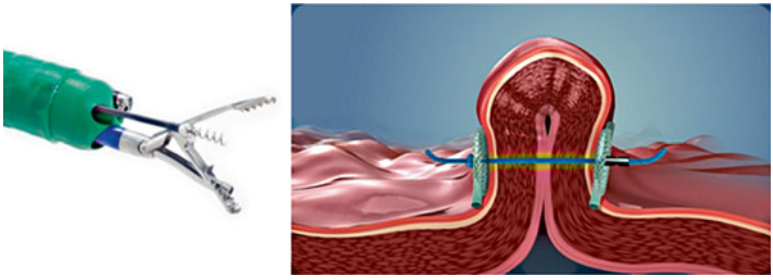

Fig. 25.3. EOS-Endosurgical Operating System (currently known as the IOP™-Incisionless Operating Platform™) and Snowshoe® Suture Anchors. Copyright: USGI Medical, San Clemente, CA, with permission.

it has difficulty reaching the fundus secondary to the rigidity of the overall apparatus. In addition, because of the large size of the device, obtaining tissue plication at different levels within the pouch was technically challenging.

Endosurgical Operating System—EOS (USGI Medical, San Clemente, CA)

The EOS is a transport® with four large channels (Fig. 25.3). This multi-lumen system has one channel for an endoscope and three operating channels and has been used extensively for stoma reduction and pouch reduction after RYGB in a procedure called ROSE (restorative obesity surgery endoscopic). The procedure starts with insertion of the TransPort® through the esophagus. The tissue approximator, called the g-Prox®, is advanced through the TransPort® and into the gastric pouch. A small corkscrew tissue grasper, called the g-Lix™, is also advanced through a channel in the TransPort® and used to secure tissue at the rim of the gastrojejunostomy anastomosis or gastric pouch and pull the tissue into the open tissue approximator. The tissue approximator is then closed on the tented tissue, creating a full-thickness tissue fold. A needle catheter within the tissue approximator is then driven through the secured tissue fold, and the first self-expanding tissue anchor, made of biocompatible nonabsorbable suture and nitinol, is advanced through the catheter and deployed. The tissue approximator is then opened and

the proximal tissue anchor released. Suture material connecting the TWO anchors is then tightened, thereby completing the tissue plication. In 2009 Ryou et al. [36] reported a pilot study of five patients. The procedure was feasible and safe without complications. The weight loss average was 7.8 kg after 3 month. Later that year a study of 20 patients from the same group was published [37]. Those patients had either regained weight from their post-bypass nadir (mean 13.4 kg regain) or didn't have adequate weight loss and also reported poor satiety after surgery. All patients had a dilated gastrojejunostomy averaging 25 mm (range 8–33 mm). This technique facilitated stoma diameter reduction by an average of 1.7 cm. An average pouch length of 7 cm (range 4–14 cm) was reduced by an average of 2.5 cm. Patients lost 5.8 kg at 1 month and 8.8 kg at 3 month. The procedure was completed in 17 patients out of 20. In one patient there was an equipment malfunction and in the other two, failure was related to difficulty maneuvering the tissue approximator (g-Prox) within a narrow pouch. The largest ROSE study was published in 2010 [38]. This was a multicenter study that enrolled at nine different institutions. Technical success was achieved in 112 out of 116 cases (97 %). In four cases, failure was due to anatomic limitation or device malfunction. All procedures were performed under general anesthesia and the majority of them (88 %) in the operating room. Three patients (<3 %) experienced an intraoperative superficial distal esophageal tear. One of them had an endoscopic clip placed as a precautionary measure. Of the 116 patients, 99 (85 %) were discharged the same day. The most common minor adverse events were pharyngitis (41 %), nausea and vomiting (12 %), and abdominal pain (13 %). All discharge complaints resolved during the post-procedural day. The stoma and pouch diameter and length were reduced by 50 % and 44 %, respectively. At 6 months after the procedure patients ($n=97$) had lost 18 % of excess weight (average 6.5 kg), representing 32 % of the weight regained since the nadir after gastric bypass. A longer follow-up on these patients weight loss at 12 month ($n=73$) was published [14]. Mean weight loss was 5.9 kg (14.5 % excess weight loss). Anchor presence was confirmed endoscopically in 61 of 66 patients (92 %) at 1 year.

The ROSE procedure seemed to be more easily applied to gastric pouch plication rather than the anastomosis and this may explain its limited utility. Currently the device is not commercially available in the United States but continues to be used by several investigators.

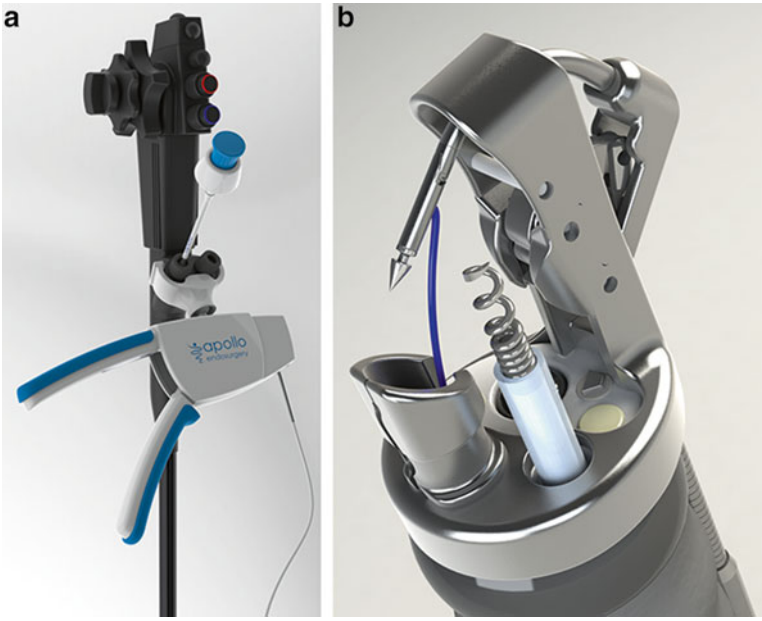

Fig. 25.4. OverStitch™ Endoscopic Suturing System. (**a**) OverStitch on Scope (**b**) OverStitch Endcap with Helix. Copyright: © 2014. Apollo Endosurgery. Austin, TX, with permission.

Overstitch™ Endoscopic Suturing System (APOLLO Endosurgery, Inc., Austin, TX)

The OverStitch™ is an endolumenal suturing system that mounts onto a double channel endoscope. The Overstitch™ is approved in the United States for approximation of tissue within the gastrointestinal tract and allows placement of sutures around the gastrojejunostomy which are then tightened to reduce the anastomotic aperture. The device is also able to create full-thickness tissue plication in the gastric pouch, which provides further volume reduction (Fig. 25.4). A US series reported their experience in performing outlet reductions in 25 patients with dilated gastrojejunostomy using the Overstitch™ [39]. Patients with weight regain after RYGB who had a dilated gastrojejunostomy, defined as an anastomosis diameter of >15 mm, were eligible for the procedure.

Interrupted stitches were placed transmurally at the anastomosis from the lower to upper margin and from right to left. In patients with a large pouch, pouch reduction was then performed with interrupted stitches placed in the distal pouch. The goal diameter of anastomotic reduction was reaching <12 mm. All 25 patients had a successful anastomotic diameter reduced to <12 mm, by placement of a mean of three interrupted stitches (range 1–7) at the anastomosis and two interrupted stitches (range 1–5) to reduce the pouch size. At the end of the procedure the mean anastomosis diameter was 6 mm (range 3–10). Three intraprocedural complications were reported including a small esophageal abrasion from the overtube that was successfully treated with fibrin glue. Two patients had arterial bleeding after stitch placement. The bleeding stopped upon tissue plication and no further therapy was needed. Several post-procedural complications occurred including bleeding in two patients, one of which required transfusion. Four patients also reported post-procedural nausea and emesis with two patients experiencing severe emesis with upper endoscopy showing torn stitches. One of the four patients had stenosis of the gastrojejunostomy and required balloon dilation. The mean weight loss at 3 month ($n=21$), 6 month ($n=17$), and 12 month ($n=16$) was 11.5 kg (range 1.4–36.3), 11.7 kg (range 2.3–27.2), and 10.8 kg (range 0.7–27.2), respectively. A recent comparison by the same group compared the Overstitch™ to a superficial thickness device—the Bard EndoCinch™ (C.R. Bard, Inc., Murray Hill, NJ) [40]. In this matched cohort trial, 59 patients in each group who had dilated gastrojejunostomy apertures (>20 mm) and who had experienced weight regain after RYGB were studied. Significantly fewer stitches were required to achieve smaller GJ anastomosis diameters in the Overstitch™ than the TORe group. Excess weight loss was significantly greater in this group. At 6 months the EWL was 20.4 ± 3.3 % after Overstitch™ TORe versus 8.1 ± 2.5 % after EndoCinch™ TORe; $P<0.01$. EWL at 1 year was 18.9 ± 5.4 % after Overstitch™ versus 9.1 ± 2.3 % after EndoCinch™ $P=0.03$. Both groups had one patient each who required blood transfusion due to bleeding. This study shows an advantage of the Overstitch™ as a full-thickness device over the superficial device in terms of weight loss.

The Overstitch™ procedure for gastrojejunostomy diameter and pouch reduction seems to be feasible and generally well tolerated. The device is capable of grasping larger and deeper tissue bites which makes approximation technically attainable. The system showed it is capable of treating bariatric complications such as leaks and marginal ulcers as

well, though this evidence is not currently robust. The device is available for use in the United States and is used by numerous practices in the management of weight regain after RYGB. The durability of this treatment, though, remains uncertain.

Over the Scope (OTSC®-clip)

The OTSC®-clip (Ovesco AG, Tübingen, Germany) is made of Nitinol and is mounted on a transparent applicator cap placed on the tip of an endoscope (over the scope). Tissue is approximated by two endoscopic forceps. The clip is released and the resultant closure clamps the tissue in place. There are several versions of this clip, including blunt toothed, sharp-toothed, and long-toothed (Fig. 25.5). The OTSC®-clip provides more durable closure than standard clips because of its wider mouth and ability to grasp larger amounts of tissue [41]. In addition, full-thickness closure is achievable because of greater compressive force [42].

In 2011 Heylen et al. reported the results of the OTSC®-clip used in 94 patients with a dilated gastrojejunostomy and 10 % weight gain after RYGB [43]. The mean stoma diameter reduced from 35 mm to 8 mm after one or two clips placement without intraprocedural complications.

Fig. 25.5. The OTSC® clip. Copyright: Ovesco Endoscopy AG, Tuebingen/Germany, with permission.

Five patients suffered from post-procedure dysphagia. Endoscopic dilatation was required in two patients who had unresolved symptoms. The mean BMI at 3-month follow-up dropped from 45 kg/m^2 to 29.7 kg/m^2. At 1 year the mean BMI was 27.4 kg/m^2. An oral contrast radiographic study at 3-month post-procedure identified clips in 27 patients (29 %). This may not reflect the true number present, however, due to the clip's low level of radio-opacity.

Data regarding this technique for resizing pouch and stoma diameter are extremely sparse. This commercially available device may be more applicable in the management of complications such as leaks and fistulas. A multicenter experience with OTSC® clipping for endoscopic management of GI defects was recently published [44]. OTSC® clips were attempted to close fistulas, perforation, and leaks. Successful closure of perforations (90 %) and leaks (73 %) was significantly higher than that of fistulas (42.9 %) ($P > 0.05$). Patients who had a rescue therapy and those who had the clip placed for fistula were significantly more likely to fail in the long term.

Endoscopic Management of Bariatric Surgery Complications

Gastrogastric Fistula

Gastrogastric fistula (GGF) is a potential complication after RYGB. The incidence ranges between 0.6 and 16 % [45]. The GGF etiologies include leak, abscess, staple line failure, ischemia, ulceration, and incomplete gastric pouch transection. Patients with GGF may be asymptomatic or have nonspecific abdominal pain, weight regain, or marginal ulcer at the gastrojejunostomy. A high index of suspicion is the key to diagnosis. Flexible upper endoscopy and upper gastrointestinal contrast studies are complementary modalities for the diagnosis of GGF. GGF is located at the proximal pouch in the majority of cases [46]. The indication for intervention depends on the extent of symptoms present. Some symptomatic patients require revisional surgical procedures which are technically challenging and associated with high morbidity and mortality [17–21]. An endoscopic approach for GGF treatment has been shown to be a procedure with much less morbidity but technical feasibility and durability present challenges with this

approach. The endoscopic techniques include clip placement, gluing, stent placement, gastrojejunostomy dilatation, and suturing. Fernandez-Esparrach et al. reported their endoscopic experience with various techniques [46]. In this study 95 patients with GGF after RYGB were treated. The GGF were successfully closed initially in 90 (95 %) patients. 75 % were treated by EndoCinch suturing and 25 % by hemoclips. In some cases, tissue fibrin glue or argon plasma coagulation was also ingaged. Of the 90 patients, GGF was reopened in 59 patients (65 %) that had an endoscopy at an average follow-up of 177 ± 202 days. Of the 59 patients, 28 underwent repeated endoscopic treatment but 20 of these presented later with recurrence once more. The only significant predictor for GGF recurrence in this study was a fistula diameter >20 mm. Other reports didn't show any better results for GGF endoscopic closure [47, 48]. Despite higher risks, surgical therapy for large symptomatic GG fistulas remains standard practice although endoscopic therapy may be more appropriate as a lower risk strategy in selected cases.

Summary

As the number of surgical procedures for treatment of obesity and its comorbidities increases, so will the number of patients with weight regain or suboptimal weight loss. Endolumenal procedures after a bariatric surgery as summarized in Table 25.1 are far from being the sole solution for this problem and results have been largely disappointing thus far. However, when considering obesity as a lifelong disease, the ability to repeat endolumenal interventions with a relatively low risk of morbidity may provide the justification to continue pursuing this technology and these types of procedures. More controlled trials are necessary to assess the long-term potential of endolumenal revisions after weight loss procedures.

Table 25.1. Endoscopic device characteristics.

Device	Safety	Full-thickness tissue approximation	Pouch reduction	Gastrojejunostomy diameter reduction	Experience	Repeatability	Durability	Availability	Comments
Sclerotherapy	++	–	–	+	Spaulding [23], Loewen and Barba [25], Catalano [26], Madan [27], Abu Dayyeh [28],	++	–	+	
EndoCinch	+	–	–	+	Thompson [29], Schweitzer [30], Thompson (Restore Trial) [31]	++	–	–	Suction-based device
StomaphyX	+	+	+	+	Mikami et al. [32], Leitman et al. [33], Manouchehri [34], Eid [35]	++	–	–	Large size device Hard to reach the fundus

EOS	+	+	++	+	Ryou [36], Mullady et al. [37], Horgan et al. [38]	++	−	−	Easier for plication More difficult for stoma reduction
Overstitch	+	+	+	+	Jirapinyo et al. [39]	++	−	+	Currently available for tissue approximation within the GI tract
OTSC-clip	++	+	−	+	von Renteln et al. [41], Heylen et al. [43], Banerjee 2012, Haito-Chavez [44]	++	−	+	More applicable for leaks than weight regain

From Dakin GF et al. Endoluminal revision of gastric bypass for weight regain—a systematic review. Surg Obes Relat Dis. 2013 May–Jun;9(3):335–42. With permission from Elsevier Limited

References

1. World Health Organization. A.f. Obesity and overweight. http://who.int/mediacenter/factsheets/fs311/en/. Accessed Sept 2011.
2. Brolin RE. Bariatric surgery and long-term control of morbid obesity. JAMA. 2002;288(22):2793–6.
3. Sjostrom L et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004;351(26):2683–93.
4. Sjostrom L et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med. 2007;357(8):741–52.
5. Schauer PR et al. Bariatric surgery versus intensive medical therapy for diabetes—3-year outcomes. N Engl J Med. 2014;370(21):2002–13.
6. Livingston EH. The incidence of bariatric surgery has plateaued in the U.S. Am J Surg. 2010;200(3):378–85.
7. Buchwald H, Oien DM. Metabolic/bariatric surgery worldwide 2011. Obes Surg. 2013;23(4):427–36.
8. Buchwald H et al. Bariatric surgery: a systematic review and meta-analysis. JAMA. 2004;292(14):1724–37.
9. Elder KA, Wolfe BM. Bariatric surgery: a review of procedures and outcomes. Gastroenterology. 2007;132(6):2253–71.
10. Magro DO et al. Long-term weight regain after gastric bypass: a 5-year prospective study. Obes Surg. 2008;18(6):648–51.
11. Christou NV, Look D, Maclean LD. Weight gain after short- and long-limb gastric bypass in patients followed for longer than 10 years. Ann Surg. 2006;244(5):734–40.
12. Chikunguwo SM et al. Analysis of factors associated with durable remission of diabetes after Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2010;6(3):254–9.
13. Heneghan HM et al. Influence of pouch and stoma size on weight loss after gastric bypass. Surg Obes Relat Dis. 2012;8(4):408–15.
14. Thompson CC et al. Stoma size critical to 12-month outcomes in endoscopic suturing for gastric bypass repair. Surg Obes Relat Dis. 2012;8(3):282–7.
15. Roberts K et al. Size matters: gastric pouch size correlates with weight loss after laparoscopic Roux-en-Y gastric bypass. Surg Endosc. 2007;21(8):1397–402.
16. Abu Dayyeh BK, Lautz DB, Thompson CC. Gastrojejunal stoma diameter predicts weight regain after Roux-en-Y gastric bypass. Clin Gastroenterol Hepatol. 2011;9(3):228–33.
17. Khaitan L et al. Laparoscopic revision of bariatric procedures: is it feasible? Am Surg. 2005;71(1):6–10. discussion 10–2.
18. Gagner M et al. Laparoscopic reoperative bariatric surgery: experience from 27 consecutive patients. Obes Surg. 2002;12(2):254–60.
19. Hamdi A et al. Midterm outcomes of revisional surgery for gastric pouch and gastrojejunal anastomotic enlargement in patients with weight regain after gastric bypass for morbid obesity. Obes Surg. 2014;24(8):1386–90.
20. Linner JH, Drew RL. Reoperative surgery—indications, efficacy, and long-term follow-up. Am J Clin Nutr. 1992;55(2 Suppl):606S–10S.

21. Jones Jr KB. Revisional bariatric surgery—potentially safe and effective. Surg Obes Relat Dis. 2005;1(6):599–603.
22. Naritaka Y et al. Long-term results of endoscopic injection sclerotherapy in 602 patients with esophageal varices. Hepatogastroenterology. 2008;55(88):2096–102.
23. Spaulding L. Treatment of dilated gastrojejunostomy with sclerotherapy. Obes Surg. 2003;13(2):254–7.
24. Spaulding L, Osler T, Patlak J. Long-term results of sclerotherapy for dilated gastrojejunostomy after gastric bypass. Surg Obes Relat Dis. 2007;3(6):623–6.
25. Loewen M, Barba C. Endoscopic sclerotherapy for dilated gastrojejunostomy of failed gastric bypass. Surg Obes Relat Dis. 2008;4(4):539–42. discussion 542–3.
26. Catalano MF et al. Weight gain after bariatric surgery as a result of a large gastric stoma: endotherapy with sodium morrhuate may prevent the need for surgical revision. Gastrointest Endosc. 2007;66(2):240–5.
27. Madan AK et al. Endoscopic sclerotherapy for dilated gastrojejunostomy after gastric bypass. J Laparoendosc Adv Surg Tech A. 2010;20(3):235–7.
28. Abu Dayyeh BK et al. Endoscopic sclerotherapy for the treatment of weight regain after Roux-en-Y gastric bypass: outcomes, complications, and predictors of response in 575 procedures. Gastrointest Endosc. 2012;76(2):275–82.
29. Thompson, CC. Novel endoscopic approaches to common bariatric postoperative complications. Digestive Disease Week, AGES Video forum. 2004. New Orleans, LA
30. Schweitzer M. Endoscopic intraluminal suture plication of the gastric pouch and stoma in postoperative Roux-en-Y gastric bypass patients. J Laparoendosc Adv Surg Tech A. 2004;14(4):223–6.
31. Thompson CC et al. Endoscopic suturing for transoral outlet reduction increases weight loss after Roux-en-Y gastric bypass surgery. Gastroenterology. 2013;145(1): 129–37. e3.
32. Mikami D et al. Natural orifice surgery: initial US experience utilizing the StomaphyX device to reduce gastric pouches after Roux-en-Y gastric bypass. Surg Endosc. 2010;24(1):223–8.
33. Leitman IM et al. Early results of trans-oral endoscopic plication and revision of the gastric pouch and stoma following Roux-en-Y gastric bypass surgery. JSLS. 2010;14(2):217–20.
34. Manouchehri N et al. Natural orifice surgery: endoluminal pouch reduction following failed vertical banded gastroplasty. Obes Surg. 2011;21(11):1787–91.
35. Eid GM et al. StomaphyX vs a sham procedure for revisional surgery to reduce regained weight in Roux-en-Y gastric bypass patients: a randomized clinical trial. JAMA. 2014;149(4):372–9.
36. Ryou M et al. Pilot study evaluating technical feasibility and early outcomes of second-generation endosurgical platform for treatment of weight regain after gastric bypass surgery. Surg Obes Relat Dis. 2009;5(4):450–4.
37. Mullady DK, Lautz DB, Thompson CC. Treatment of weight regain after gastric bypass surgery when using a new endoscopic platform: initial experience and early outcomes (with video). Gastrointest Endosc. 2009;70(3):440–4.
38. Horgan S et al. Incisionless revision of post-Roux-en-Y bypass stomal and pouch dilation: multicenter registry results. Surg Obes Relat Dis. 2010;6(3):290–5.

39. Jirapinyo P et al. Evaluation of an endoscopic suturing device for transoral outlet reduction in patients with weight regain following Roux-en-Y gastric bypass. Endoscopy. 2013;45(7):532–6.
40. Kumar N, Thompson CC. Comparison of a superficial suturing device with a full-thickness suturing device for transoral outlet reduction (with videos). Gastrointest Endosc. 2014;79(6):984–9.
41. von Renteln D, Vassiliou MC, Rothstein RI. Randomized controlled trial comparing endoscopic clips and over-the-scope clips for closure of natural orifice transluminal endoscopic surgery gastrotomies. Endoscopy. 2009;41(12):1056–61.
42. Committee AT et al. Endoscopic closure devices. Gastrointest Endosc. 2012; 76(2):244–51.
43. Heylen AM et al. The OTSC(R)-clip in revisional endoscopy against weight gain after bariatric gastric bypass surgery. Obes Surg. 2011;21(10):1629–33.
44. Haito-Chavez Y et al. International multicenter experience with an over-the-scope clipping device for endoscopic management of GI defects (with video). Gastrointest Endosc. 2014;80(4):610–22.
45. Csendes A et al. Incidence of marginal ulcer 1 month and 1 to 2 years after gastric bypass: a prospective consecutive endoscopic evaluation of 442 patients with morbid obesity. Obes Surg. 2009;19(2):135–8.
46. 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.
47. Spaun GO et al. Endoscopic closure of gastrogastric fistulas by using a tissue apposition system (with videos). Gastrointest Endosc. 2010;71(3):606–11.
48. Bhardwaj A et al. Endoscopic repair of small symptomatic gastrogastric fistulas after gastric bypass surgery: a single center experience. Obes Surg. 2010;20(8):1090–5.

26. Natural Orifice Transluminal Endoscopic Surgery (NOTES™)

Eric G. Sheu and David W. Rattner

Introduction

Natural orifice transluminal endoscopic surgery (NOTES) refers to the performance of surgical procedures using transvisceral access to the body cavities. By eliminating body wall incisions, NOTES offers the potential for less postoperative pain, improved cosmesis, and faster functional recovery.

Less than a decade after the first report of a NOTES procedure in an animal model, an explosion of research has lead to the development of several novel procedures. This work has left the lab and is already being translated to the bedside. Thousands of NOTES procedures have been performed across the globe. Peroral endoscopic myotomy (POEM) is a procedure not even imagined 10 years ago already threatening to replace traditional Heller myotomy as first line therapy for achalasia. Moreover, the interest spurred by NOTES has had major "trickle-down" effects, with spillover benefits for interventional flexible endoscopic and laparoscopic surgery.

This chapter will review the history of NOTES, the role of SAGES/ASGE (The Society of American Gastrointestinal Surgeons/American Society of Gastrointestinal Endoscopy) in fostering NOTES, a brief update on the current status of various NOTES procedures, and highlight remaining challenges for the future.

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History

The first pure NOTES procedure—a transgastric peritoneoscopy in a porcine model—was published in 2004 [1]. Subsequently, a video case report of a human transgastric appendectomy was presented at the 2005 SAGES meeting [2]. These reports spurred an explosion of laboratory work that demonstrated multiple other NOTES procedures could be safely performed in animal models [3–5].

In October 2005, a joint meeting sponsored by SAGES and ASGE was held in New York City. This meeting spawned the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR). NOSCAR was founded to facilitate research and communication among investigators, thereby promoting the safe development of NOTES procedures for clinical practice.

One outcome of the initial October 2005 meeting was the drafting of the first White Paper on NOTES [6]. This paper defined the initial barriers to NOTES—including safe access to the peritoneum, gastric closure, prevention of peritoneal infection, development of a multitasking platform, and the management of complications related to peritoneal insufflation. The group also identified several key research questions to be answered to overcome these barriers.

Five years later, the 2nd SAGES/ASGE NOTES white paper was published and summarized the progress made in surmounting the originally identified challenges [7]. All the key research questions had been tackled—most with NOSCAR sponsorship. Of the initially identified barriers, several had been answered completely (e.g., peritoneal infection, physiologic complications) while significant technologic progress had been made to address the others (Table 26.1).

Clinical Trials

Transvaginal NOTES vs. laparoscopic cholecystectomy
Transanal NOTES hybrid sigmoid colectomy
Transvaginal NOTES sleeve gastrectomy
Transvaginal ventral hernia repair
Transrectal NOTES appendectomy

Table 26.1. Progress on seminal questions of first NOTES white paper.

Question	Progress
Peritoneal access	All access points in human clinical practice
Gastric closure	New devices for closure developed, testing in animal models
Prevention of infection	Minimal peritoneal contamination demonstrated after transgastric access
Suturing and anastomotic devices	New devices approved or in pipeline
Maintaining spatial orientation	Image registration and other techniques being explored
Development of a multitasking platform	Device prototypes in development
Management of intra-peritoneal complications and hemorrhage	Currently through laparoscopic rescue in hybrid approaches. Better instrumentation still required
Physiologic untoward events caused by NOTES	Risks, physiology, and treatment documented in animal and humans
Training	Advanced flexible endoscopic fellowships

Amazingly, in only 5 years, over six human clinical trials of NOTES procedures were underway in the US alone, some for procedures not envisioned at the first NOSCAR meeting.

The pace of innovation with NOTES procedures was rapid during the early years, but the current economic and regulatory environment have slowed the rate of innovation in the past several years (Fig. 26.1).

Current Status of Procedures

The procedures and operations that have been attempted with a NOTES approach are too exhaustive to document here. Suffice to say that nearly every conceivable abdominal, pelvic, and thoracic operation has been attempted with a NOTES approach in animal models. Below we will focus on the most common or promising NOTES operations in development today, grouped by visceral access point (Table 26.2).

Transesophageal

The best example of transesophageal access is peroral endoscopic myotomy (POEM) (Fig. 26.2). POEM was first described in 2007 in an animal model [8]. Subsequently, POEM has become the most clinically

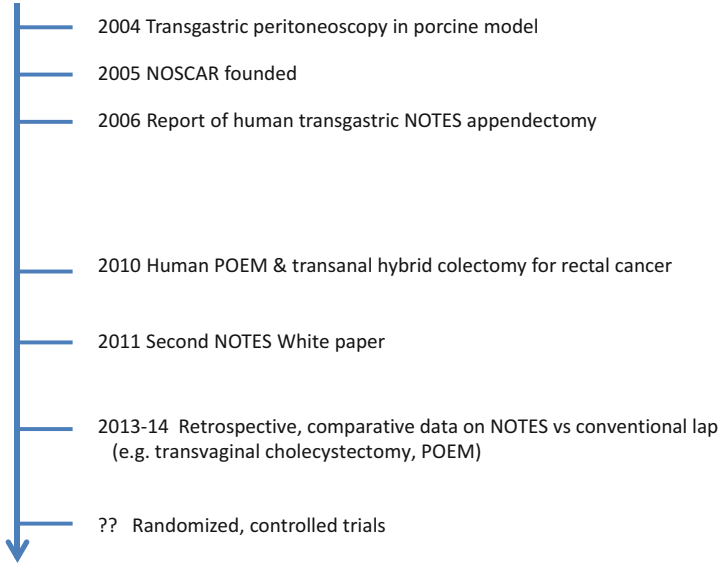

Fig. 26.1. Timeline of NOTES progress.

Table 26.2. Prototype NOTES procedures grouped by visceral access site.

Visceral access	Prototype procedure
Esophagus	Heller myotomy (POEM)
Stomach	Diagnostic peritoneoscopy
Vagina	Cholecystectomy
Rectum	Proctocolectomy

successful NOTES procedure, driven initially by Dr. Haru Inoue in Japan [9].

The technical details of POEM are reviewed elsewhere in this book. It is now clear that POEM is safe in experienced hands and, at least in the medium term, an effective treatment for achalasia. There had been initial concern that the lack of an accompanying anti-reflux procedure with POEM might lead to increased rates of GERD and, potentially, recurrent dysphagia. Thus far, retrospective, non-controlled studies have not observed high rates of symptomatic reflux [10]. Long term and

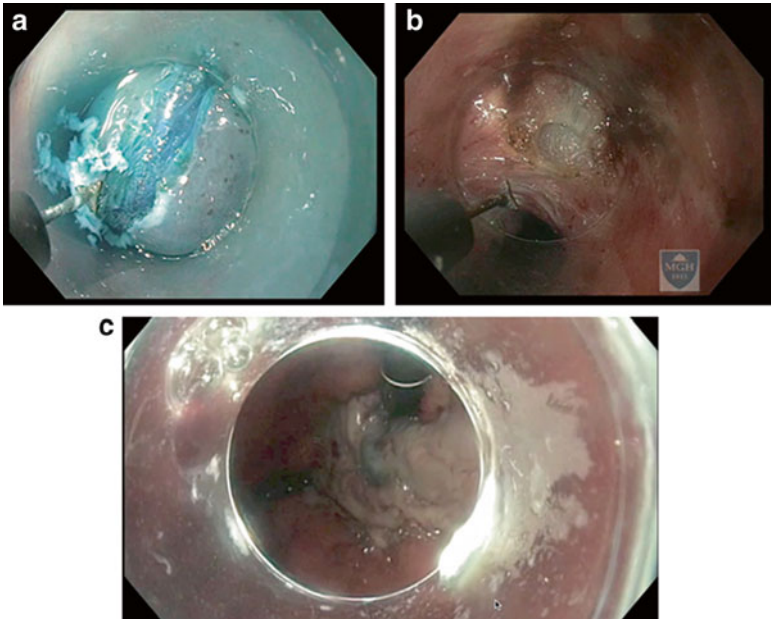

Fig. 26.2. Per oral endoscopic myotomy. (**a**) Creation of the esophageal mucosotomy. (**b**) Division of circular esophageal muscle fibers within submucosal tunnel. (**c**) Retroflexed view within stomach showing the completed myotomy extending past the GE junction.

randomized, controlled studies comparing POEM and laparoscopic Heller myotomy are still needed.

Transesophageal access has also been explored for mediastinal and thoracic procedures. Using a submucosal flap tunnel method, like POEM, transesophageal NOTES has been used for mediastinal lymph node biopsy and lymphadenectomy, pericardial windows, and pleural biopsy in animal models [11]. One of the limitations of transesophageal access is the consequences of an esophageal leak. Although these can frequently be managed nonsurgically, the morbidity of mediastinitis is significant. Another limitation of transesophageal access is the restricted flexibility imposed by the narrow intramural esophageal tunnel used to transgress the esophageal wall. Finally, since the esophagus cannot be fully sterilized, it is not a good route for placing foreign bodies or implants.

Transgastric

The first NOTES procedures used transgastric access to the peritoneal cavity. Diagnostic peritoneoscopy, appendectomy, cholecystectomy, oopherectomy, and more complex procedures such as splenectomy have all been successfully performed via transgastric access in animal models.

Many of the initial barriers delineated in the 1st SAGES white paper dealt with transgastric access. These barriers continue to limit full use of transgastric NOTES. Formation of the gastrotomy has been complicated by high rates of iatrogenic injury to the abdominal wall, viscera, or vessels [12]. Performance of procedures in the upper abdomen requires a retroflexion of the gastroscope which limits mobility, and hence, this access route can add technical challenges not present in laparoscopy. Thus far, human transgastric NOTES has been limited to less technically complex procedures where the endoscope can be used in an in-line, or straight, position such as appendectomy or peritoneoscopy.

Significant progress towards improving gastrotomy closure has been made, with several new devices being tested. Importantly, animal studies have shown that peritoneal contamination is not likely to be clinically significant from transgastric access—akin to a clean-contaminated open or laparoscopic case [13, 14]. However, given that transgastric NOTES is being pursued to replace clean operations, the reliability of visceral closure will need to be extremely high to allow routine clinical practice. Nevertheless, transgastric staging peritoneoscopy remains an enticing approach for evaluating malignancies that require biliary stenting or other endoscopic interventions in preparation for aggressive local therapies such as surgery or radiotherapy. The procedure was among the top candidates listed for initial human application at the 2010 NOSCAR meeting, given its wide potential application and benefit, as well as the availability of appropriate instrumentation [7].

Transvaginal

Transvaginal access has gained significant traction due to its advantages of an in-line endoscopic view for abdominal operations and a reliable and safe visceral closure method derived from long experience in the gynecologic field. Indeed, one of the first NOTES-types procedures was a hybrid transvaginal cholecystectomy performed during vaginal hysterectomy incorporating transvaginal and abdominal ports [15].

Transvaginal cholecystectomy has become the most common clinical hybrid NOTES procedure. It is estimated over 4000 have been performed worldwide [3]. A large experience has been reported in Europe through the German registry [16]. In many parts of the world, transvaginal cholecystectomy is considered a fairly standard approach. To date, primarily due to instrument limitations, transvaginal cholecystectomy is still a hybrid NOTES procedure, with abdominal ports used for securing the bile duct and vascular supply.

Dissemination of this technique is hindered by its applicability only to women, as well as residual functional and cultural concerns over transvaginal access. Injuries to the ureter, bladder, and rectum have been reported, although in most studies, the overall complication rate with NOTES transvaginal cholecystectomy is equivalent to laparoscopic cholecystectomy. Some critics have raised concerns about the impact of transvaginal access on sexual and reproductive function. Several studies addressing this topic in transvaginal cholecystectomy have not borne these concerns out, and there is fairly extensive data in the gynecologic literature that should also allay concerns [17, 18].

A small randomized trial of transvaginal vs. multi-trocar needlescopic cholecystectomy showed decreased pain scores and improved cosmesis with the NOTES approach. There was no observed difference in return to work or complications, although the study was underpowered [19]. A larger multi-institution clinical trial comparing NOTES transvaginal cholecystectomy with laparoscopic cholecystectomy sponsored by NOSCAR is underway.

Transanal

Transanal access, particularly for colorectal resection, offers many potential advantages. Most importantly, the access viscerotomy is through the target organ and is removed at the time of resection. Multiple tested and reliable means of closure are available, included stapled anastomosis or hand-sewn coloanal anastomosis. With the transanal endoscopic microsurgery (TEM) experience, a multitasking instrumentation platform is available and familiar to many surgeons. Lastly, transanal access provides immediate access to the correct tissue planes for dissection, allowing potentially improved visualization for a “bottom-up” dissection in the pre-sacral space for low rectal resections (Fig. 26.3) [20].

The first hybrid NOTES transanal rectal resection with laparoscopic assistance was reported in 2010 [21]. Since that time, several series of

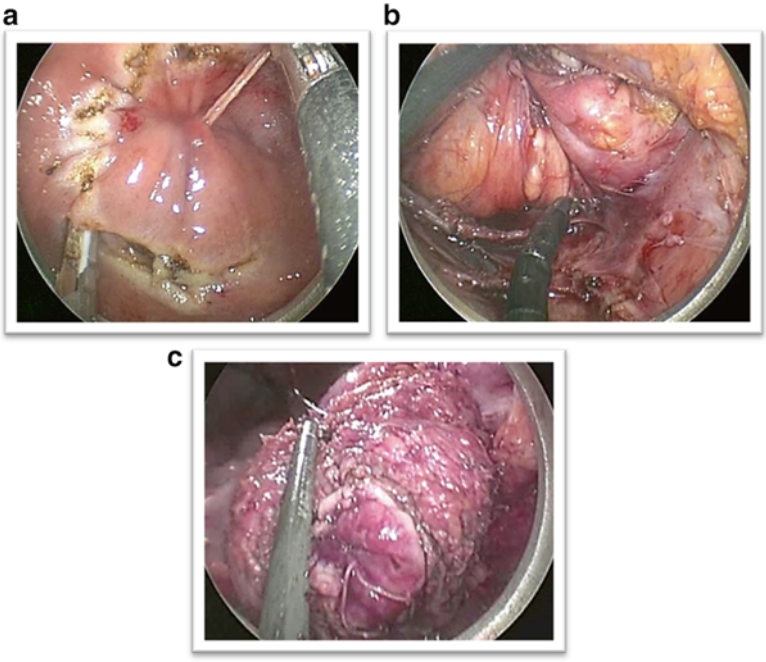

Fig. 26.3. Transanal NOTES colectomy. (**a**) Transrectal access by full thickness circumferential rectal division using the ultrasonic dissector. The purse string suture marks the distal resection margin. (**b**) "Bottom-up" NOTES dissection of the pre-sacral space. (**c**) Transanal extraction of rectal resection specimen.

hybrid NOTES colorectal resection for rectal cancer have been reported, and it is estimated >400 human procedures have been performed worldwide [20, 22]. These series have demonstrated feasibility and safety. Importantly, they have demonstrated excellent oncologic outcomes, with good lymph node harvest and negative pathologic margins.

Due to current limitations with instrumentation, laparoscopic assistance is still required for splenic flexure takedown and vascular pedicle ligation. However, transanal sigmoid resection offers considerable promise for benefits: the transanal view allows precise identification of the distal tumor resection margin, improved visualization for dissection in obese patients and the narrow pelvis, and NOTES specimen extraction eliminates the problems associated with a larger abdominal incision, including increased pain, wound infections, and hernia. Future trials will need to confirm whether these benefits are realized and importantly, assess long-term oncologic outcomes.

Ongoing Challenges

As discussed, considerable progress has been made towards overcoming the challenges associated with NOTES. In particular, concerns over physiologic and infectious complications of transvisceral access to the peritoneum have largely been addressed. Several of the other obstacles noted in the 1st NOTES white paper have been lowered but remain.

Future Challenges

- Transgastric access and closure
- Regulatory hurdles to device development
- Reimbursement and cost incentives
- Improved instrumentation and platform to go from hybrid to pure NOTES
- Training paradigm
- Randomized data to assess outcomes

Technical challenges related to placement and closure of viscerotomy—particularly for transgastric access—still exist. Devices for gastrotomy closure have improved and been tested with some reliability including over the scope clips. It is likely feasible to safely achieve natural orifice access with laparoscopic assistance to guide placement of the viscerotomy and to test closure. However, a reliable method for safely creating and orienting the viscerotomy, particularly in the stomach, using a pure NOTES approach is lacking. Similarly, a pure NOTES or endoscopic method to test the integrity visceral closure intra-procedurally has not yet been described.

Technical problems related to instrumentation deficiencies that would allow pure NOTES procedures are currently being overcome by use of hybrid laparoscopic assisted procedures. In particular, current instrumentation for hemostasis—clip appliers, vessel sealing, and other energy devices—remain inferior on flexible NOTES platforms. Endoscopic stapling and anastomotic devices have been introduced but remain suboptimal. The ongoing development of endoscopic suturing devices, however, has been more successful with commercially available devices now on the market.

Likely the greatest challenge to NOTES is the current regulatory and financial environment, which could slow development of needed new devices and technology. Previously, devices could be more quickly approved using the FDA 510K process. Physicians were allowed to use approved devices for "off-label" indications. Increasing scrutiny is being applied to this process, and more devices are being required to undergo the more arduous, costly, and time-consuming pre-marketing approval application (PMA). As many of the companies focusing on NOTES device development are smaller start-ups with smaller budgets, these regulatory changes are major challenges to further innovation.

Finally, with the recent changes of healthcare reform, greater attention will be paid going forward to the costs of new procedures. It must be understood that the initial costs of a new, innovative procedure will be greater at its outset than in its final form. We must not lose sight of the potential longer term benefits of a new procedure, particularly in societal costs that are often not captured with current studies (e.g., disability, return to work, long-term complication and re-op rates). In the early days of laparoscopic cholecystectomy, costs were higher than open surgery, but over time, the cost-benefit ratio has clearly swung in favor of laparoscopy. Developing a viable financial strategy to nurture innovative procedures through their more costly infancy must be a priority for hospital and medical leaders.

Future Directions

NOTES currently stands at an exciting transitional phase. Many of the initial physiologic concerns and technical limitations have been addressed or have promising solutions in the pipeline. Many NOTES procedures have graduated from the lab and been successfully introduced into human practice. Going forward, our goal must be to continue clinical translation, optimize technique and costs, and rigorously assess NOTES procedures for safety and comparative efficacy.

The "trickle down" benefits associated with NOTES have been significant. Many instruments and devices developed with NOTES in mind have found uses in interventional endoscopy and single site laparoscopic surgery. Cross-fertilization between these fields, particularly in training and development of technical skills, will be critical to the future of endoscopic surgery. Of interest is the potential application of robotics for single port and endoscopic surgery. Articulated, flexible robotic instrumentation could aid in overcoming some of the triangulation and

visualization challenges associated with current single-site laparoscopic platforms. The cost of the current computer assisted surgery systems is prohibitive, but if these costs come down there may be potential applicability for this technology in NOTES. Improvements in instrumentation will be necessary to drive the transition from hybrid to pure NOTES procedures.

The 2nd NOTES white paper noted debate on the ideal entry procedure for NOTES. Since that time, POEM has clearly succeeded as the first pure NOTES operation in widespread practice. Transanal NOTES colectomy remains technically challenging but has many conceptual advantages supporting its candidacy as the second NOTES procedure to enter wider clinical practice. It is critical that clinical entry continue in the hands of experienced teams with prospective documentation of outcomes.

The past decade has seen development of NOTES procedures that are safe and effective. The next major hurdle is to put NOTES to the test in randomized clinical trials against standard laparoscopy. The time is nearing to see whether NOTES will offer the originally envisioned patient benefits of reduced pain, improved cosmesis, and faster functional recovery.

References

1. Kalloo AN, Singh VN, Jagannath SB, et al. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. Gastrointest Endosc. 2004;60:114–7.
2. Rao G, Reddy N. Transgastric appendectomy in humans. Oral presentation at the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) conference. 26–29 April 2006, Dallas, Texas.
3. Khashab MA, Kalloo AN. NOTES: current status and new horizons. Gastroenterology. 2012;142:704–10.
4. Liu L, Chiu PWY, Reddy N, et al. Natural orifice transluminal endoscopic surgery (NOTES) for clinical management of intra-abdominal diseases. Dig Endosc. 2013; 25:565–77.
5. Garud SS, Willingham FF. Natural orifice transluminal endoscopic surgery. Gastrointest Endosc. 2012;76:491–5.
6. Rattner D, Kalloo A, et al. ASGE/SAGES working group on natural orifice translumenal endoscopic surgery October 2005. Surg Endosc. 2006;20:329–33.
7. Rattner DW, Hawes R, Schwaitzberg S, et al. The second SAGES/ASGE white paper on natural orifice transluminal endoscopic surgery: 5 years of progress. Surg Endosc. 2011;25:2441–8.

8. Pasricha PJ, Hawari R, Ahmed I, et al. Submucosal endoscopic esophageal myotomy: a novel experimental approach for the treatment of achalasia. Endoscopy. 2007; 39:761–5.
9. Inoue H, Minami H, Kobayashi Y, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42:265–71.
10. Bhayani NH, Kurian AA, Dunst CM, et al. A comparative study on comprehensive, objective outcomes of laparoscopic Heller myotomy with per-oral endoscopic myotomy (POEM) for achalasia. Ann Surg. 2014;259:1098–103.
11. Gee DW, Rattner DW. Transmediastinal endoscopic intervention. J Gastrointest Surg. 2011;15:1303–5.
12. Sohn DK, Turner BG, Gee DW, et al. Reducing the unexpectedly high rate of injuries caused by NOTES gastrotomy creation. Surg Endosc. 2010;24:277–82.
13. Nau P, Ellison EC, Muscarella Jr P, et al. A review of 130 humans enrolled in transgastric NOTES protocol at a single institution. Surg Endosc. 2011;25:1004–11.
14. Memark VS, Anderson JB, Nau PN, et al. Transgastric endoscopic peritoneoscopy does not lead to increased risk of infectious complications. Surg Endosc. 2011;25:2186–91.
15. Tsin DA, Sequeria RJ, Giannikas G. Culdolaparoscopic cholecystectomy during vaginal hysterectomy. JSLS. 2003;7:171–2.
16. Lehmann KS, Ritz JP, Wibmer A, et al. The German registry for natural orifice translumenal endoscopic surgery. Report of the first 551 patients. Ann Surg. 2010; 252:263–70.
17. Donatsky AM, Jorgensen LN, Meisner S, et al. Sexual function after transvaginal cholecystectomy: a systematic review. Surg Laparosc Endosc Percutan Tech. 2014;24:290–5.
18. Van den Boezem PB, Velthuis S, Lourens HJ, et al. Hybrid transvaginal cholecystectomy, clinical results and patient-reported outcomes of 50 consecutive cases. J Gastrointest Surg. 2013;17:907–12.
19. Bulian DR, Knuth J, Cerasani N, et al. Transvaginal/transumbilical hybrid-NOTES-versus 3-trocar needlescopic cholecystectomy: short-term results of a randomized clinical trial. Ann Surg. 2013;00:1–8.
20. de Lacy AM, Rattner DW, Adelsdorfer C, et al. Transanal natural orifice transluminal endoscopic surgery (NOTES) rectal resection: “down-to-up” total mesorectal excision (TME)—short-term outcomes in the first 20 cases. Surg Endosc. 2013;27:3165–72.
21. Sylla P, Rattner DW, Delgado S, et al. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. Surg Endosc. 2010;24:1205–10.
22. Sylla P, Bordeianou LG, Berger D, et al. A pilot study of natural orifice transanal endoscopic total mesorectal excision with laparoscopic assistance for rectal cancer. Surg Endosc. 2013;27:3396–405.

27. Future Directions for Endoscopic Operations

Carter Lebares and Silvana Perretta

Introduction

Over the past 20 years there has been a slow but continuous migration from open surgery to less invasive, more patient-friendly therapeutic options. Surgery is evolving away from the purely tactile craft of the twentieth century, towards a less invasive métier augmented by robotics and image-guidance. The future of surgery embraces a flexible, technology-enabled, and image-based approach. It will focus on less invasive approaches with the aim of cost-effective care. Therefore, modern surgical thinking needs to go further than laparoscopic or endoscopic replications of open established surgical techniques. The real act of discovery consists not only in finding new lands but in seeing with new eyes. Therefore, the idea of decreasing the morbidity of an operation challenges not only the way the intervention is delivered but also the surgical strategy itself. Because of advances in techniques and technology, what was once a fantasy is now a realistic goal: to safely and adequately address surgical issues with minimal or no anesthesia, in a same day facility, leaving little or no scar, and returning our patients to normal life the next day.

In the near future, the availability of sophisticated new diagnostic and functional imaging modalities should allow us to use flexible endoscopy, laparoscopy, and perhaps even nonsurgical image-guided access to deliver surgery and treatments in a more personalized, targeted, and minimally invasive way. Imaging modalities once purely diagnostic become powerful treatment tools, capable of delivering therapy while sparing surrounding tissue. An example of such is high-intensity, focused ultrasound beam that heats and precisely destroys targeted tissue, noninvasively, while continuously monitoring the tissue effect [1].

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Future Directions

Already, substantial gains have been made in reducing surgical trauma: hospital stays and operative complications have decreased through the transitioning of many open procedures to equivalent laparoscopic procedures over the last 25 years. As our skills and imaging resources have evolved, minimally invasive surgery has become the new standard, transforming the surgical management of many diseases into short-stay or out-patient procedures.

So it is with flexible surgical endoscopy, the crux of another grand evolutionary surgical step, akin to laparoscopy in the 1990s. In some instances the endoscopic approach has already become commonplace; there is nothing futuristic about how we treat Zenker's diverticulum, esophageal varices or perform enteral access percutaneous endoscopic gastrostomy (PEG). In other cases, the flexible endoscopic approach is becoming a dependable adjunct to laparoscopic and even open surgery, frequently allowing us to minimize more morbid laparoscopic or open approaches. Such is the case in the treatment of surgical complications through the use of endoscopic clips and stents for gastrointestinal leaks and fistulas or even endoscopic suturing [2, 3].

Finally, there are those areas of flexible surgical endoscopy that are neither commonplace nor complementary but rather novel approaches to old problems, in every single surgical field, expanding our horizons in unexpected ways, mixing surgical thinking, endoscopic tools and image guidance.

For example, endolumenal therapy represents an intriguing strategy for bariatric patients with weight regain after gastric bypass. It may offer a durable or repeatable, cost-effective alternative to surgery [4]. Another striking example in hepatobiliary surgery is the combined endoscopic and percutaneous approach for securing intra- and extra-hepatic biliary access via rendezvous techniques. These procedures have become more widely utilized in recent years as a salvage approach for common bile duct injuries, post-transplant biliary stricture, and biliary leaks following partial hepatectomy [5, 6]. This novel "work-around" has only increased in applicability with the development of more advanced Endoscopic Ultrasound (EUS) techniques. The recent retrospective review of 240 patients from six international centers the InEBD Study Group, shows that the evolution of EUS has allowed the development of biliary access via hepaticogastrostomy, hepaticoesophagostomy, and choledochoduodenostomy, complementing EUS-endoscopic retrograde cholangiopancreatography (ERCP) transpapillary rendezvous proce-

dures [7]. These hybrid approaches are important options when standard ERCP fails [8, 9]. Image guided flexible approaches may also touch areas that are "daily bread" for laparoscopic surgeons, such as cholecystectomy. Perez-Miranda [10] has described the creation of a transgastric cholecysto-gastrostomy to address gallbladder disease from an endoluminal approach. Although currently intended for patients unable to undergo laparoscopy, it represents a potential change in management of a pathology that is nearly synonymous with surgeons.

The future direction of surgical endoscopy is less the development of a new frontier than the renaissance of an old one. Many of us do not realize that a striking number of landmark endoscopic innovations were made by surgeons. In 1963 Turell used a modified gastroscope to obtain the first "colonscopic" view of the colon [11]. In 1973, Wolff and Shinya published their novel experience with endoscopic polypectomy [12]. In 1979, Gaisford first described endoscopic electrohemostasis to treat active upper GI bleeding [13] and was followed by Sugawa, in 1986, who described parallel treatment obtained by endoscopic injection of dehydrated ethanol [14]. McCune first performed endoscopic cannulation of the ampulla of Vater in 1968 [15] and PEG was invented by the team of Ponsky and Gauderer, in 1979 [16].

Most recently, in 2010, Inoue, a surgical endoscopist, introduced the Peroral Endoscopic Myotomy (POEM) as a treatment for achalasia [17] building on the tools and techniques of Endoscopic Submucosal Dissection (ESD) and changing how we view submucosal disease of the digestive tract. POEM is an example of the shape of things to come; a flexible surgical endoscopy approach to disease that is equivalent or perhaps superior to its laparoscopic or open alternative. The development of POEM proved to be a gateway for transitioning the endoscope to a more interventional tool. In the first few years of the twenty-first century, The Mayo Clinic, the Apollo Group, the Submucosal Inside Out Project and the Pasricha lab explored the submucosal working space and described the first experience with submucosal endoscopic esophageal myotomy in an experimental setting [18]. By 2010, Inoue had developed his POEM procedure, selectively dividing the esophageal circular muscle via a long submucosal tunnel. Since then, more than 4000 POEM procedures have been performed worldwide with limited complications and solid efficacy [19]. This technique received early harsh criticism and subsequently grew under strict scrutiny, a similar story to laparoscopy. As with laparoscopy, our skills and resources have advanced, making the procedure progressively more precise and more effective as we learned to fear less and think more. We can now measure

physiologic results intraoperatively tailoring the myotomy to the "obstruction" with new methods that measure the distensibility of the esophagogastric junction (EGJ) with a functional lumen imaging probe, EndoFLIP® (Crospon, Galway, Ireland) [20].

This concept may have an impact on postoperative oesophageal emptying and development of postoperative gastroesophageal reflux and is currently under investigation. We can now assess the disease anew and tailor the myotomy length using confocal endomicroscopy guidance to track myenteric neuronal network within the submucosal tunnel [21]. The development of submucosal endoscopy, coupled with technical advances, has opened the door to more aggressive endoscopic techniques. Several endoscopic procedures derived from ESD, and fusion procedures of endoscopy and laparoscopy, have recently emerged for upper gastrointestinal submucosal tumors and even cancers. These include endoscopic muscularis dissection, submucosal endoscopic tumor resection, endoscopic submucosal tunnel dissection and endoscopic full-thickness resection [22].

Clearly, the future direction of surgical endoscopy is towards more focused treatment and nowhere is this demonstrated more profoundly than in our approach to gastrointestinal cancer. Here we have the most exciting glimpse of surgical endoscopy's future, centered on the principle: *Diagnose early to treat early*.

Over the last decade, the endoscopic approach to early gastrointestinal malignancy has become well-established in Asia. Of one million cases of gastric cancer worldwide, in 2012, 50 % were in East Asia. The high incidence of gastric cancer in Japan and South Korea lead to national screening programs which resulted in early diagnosis and a substantial subsequent increase in the proportion of cancers successfully treated with ESD. As indication for ESD have been expanding, concerns have been asked to achieve curative resection for early gastric cancer while guaranteeing precise prediction of lymph node metastasis. Moreover recently, new techniques including ESD or endoscopic full-thickness resection combined with sentinel node navigation enable minimal tumor resection and a laparoscopic lymphadenectomy in cases of early gastric cancer with high risk of lymph node metastasis [23]. A similar story is true for colorectal cancer, with ESD providing an organ-preserving functional "alternative" for cancer that is diagnosed early [24].

In the West, we grapple more with esophageal carcinoma, on the rise over the last three decades and still an aggressive disease with overall 5 year survival ~15 % [25]. Nonetheless, management of esophageal

adenocarcinoma (EAC) has likewise benefited profoundly from advances in surgical endoscopy. Established and evolving endoscopic innovations have made EAC the quintessential example of how close we are to the goal of scarless, same-day, organ-sparing cancer surgery. Historically, radical esophagectomy with nodal dissection has been the standard of care. However, despite its effectiveness in providing definitive and curative treatment, esophagectomy is associated with substantial morbidity [26, 27]. The general assumption behind this approach for early cancer is that regional or systemic lymphadenectomy is appropriate for clinically suspicious or pathologically proven metastases to regional lymph nodes. Thus, when there is no possibility of metastases to regional lymph nodes, organ-sparing resection (such as ESD) with or without lymphadenectomy should be sufficient for selected patients. As such, there has been a drive towards attempting esophageal preservation in patients with intramucosal neoplastic lesions in which lymphatic involvement is unlikely [28, 29]. The early success of recently introduced endoscopic approaches such as endoscopic resection and radiofrequency ablation has resulted in a demand for definitive treatments, which ultimately preserve the esophagus.

Ablation or ESD has become standard of care for high grade dysplasia (HGD) of the esophagus. This represents a major departure from the recent past when all esophageal pathology, from dysplasia to frankly invasive cancer, was met with highly morbid radical resection. T1b lesions, though, remain subject to esophagectomy due a low but unacceptably high rate of lymph node metastases. Indeed, 45 % of T1b lesions have associated lymphatic invasion at the time of surgery [30–33]. Which, put another way, means that 55 % of patients with EAC T1b lesions are getting an esophagectomy they do not need. While no one would suggest lesser treatment in a population at such high risk, this does beg the question: what if we could tell those who have nodal metastases apart from those who do not? In the era of endoscopic resection, lymph node status makes all the difference [34]. The sentinel node concept may allow less invasive operation with selective lymphadenectomy, or in node negative patients, organ-preserving cancer resection by totally endoscopic techniques (e.g., endoscopic mucosal and submucosal dissection). Combined dye-magnetic resonance imaging may provide a new tool for systematic sentinel node basin identification; completely noninvasive requiring no preliminary aggressive dissection and without ionizing radiation [35–37]. If proved sufficiently reliable, it may represent a step further towards an image guided solely endoscopic node harvest, diagnosis and resection of the primary tumor.

As endoscopic resection become more aggressive and indication for organ sparing techniques are established for early stage esophageal tumors, reconstruction techniques are also warranted. Regenerative medicine approach may enable more aggressive resection of neoplastic tissue without the need for radical esophagectomy and its associated complications.

Biological and synthetic scaffolds can have been used to promote tissue remodeling and growth in the case of esophageal repair. Extracellular matrix scaffolds have proven to be effective for the reconstruction of small patch defects, and the prevention of stricture formation after endoscopic resection [38].

Conclusions

The boundaries between surgery and endoscopy get narrower every day. "No scar surgery opened the way to using flexible endoscopy to treat gastrointestinal diseases, internalizing surgical access and bringing the surgeon much closer to the pathology. This minimizes the "collateral damage" that operating on the gastrointestinal system typically entails. Already, procedures that in the past were only performed by radical surgery can now be performed with endolumenal treatments and flexible scopes. "Scar less surgery" with its preservation of the skin, has ultimately led to preservation of the organ. Common sense suggests that the foregut surgeon who loses the opportunity to learn and practice endoscopy will soon disappear. The future of surgery is "flexible" and lies in the reduction of the invasiveness where appropriate, the development of innovative surgical concepts where possible and revision of old surgical dogmas where indicated. In order to partake in the definition and guidance of this new direction for gastrointestinal surgeons, we need to educate ourselves and formally train our residents.

References

1. Maloney E, et al. Emerging HIFU applications in cancer therapy. Int J Hyperthermia. 2014;4:1–8.
2. Gonzalez JM, et al. Double-type metallic stents efficacy for the management of postoperative fistulas, leakages and perforations of the upper gastrointestinal tract. Surg Endosc. 2015;29(7):2013–8.

3. Kurian AA, et al. Endoscopic suture repair of full-thickness esophagotomy during per-oral esophageal myotomy for achalasia. Surg Endosc. 2013;27(10):3910.
4. Jirapinyo P, et al. Evaluation of an endoscopic suturing device for transoral outlet reduction in patients with weight regain following Roux-en-Y gastric bypass. Endoscopy. 2013;45(7):532–6.
5. Nasr JY, et al. Rendezvous procedure for the treatment of bile leaks and injury following segmental hepatectomy. Dig Liver Dis. 2013;45:433–6.
6. Salama IA, et al. Iatrogenic biliary injuries: multidisciplinary management in a major tertiary referral center. HPB Surg. 2014;2014:12.
7. Gupta K, Perez-Miranda M, Kahaleh M, Artifon EL, Itoi T, Freeman ML, de-Serna C, Sauer B, Giovannini M, InEBD STUDY GROUP. 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.
8. Kim YS, et al. Endoscopic ultrasound rendezvous for bile duct access using a transduodenal approach: cumulative experience at a single center. Endoscopy. 2010; 42(6):496–502.
9. Perez-Miranda M, et al. Transenteric anastomosis with lumen-apposing metal stent as a conduit for iterative endotherapy of malignant biliary obstruction in altered anatomy. Gastrointest Endosc. 2014;80(2):342.
10. Peñas-Herrero I, de la Serna-Higuera C, Perez-Miranda M, et al. Endoscopic ultrasound-guided gallbladder drainage for the management f acute cholecystitis (with video). J Hepatobiliary Pancreat Sci. 2014;22(1):35–43.
11. Turell R. Fiber optic colonoscope and sigmoidoscope. Am J Surg. 1963;105:133–6.
12. Wolff WI, et al. A new approach to colonic polyps. Ann Surg. 1973;178(3):367–78.
13. Gaisford JC, et al. Endoscopic electrohemostasis of active upper gastrointestinal bleeding. Am J Surg. 1979;137(1):47–53.
14. Sugawa C, et al. Endoscopic hemostasis of bleeding of the upper gastrointestinal tract by local injection of ninety-eight per cent dehydrated ethanol. Surg Gynecol Obstet. 1986;162(2):159–63.
15. McCune WS, et al. Endoscopic cannulation of the ampulla of Vater: a preliminary report. Ann Surg. 1968;167(5):752–6.
16. Ponsky JL, Gauderer MW, Stellato TA. Percutaneous endoscopic gastrostomy. Review of 150 cases. Arch Surg. 1983;118(8):913–4.
17. Inoue H, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42(4):265–71.
18. Pasricha PJ, et al. Submucosal endoscopic esophageal myotomy: a novel experimental approach for the treatment of achalasia. Endoscopy. 2007;39(9):761–4.
19. NOSCAR POEM White Paper Committee, Stavropoulos SN, Desilets DJ, Fuchs KH, Gostout CJ, Haber G, Inoue H, Kochman ML, Modayil R, Savides T, Scott DJ, Swanstrom LL, Vassiliou MC. Per-oral endoscopic myotomy white paper summary. Gastrointest Endosc. 2014;80(1):1–15.
20. Rieder E, et al. Intraoperative assessment of esophagogastric junction distensibility during per oral endoscopic myotomy (POEM) for esophageal motility disorders. Surg Endosc. 2013;27(2):400–5.

21. Neumann H, et al. Confocal laser endomicroscopy guided endoscopic myotomy. Gastroenterology. 2014;147(1):31–2.
22. Kim MY, Cho JH, Cho JY. Ever-changing endoscopic treatment for early gastric cancer: yesterday-today-tomorrow. World J Gastroenterol. 2014;20(37):13273–83.
23. Kim MY, et al. ESD around the world: Asia. Gastrointest Endosc Clin N Am. 2014;24(2):283–93.
24. Saito Y, Otake Y, et al. Indications for and technical aspects of colorectal endoscopic submucosal dissection. Gut Liver. 2013;7(3):263–9.
25. Global cancer facts & figures. 2. Atlanta, GA: American Cancer Society; 2011.
26. Thomas P, et al. Esophageal cancer resection in the elderly. Eur J Cardiothorac Surg. 1996;10:941–6.
27. Fujita H. Mortality and morbidity rates, postoperative course, quality of life and prognosis after extended radical lymphadenectomy for esophageal cancer: comparison of three-field with two-field lymphadenectomy. Ann Surg. 1995;222:654–62.
28. Holscher AH, et al. Early adenocarcinoma in Barrett's oesophagus. Br J Surg. 1997;84:1470–3.
29. Oh DS, Hagen JA, Chandrasoma PT, Dunst CM, Demeester SR, Alavi M, Bremner CG, Lipham J, Rizzetto C, Cote R, Demeester TR. Clinical biology and surgical therapy of intramucosal adenocarcinoma of the esophagus. J Am Coll Surg. 2006; 203:152–61.
30. Pohl H, et al. The role of overdiagnosis and reclassification in the marked increase of esophageal adenocarcinoma incidence. J Natl Cancer Inst. 2005;97:142–6.
31. Brown LM, et al. Incidence of adenocarcinoma of the esophagus among White Americans by sex, stage, and age. J Natl Cancer Inst. 2008;100:1184–7.
32. Rice TW, et al. Role of clinically determined depth of tumor invasion in the treatment of esophageal carcinoma. J Thorac Cardiovasc Surg. 2003;125:1091–102.
33. Rice TW, et al. Esophageal carcinoma: depth of tumor invasion is predictive of regional lymph node status. Ann Thorac Surg. 1998;65:787–92.
34. Schlag PM, et al. Sentinel node biopsy in gastrointestinal tract cancer. Eur J Cancer. 2004;40:2022–32.
35. Yuasa Y, et al. Sentinel lymph node biopsy using intraoperative indocyanine green fluorescence imaging navigated with preoperative CT lymphography for superficial esophageal cancer. Ann Surg Oncol. 2012;19:486–93.
36. Hyung WJ, et al. Preoperative imaging of sentinel lymph nodes in gastric cancer using CT lymphography. Yonsei Med J. 2010;51(3):407–13.
37. Yamamoto S, et al. Intraoperative detection of sentinel lymph nodes in breast cancer patients using ultrasonography-guided direct indocyanine green dye-marking by real-time virtual sonography constructed with three-dimensional computed tomography-lymphography. Breast. 2013;22:933–7.
38. Hoppo T, et al. Esophageal preservation in esophageal high-grade dysplasia and intramucosal adenocarcinoma. Thorac Surg Clin. 2011;21(4):527–40.

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