Multidisciplinary Approaches to Common Surgical Problems

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I would like to dedicate this book to my children, all of whom I'm extremely proud of.
Grace, who has a beautiful, Christ-centered heart, and she has been smarter than me since she was two.
Alec, who has a gentle, sweet soul and empathy for the less fortunate that started several years ago.
Viktoria, who despite her physical limitations always greets everyone with a smile and a happy face, and
Luke, who keeps our family together with his laughter, hugs, and an undying willingness to help out.
I am blessed so much more than I deserve.

Preface

Just two and a half decades ago when I started my residency training, the decisions made for acute general surgery problems used to require only a single provider, the general surgeon. While surgery, at that time, often afforded the patient the best chance to survive a perforated diverticulitis or a bleeding duodenal ulcer, there was still a high morbidity rate and survivors endured a long hospitalization and recovery. With the advancement of surgical techniques, radiologic technology, endolumenal therapy, radiation therapy, and chemotherapy, many of the acute surgical diseases require a multidisciplinary approach and are even now managed primarily by other specialties. This has changed the skill set of the general surgeon. They now require more laparoscopic and endolumenal skills and, cognitively, they have to be familiar and aware of the advantages, disadvantages, and limitations of other modalities. This can also mean that the patient who eventually comes to needing urgent surgical intervention will be the sickest population and in the most urgent need of surgery because all other options have been unsuccessful. The general surgeon will also have to be familiar with the concept and techniques of damage control surgery in these situations.

In the case of upper gastrointestinal (GI) bleeding, providers used to put a limit on the number of packed red blood cell transfusions the patient could receive before deciding to operate. Now patients will often undergo several attempts at endolumenal and interventional radiology therapy provided they are resuscitated appropriately and remain hemodynamically stable. Surgery is reserved, therefore, for the patient who continues to bleed despite the best efforts of the other specialties or for the patient who is unstable. Prompt intervention will be needed, and therefore the general surgeon must be vigilant and ready to operate quickly.

The complications of gallstones are another entity that will typically require a gastroenterologist, a radiologist, and a general surgeon. A similar team can be utilized for diverticulitis and in the treatment of inflammatory bowel disease. For the latter, the surgeon should, in particular, be familiar with the medical treatment modalities and their efficacy when deciding whether or not to perform surgery.

This multidisciplinary approach can also be seen in GI malignancies that present with obstruction or bleeding. While the patient may eventually come to need surgery, the use of endolumenal stents can temporarily treat the obstruction and allow the use of neoadjuvant chemo- and radiation therapy. This, in turn, may decrease the tumor burden allowing a less invasive and

earlier approach to ultimately treat the cancer, as with esophageal, liver, and rectal tumors. In other instances, it may preclude the need for surgery entirely as with anal cancers.

The ubiquity of bariatric surgery represents another area where a multidisciplinary approach is required. These patients often have multiple comorbidities that need attention and even those with successful weight loss and control of their comorbidities may have acute nutritional and psychological derangements. These patients often have limited physiologic reserve also, so acute issues need to be identified and addressed quickly to prevent hemodynamic collapse. Identification requires an awareness of the possible complications by an emergency physician and appropriate radiologic testing with attention paid to the bariatric procedure. Bariatric patients, for instance, will not be able to take in a liter of oral contrast for an abdominal CT scan. Today's endoscopist is typically the first line for treatment of complications like anastomotic strictures, leaks, and marginal ulcers.

There will always be acute nonobstetric surgical issues in the pregnant patient. Any surgical disease process that risks septic shock or hemodynamic collapse should supersede any fear that surgery and/or anesthesia will compromise the fetus. This is because the risk of fetal demise increases greatly when sepsis or perforation occurs. However, this approach does require knowledge of pregnancy physiology, appropriate diagnostic imaging, and the clinical acumen of when to best intervene. Surgery, in general, is safe in all trimesters but again requires a multidisciplinary approach.

Finally, there will be less common but no less dangerous occurrences that require more than one specialty to successfully treat the patient. This includes bleeding in cirrhotic patients, strangulated paraesophageal hernias, significant bleeding from idiopathic thrombocytopenia, end-stage achalasia, mesenteric ischemia, complicated empyemas, and a hypertensive crisis from a pheochromocytoma.

The purpose of this book is to help all members of these multidisciplinary teams understand the role and the limitations of the other specialties. The chapters were authored by clinically active specialists in their fields, to include gastroenterology, interventional radiology, radiology, obstetrics, endocrinology, medical oncology, and pulmonary/critical care. It is meant to give the clinician a different perspective of the same disease. It is the hope that this book will make patient care more efficient, will make consultations more appropriate, and will help all members recognize when emergent intervention needs to be done and when intervention can be delayed for a few hours. Ultimately this book is for the patients. While tremendous advancements have occurred in medicine over the past 25 years, emergency general surgery alone remains an independent risk factor for mortality and complications.[1]

With the exception of the pregnant patient, the diseases covered in this book represent areas where I feel the treatment paradigm has shifted away from a surgery-first approach. As such, diseases like small bowel obstructions

[1]Havens JM, Peetz AB, Do WS, et al. The excess morbidity and mortality of emergency general surgery. J Trauma Acute Care Surg. 2015 Feb;78(2):306-11.

and appendicitis were not covered. Many more diseases could probably be included and perhaps in the next decade the treatment paradigm will shift again. But I have also chosen these because they have personally caused me a lot of sleepless nights wondering what else can be done to improve this kind of care. As such, this book would not be possible without the love and support of my beautiful, graceful, and kind-hearted wife Lisa. Her heart is endless and I owe all of my success to her wonderful spirit.

Honolulu, HI, USA Robert Lim

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Part I

Bariatric Complications

1 Surgery for Acute Bariatric Complications

Mohamad Rassoul A. Abu-Nuwar, Souheil Adra, and Daniel B. Jones

Introduction

Morbid obesity is an epidemic with nearly 230,000 weight loss procedures performed each year. While bariatric surgery has evolved over the past few decades with practice guidelines, complications still occur and can be life-threatening. Familiarity with weight loss surgery is a growing necessity [1].

Patients presenting to the ED need to be assessed with more scrutiny and a wider differential in mind. Bariatric patients may travel to undergo weight loss surgery at accredited facilities far away from where they live. However, when complications arise the patients will be transported to the nearest facility, which may not have a bariatric surgeon. For this reason, all general surgeons should be able to manage the emergent bariatric complication, and if needed, damage control surgery be performed.

Many emergency physicians are unaware of the complications associated with weight loss surgery. However, as weight loss surgical procedures are performed more commonly, emergency physicians and general surgeons will need to recognize, diagnose, and manage patients with complications after weight loss surgery. We aim to highlight some of the most common and dreaded complications related to bariatric surgery, as well as the safest ways to manage them surgically, emphasizing some pitfalls. This chapter will explain the importance of having a relatively low threshold to aggressively evaluate the weight loss surgery patient in distress.

Initial Assessment and Workup

It is paramount that all hospitals have a system in place for early detection of possible weight loss surgery-related complications. The ASMBS has a poster titled "Clinical Pearls for Emergency Care of the Bariatric Patient," which is a valuable aid. These pearls help to guide healthcare providers to pick up on early signs of complications and improve outcomes [2]. These posters could be hung in clinical areas where they could be consulted as a quick reference.

Initial history can help focus an otherwise complicated presentation. Type of procedure, time since procedure, diet, recent band adjustments, etc. shed light on the most common problems after weight loss surgery. Whenever possible, surgical records should be obtained. This becomes especially important in patients who may have undergone multiple explorations in the past. A detailed review of medications is especially relevant with attention to NSAID use (Ibuprofen,

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Naproxen, etc) and immunosuppressive medications (steroids, immunomodulators,...). Sustained tachycardia greater than 120 bpm non-responsive to resuscitation is an ominous sign especially in the early postoperative period and should always raise a suspicion for an underlying leak, bleeding, a myocardial infarction, and a pulmonary embolism. Physical examination can be challenging in patients with morbid obesity but nonetheless is paramount with an attention to mental status, signs of dehydration, possible hernias, and assessment of port sites while keeping in mind that the classical signs and symptoms of peritonitis may not be evident.

Blood counts and chemistry are always a necessity. Restrictive and malabsorptive procedures leave patients particularly vulnerable to dehydration and electrolyte imbalances. Lactate and an arterial blood gas may provide clues to a septic or ischemic process that may be underway. Nutritional labs must not be overlooked; bariatric patients even prior to surgery are at risk of nutritional deficiencies, and this is only compounded by their procedure. A full set of nutritional labs (vitamin B1 and B12, folate, Ca, iron, copper, vitamin D, and zinc) is highly recommended, and deficiencies should be assumed and corrected empirically, i.e., intravenous infusion of isotonic solution with a multivitamin, thiamine, magnesium, and folic acid (banana bag) in patients with ongoing vomiting or PO intolerance.

The ubiquitous availability of CT scan in the ED to assess abdominal pain is instrumental. There are multiple imaging modalities that are quicker, cheaper, and place less burden on resources. One has to remember that those may have limited sensitivity with the habitus of a bariatric patient. Baseline ECG and a chest X-ray can assess for cardiac and respiratory complications as well as looking for free air. An upper GI (UGI) swallow study under fluoroscopy is very helpful; however availability may be limited, especially after hours. It can assess band placement migration, leaks, obstructions, and anatomy. A CT is recommended with dual contrast, helping to elucidate in addition to the above, collections, distal leaks, and internal hernias. Its superior sensitivity and resolution in the patients gives it a central role in the evaluation of the bariatric postoperative patient (see Chap. 2: Radiology in the Acute Bariatric Patient).

Patients' resuscitation should start off with dual large bore cannulas; patient habitus may make this difficult along with collapsed veins due to dehydration. Early placement allows rapid fluid corrections and blood product transfusion if necessary. Patient should be made NPO, and a strict input/output chart should be recorded and fluid deficits corrected as appropriate. Given the clinical scenario, NGT placement may be necessary, but attention must be given to the type of procedure the patient has undergone, particularly in patients with gastric bands and gastric bypass. Often it may not be necessary to place an NG tube, especially in a patient who is not vomiting. Remember never to force the NGT, as to minimize the risk of perforation. Placement of the NG tube under fluoroscopy guidance may help improving the safety of this procedure. Relevant home medications should be replaced with IV counterparts. Pain should be assessed and treated appropriately.

Once adequately stabilized and evaluated, it is appropriate to transfer these patients to nearby accredited bariatric centers. It is the responsibility of these centers to ease the transfer process and for the bariatric surgeon to be accommodating [3]. A patient whose workup cannot be completed in a timely fashion should be transferred rather than potentially delaying their care waiting for radiologic studies.

General Complications

It is important to remember that bariatric patients may have an unusual presentation with some crossover findings for complications as compared to their general surgical counterparts. A pulmonary embolism may present as abdominal pain or a leak as dyspnea. Some bariatric complications are similar to general surgery procedures.

In the bariatric population, given the preexisting comorbidities and technical difficulties imposed by their body habitus, some complications occur with a higher frequency.

The risk of DVT and PE is increased especially in patients with an exceptionally high BMI (>60), severe sleep apnea, and poor ambulation or functional dependence [4]. Nearly 50% of deaths in the perioperative period are attributed to PE, making it the most common cause of mortality [5]. Regardless of the weight loss procedure, the rate is similar, ranging from 0.7% to 2.4% [6]. As such, it is recommended that this patient group be considered for extended prophylaxis to mitigate the risk [7]. A low threshold for PE, especially in the first 30 days post-op, is essential to recognize this potentially deadly complication. A liberal use of chest CT angiogram is usually essential to appropriately detect and initiate treatment in a timely fashion. Other modalities for evaluation of PE are usually harder to interpret in the immediate postoperative period. A V/Q scan is usually harder to obtain, and often the patients may have chronic hypoventilation and postoperative atelectasis that limit the utility of this diagnostic modality. It is easy for tachycardia to be overlooked; however, it should always prompt consideration for PE or leaks in weight loss surgery patients.

Cardiac and respiratory complications may present in a manner that precludes their early detection. As such, a detailed history and physical coupled with relatively cheap and easy to conduct investigations can help to diagnose or rule out these issues. Cardiac strain is common with an increased chance of postoperative myocardial infarction as well as decompensation of heart failure. Mortality due to cardiovascular events can be as high as 17.6% in the perioperative period making it the second most common cause of death [8]. Increased BMI and wider neck diameters put these patients at risk for obstructive sleep apnea, which many times is undiagnosed and could lead to cardiac strain. Preoperative evaluation is essential to diagnose and optimize this comorbidity. The use of perioperative CPAP decreases the cardiac complications of OSA [3].

Atelectasis and pneumonia should be part of the differential. Pulmonary complications are the third leading cause of mortality and can be a long-term risk due to aspiration especially in patients with obstruction (stomal after lap band, strictures in sleeves, or gastric bypasses) [8, 9]. Simple investigations with an ECG and chest X-ray can help provide cues.

Incisional sites in bariatric patients can be troublesome. Given the potential subcutaneous space and pressure at the abdominal wall, subcutaneous space collections may occur, and deep muscular sutures may break. Proper assessment can preclude unnecessary workup. Fat necrosis and poor hygiene can lead to surgical site infections; caution should always be given to signs of wound infection at gastric band port sites as this may be a sign of a more ominous process. In most cases simple evaluation and local wound care are all that are necessary. However, clinical evaluation is limited by the patient's body habitus. An ultrasound or CT scan may be necessary to evaluate the abdominal wall.

Procedure-Specific Complications: Gastric Banding

The adjustable gastric band is frequently advertised as having fewer complications in comparison to other weight loss surgery procedures. While this may be initially true, its lifelong presence means patients can present with complications at any point in their lives. Healthcare providers should take note of any recent band adjustments. An UGI imaging study gives the best information about the band location, gastric prolapse, and obstruction. It is generally easy to learn how to properly assess the radiological location of a gastric band, and any general surgeon should be enabled to assess that. We recommend completely unfilling any band prior to imaging study to obviate the need for repeat imaging. Should this prove to be difficult either due to inexperience or possible malpositioning of the port, accessing the port under fluoroscopic guidance is an option.

A 2 or 4 inch non-coring (Huber) needle 20–22 gauge should be used. Tensing the abdominal musculature and immobilizing the port with the non-dominant hand are helpful.

Stromal obstruction is due to an excessively tight band and can occur in up to 14% of patients during their lifetime [10]. Patients usually present with nausea, vomiting, and an inability to tolerate oral intake including secretions [10]. In the immediate postoperative period, reasons include hematoma formation, tissue swelling, and operative technique. These conditions are generally self-limiting and can be managed by observation for 4–6 days while administering IV hydration [10]. In patients with a history of a recent band fill, it is recommended to access the port for an unfill if expertise permits. Alternatively, the patient can be resuscitated and transferred to the nearest bariatric facility. The port should only be accessed under sterile technique using a Huber needle; the use of other needles can permanently damage the port. Once completely unfilled demonstrating a tolerance to PO intake is necessary, intolerance should raise the suspicion of other conditions such as gastric prolapse or strangulation of prolapsing stomach [11].

Gastric prolapse incidence varies and has been reported to be as low as 1% [10], and patients present with obstructive symptoms (Fig. 1.1a, b). An UGI study confirms the diagnosis by showing a band in an incorrect position or angle, and obstruction of contrast may also be present. There are two types of gastric prolapse (anterior and posterior); however, for this chapter their management is identical [12]. These patients should be promptly diagnosed resuscitated and referred to a bariatric surgeon. While urgent their condition is not emergent, it may become so as prolonged band prolapse predisposes to gastric strangulation [13].

Band erosion is a relatively uncommon complication, occurring in approximately 1% [14]. It may be due to pressure necrosis, infection, or gastric ischemia. The presenting symptoms are unique (Fig. 1.2). Most commonly it will present with a port site infection but may also present with peritonitis, abscess formation, or a port-cutaneous fistula [14]. Diagnosis is confirmed by endoscopy or UGI imaging, and treatment is surgical by removal of the band and closure of the gastric ulcer.

Port complications have been reported to occur as high as 14.5% of band placements [15, 16]. The port is generally placed under the largest surgical incision. Body habitus can make its palpation and access difficult. Port complications include port malfunction, malposition, and infections. While malfunctions and malpositions are hardly an emergency, infectious complications

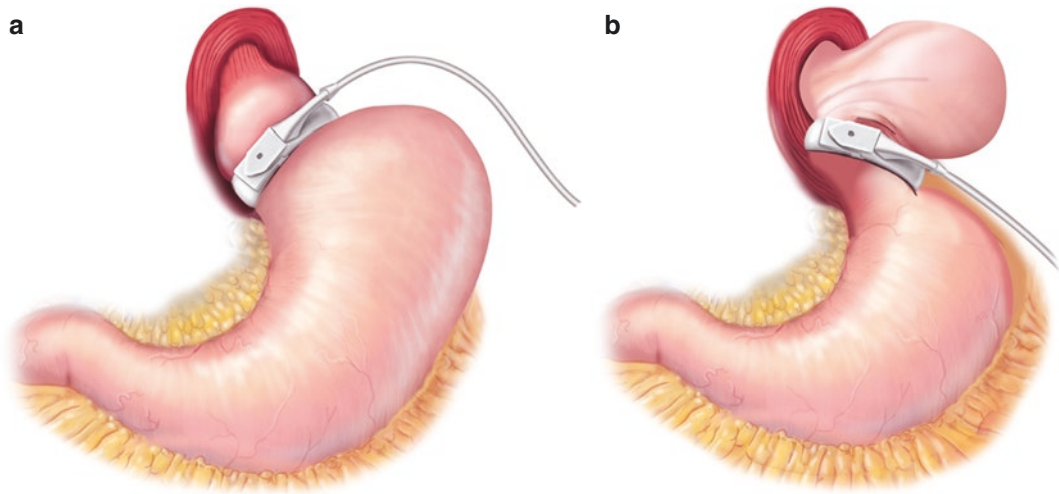

Fig. 1.1 (**a**, **b**) Normal positioned band vs gastric prolapse. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

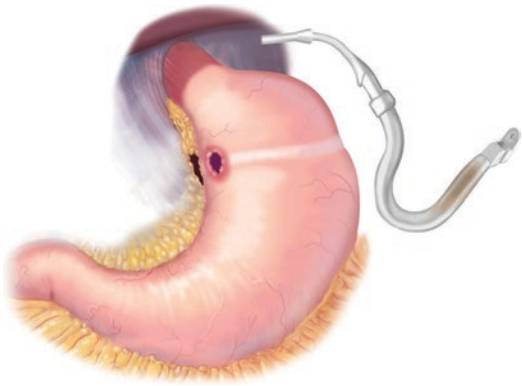

Fig. 1.2 Band erosion through gastric wall. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

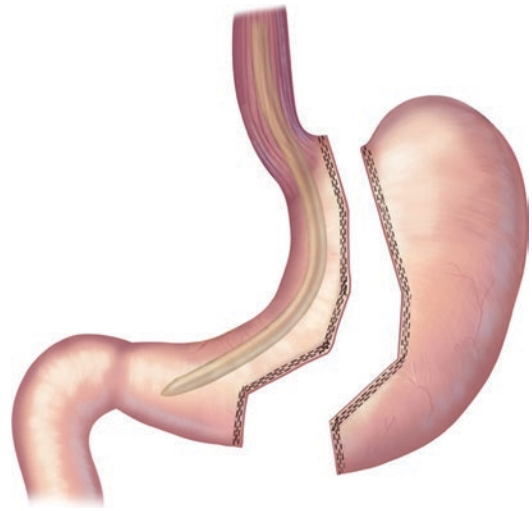

Fig. 1.3 Sleeve gastrectomy. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

can be the sign of a more ominous pathology. This may be related to band erosion, appendicitis, cholecystitis, and other intra-abdominal infections; it is recommended to remove the band at the time of surgical intervention [11]. If only a mild cellulitis is present, treatment with IV antibiotics and close observation are usually adequate.

Procedure-Specific Complications: Sleeve Gastrectomy

Sleeve gastrectomy has become the most commonly performed bariatric procedure worldwide and in the USA, transitioning from the first step in a staged procedure to a stand-alone option for weight loss surgery (Fig. 1.3). With a low complication rate and mortality of approximately 0.37% [17], the sleeve gastrectomy is relatively safe, with most complications presenting in the early postoperative period. Unlike other weight loss surgery procedures, the sleeve gastrectomy is not riddled with acute surgical emergencies later into follow-up.

The most dreaded complication of sleeve gastrectomy is development of a leak. Leak rates are reported at ranging around 1% and as high as 6.25% in revisional cases [18, 19] meaning its rate can be higher than that of a gastric bypass. Patients can present with pain, nausea, vomiting, hiccups, respiratory distress, fever, and tachycardia among many other symptoms. The most relevant is the presence of sustained tachycardia, greater than 120 bpm despite resuscitation. Most commonly leaks occur near the angle of His [20, 21]. Imaging by UGI or CT scan with gastrografin followed by thin barium is often needed to diagnose and evaluate for a leak. Management starts with gastric decompression, NPO, resuscitation, and antimicrobial coverage [22]. Ultimately, the stability of the patient will guide the management. In the stable patient, evaluation will often include endoscopy to evaluate the size and location of the leak and the need for stenting. In the appropriate patients, endoscopic stent deployment is performed (see Chap. 3: Endoscopic Management of Bariatric Emergencies). Its common complications are significant reflux and stent migration. CT-guided percutaneous drainage may be necessary if a collection has developed. In the patients where IR is unable to access a sizeable abscess, a laparoscopic washout and drainage may be necessary. Other indications for operative interventions are hemodynamically unstable patients or in chronic leaks [11]. Depending on patient hemodynamic status, chronicity of the leak, and the condition of the tissues, surgical options can be as simple as a primary repair or as complex as a complete proximal diversion with esophagojejunostomy creation.

Bleeding most commonly occurs at the suture line, and given the relatively low volume of the sleeve, high tension can be placed on the suture line causing bleeding to occur in the early post-operative period. It is recommended to reinforce areas of bleeding intra-operatively with sutures and staples [23].

Overly eager suturing particularly at the incisura or using a small bougie can result in narrowing and stenosis [24, 25]. The stenosis can also be due to twisting or kinking of the sleeve. Points of narrowing most commonly occur at the gastroesophageal junction and the angularis [26]. Patients can present with an inability to tolerate orally, vomiting, and dehydration, and diagnosis can be confirmed with an UGI imaging study or endoscopic evaluation [26, 27]. Patients should be admitted, kept NPO, resuscitated, and then proceed for endoscopic dilation (Fig. 1.4) or stenting. Should endoscopic treatment fail, surgical correction is necessary usually by conversion to another weight loss surgery procedure such as a gastric bypass. A tight stenosis can also present as a leak, the latter of which will not heal unless the stenosis is treated.

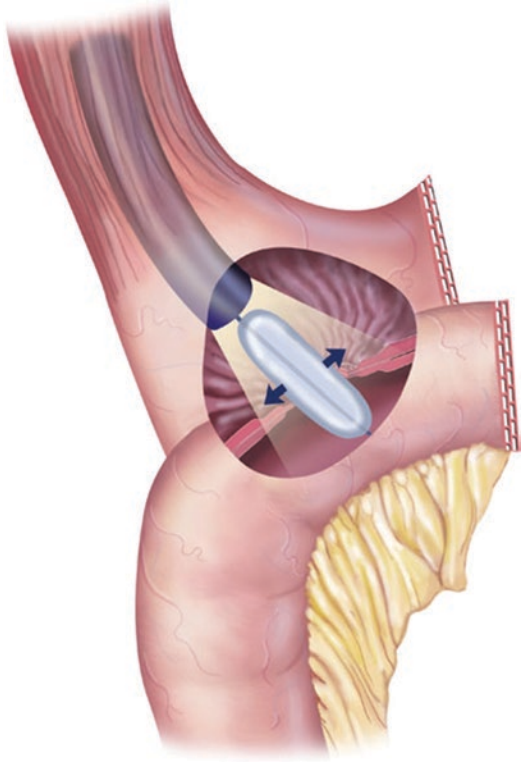

Fig. 1.4 Endoscopic dilatation. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

Procedure-Specific Complications: Roux-en-Y Gastric Bypass

The Roux-en-Y gastric bypass (RYGB) has been one of the most common weight loss surgical procedures performed and has been around for many decades. The technique has been modified throughout the years, and variants of this procedure exist, particularly in the route and anastomosis of the Roux limb. The Roux limb can pass anterior (ante) or posterior (retro) to the transverse colon; additionally, the gastrojejunal anastomosis can pass anterior (ante) or posterior (retro) to the gastric remnant (Fig. 1.5). This holds not only clinical significance but also is valuable should emergency surgery be necessary. Another variation of the RYGB is the mini-gastric bypass, which is effec-

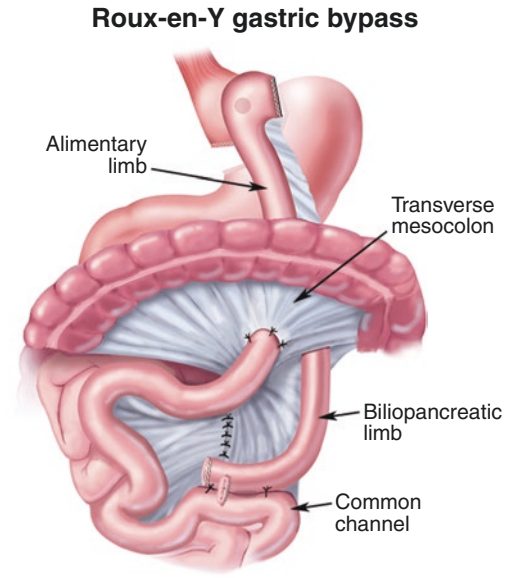

Fig. 1.5 Retrocolic antegastric Roux-en-Y gastric bypass. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

tively a loop gastrojejunostomy, similar to Billroth 2 anatomy. This is a popular procedure outside the USA. As such, it is highly recommended when possible to obtain original operative reports.

Gastrointestinal leaks occur most commonly within the first week of surgery while the remainder occurs within the first month [28]. Leak rates are similar regardless of laparoscopic or open surgery and can range from 1% to 5% [29]. Mortality from a leak is significant and has been reported in some series as high as 30% [30]. Presence of a leak also predicts an elevated risk for fistula formation, bleeding, wound infections, and cardiorespiratory complications [31]. Imaging of choice is an UGI series with gastrografin followed by thin barium to help identify large and small leaks (Fig. 1.6). Unfortunately, both CT scan and UGI imaging have proven unreliable and may miss leaks in as much as 78% of cases [31]. Exploratory laparoscopic is always a reasonable diagnostic modality if clinical suspicion is high. In the hemodynamically stable patient, attention has to be paid to rule out other conditions including cardiac ischemia, pulmonary embolism, and bleeding. Operative management includes primary repair, washout, and wide drainage [11]. Should the leak not be found, instillation of methylene blue and intraoperative endoscopy can be useful; the above principals should still be followed. It is our practice to place an NGT distal to the gastrojejunostomy and a G-tube in the gastric remnant to decompress the stomach initially as well as deliver postoperative nutrition and medications as needed (Fig. 1.7). It is reasonable to manage contained leaks in the hemodynamically stable patient with gastric decompression, NPO status, IV fluids, antibiotics, and IR drainage if feasible [32].

Marginal ulcers are reported with an incidence up to 5% [33–35]. They can occur both at the gastrojejunostomy and jejunojejunostomy site with a propensity to occur near the gastrojejunostomy (Fig. 1.8). Risk factors include smoking, NSAID,

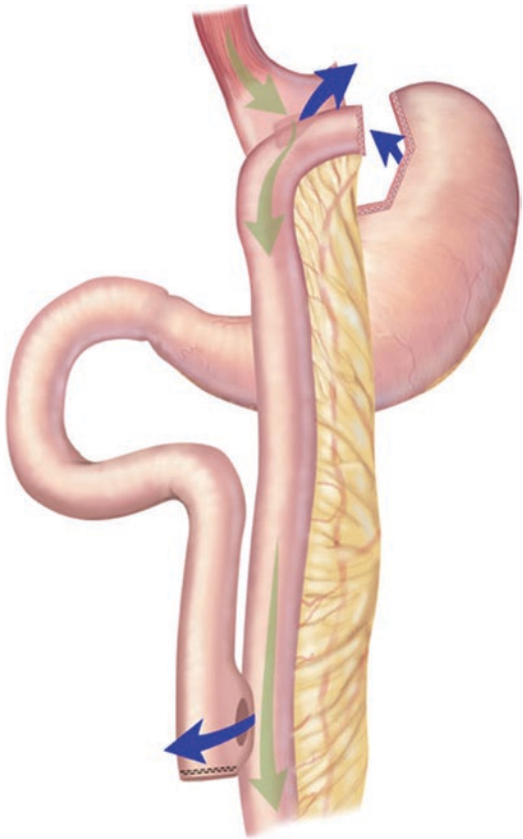

Fig. 1.6 Sites of potential leaks after Roux-en-Y gastric bypass. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

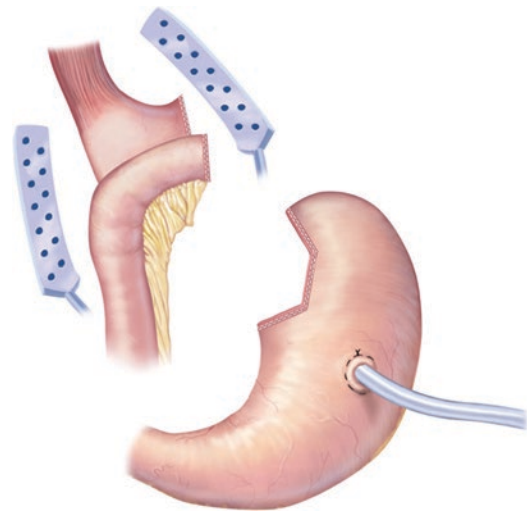

Fig. 1.7 Wide drainage around leak sites and a G-tube. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

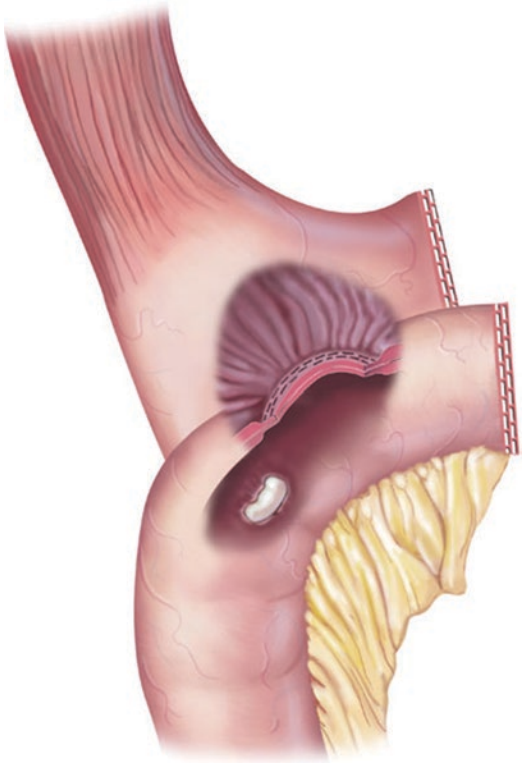

Fig. 1.8 Most common site of marginal ulcer after Roux-en-Y gastric bypass. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

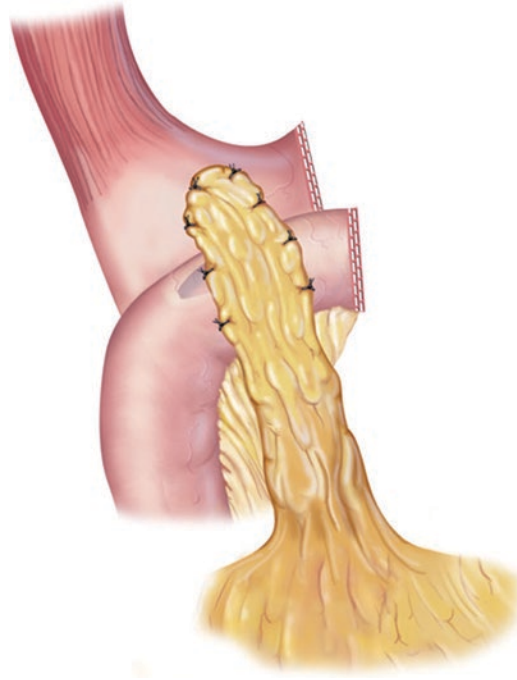

Fig. 1.9 Graham patch repair. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

corticosteroids, and the presence of a gastrogastric fistula [30, 36]. The majority of cases can be managed conservatively with stopping offending agents and starting proton pump inhibitors [34]. While patients can present with mild pain or nausea, others may present with melena or free perforation. In cases of a bleeding marginal ulcer, first steps in management are similar to any upper GI bleed: dual large bore venous access, serial hematocrit levels, correction of coagulopathic states if present, and an upper endoscopy as expeditiously as possible. Embolization may be utilized in select cases where endoscopy identifies a vessel but is unable to control it, knowing that ischemia is one of the risks of the procedure. While this manages most cases, patients may ultimately require surgery at which time a revision of the gastrojejunostomy is required; given the complexity of this procedure, it should not be taken lightly. In cases with a perforation, a repair with a Graham patch, washout, and wide drainage is the procedure of choice (Fig. 1.9).

Bowel obstructions in patients with RYGB most commonly occur between 6 months and 2 years [37]. The incidence is between 0.2% and 4.5% [33, 35, 38–40], and it is necessary to make a distinction pertaining to the timeframe from surgery. Earlier bowel obstructions (within 6 weeks) are more likely to be due to technical issues rather than adhesions; however, this should not be a deciding factor [35, 40]. Patients can present with vomiting, obstipation, and pain; chronic intermittent pain should always increase suspicion for an internal hernia [41, 42]. The quality of the vomitus may clue as to the location of the obstruction; bilious vomiting is caused by an obstruction distal to the jejunojejunostomy. UGI imaging and a CT scan are increasingly important in these cases to determine the presence of intussusception vs internal hernia vs adhesive bowel obstruction.

Common signs on CT for internal hernias include dilated proximal bowel loops, mesenteric swirling, jejunojejunostomy displacement to the right lower quadrant, and clustered small bowel loops at an otherwise abnormal location. Despite the reliability of imaging, diagnostic laparoscopy can be a valuable evaluation tool, particularly to rule out internal hernias [30, 38]. While adhesive bowel obstruction can be managed by conservative treatment, intussusception and internal hernias require surgical exploration. Internal hernias can occur at the site of jejunojejunostomy. In the case of retrocolic Roux limb, other sites of internal hernias are the transverse mesocolon defect and Petersen's defect and in the case of antecolic Roux limb, the pseudo-Petersen defect (Fig. 1.10) [11]. Emergent surgery is required, and a timely exploration avoids resection of bowel, which could become gangrenous as the presentation of internal hernias is insidious (Fig. 1.11) [41]. Once the bowel has been reduced and viability assessed, attention should be turned to the defect as well as other potential defects. Closing the defects with a nonabsorbable suture in a simple interrupted manner is adequate and has been shown to decrease rates of internal hernia from 6% to 3% [40].

An intussusception can occur at multiple points, including at the gastrojejunostomy, biliopancreatic limb, Roux limb, and most commonly the common channel [43, 44]. The exact cause of this is unknown, and its incidence increases as more weight is lost. The presentation is the same regardless of point of intussusception [45, 46]. While CT scan is the imaging of choice, it's only reliable in 80% of cases; as such a negative scan does not rule it out [47]. Emergent surgical exploration is warranted based upon the patient's clinical picture and their hemodynamic stability, with revision and pexy being the most entertained surgical options; however, should bowel necrosis be present, resection is of course necessary. The surgeon must be able to detect a spurious intussusception identified on positive CT findings without any clinical symptoms; in these cases, repeat CT is warranted to confirm resolution [47, 48].

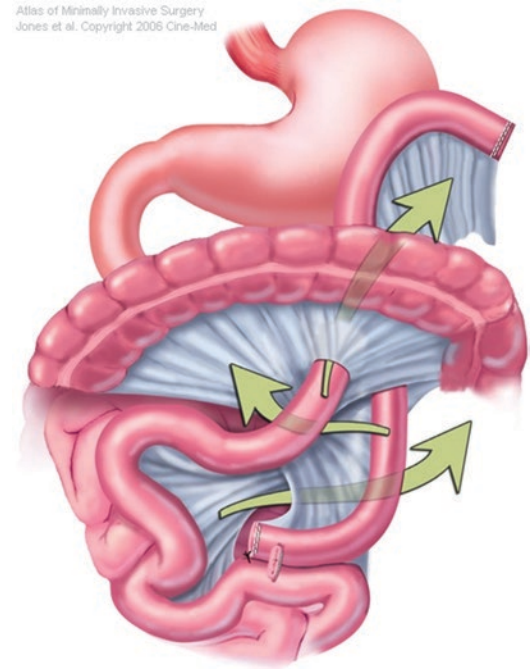

Fig. 1.10 Potential sites of internal hernias. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

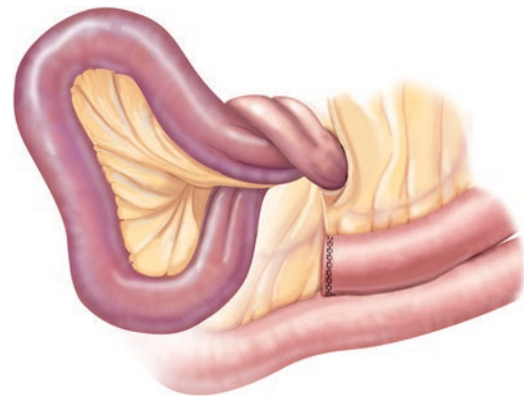

Fig. 1.11 Strangulated internal hernia. (Illustrations reprinted with permission from Atlas of Metabolic and Weight loss surgery, Jones et al. Cine-Med. 2010. Copyright of the book and illustrations are retained by Cine-Med)

Conclusion

As the prevalence of morbid obesity is on the rise, so too is the number of patients undergoing weight loss surgery procedures. Despite continuous updates to best practices and improvement in relation to outcomes, at nearly 230,000 cases operated per year, complications will occur.

Familiarity with anatomy, procedures, and complications is crucial to emergency surgery. Institutes should have systems in place for early detection starting with the ED healthcare providers. General surgeons should be familiar with presentation of weight loss surgery complication and have a relatively low threshold to explore a patient in distress. A systematic approach works best with a detailed interview and assessment of not only relevant surgical history. Operative reports should be garnered and reviewed. Both medical and surgical conditions should be fully evaluated. Appropriate use of blood works, ECG, and imaging play a vital role in early diagnosis.

Early diagnosis and resuscitation is the cornerstone of therapy. More and more complications are becoming amenable to a multidisciplinary approach consisting of endoscopic minimally invasive therapy. Most patients can be stabilized and safely transferred to an accredited bariatric facility. The general surgeon, however, will need to be prepared for the truly emergent procedures.

References

1. Estimate of Bariatric Surgery Numbers 2011–2016. Web site. https://asmbs.org/resources/estimate-of-bariatric-surgery-numbers. Updated 2016. Accessed 27 May 2018.
2. ASMBS ER Poster. Website. https://asmbs.org/resources/clinical-pathway-templates. Accessed 27 May 2018.
3. Lim RB, Baker JW, Jones DB. Patient safety. In: Nguyen NT, Blackstone RP, Morton JM, Ponce J, Rosenthal R, editors. The ASMBS textbook of bariatric surgery, vol. 1. New York: Springer; 2014. p. 119–37.
4. Sugerman HJ, Sugerman EL, Wolfe L, Kellum JM Jr, Schweitzer MA, DeMaria EJ. Risks and benefits of gastric bypass in morbidly obese patients with severe venous stasis disease. Ann Surg. 2001;234:41–6.
5. Podnos YD, Jimenez JC, Wilson SE, Stevens CM, Nguyen NT. Complications after laparoscopic gastric bypass: a review of 3464 cases. Arch Surg. 2003;138:957–61.
6. Sapala JA, Wood MH, Schuhknecht MP, Sapala MA. Fatal pulmonary embolism after bariatric operations for morbid obesity: a 24-year retrospective analysis. Obes Surg. 2003;13:819–25.
7. Lehman Center Weight Loss Surgery Expert Panel. Commonwealth of Massachusetts. Betsy Lehman Center for Patient Safety and Medical Error Reduction. Expert Panel on weight loss surgery: executive report. Obes Res. 2005;13:206–26.
8. Morino M, Toppino M, Forestieri P, Angrisani L, Allaix ME, Scopinaro N. Mortality after bariatric surgery: analysis of 13,871 morbidly obese patients from a national registry. Ann Surg. 2007;246:1002–7, discussion 1007–9.
9. Alamoudi OS. Long-term pulmonary complications after laparoscopic adjustable gastric banding. Obes Surg. 2006;16:1685–8.
10. Spivak H, Favretti F. Avoiding postoperative complications with the LAP-BAND system. Am J Surg. 2002;184(6B):31S–7.
11. Lim RB, Blackburn GL, Jones DB. Benchmarking best practices in weight loss surgery. Curr Probl Surg. 2010;47(2):92–128.
12. Keidar A, Szold A, Carmon E, Blanc A, Abu-Abeid S. Band slippage after laparoscopic adjustable gastric banding: etiology and treatment. Surg Endosc. 2005;19:262–7.
13. Chevallier JM, Zinzindohoué F, Douard R, Blanche JP, Berta JL, Altman JJ, et al. Complications after laparoscopic adjustable gastric banding for morbid obesity: experience with 1,000 patients over 7 years. Obes Surg. 2004;14:407–14.
14. Abu-Abeid S, Keidar A, Gavert N, Blanc A, Szold A. The clinical spectrum of band erosion following laparoscopic adjustable silicone gastric banding for morbid obesity. Surg Endosc. 2003;17:861–3.
15. Keidar A, Carmon E, Szold A, Abu-Abeid S. Port complications following laparoscopic adjustable gastric banding for morbid obesity. Obes Surg. 2005;15:361–5. 179.
16. Lattuada E, Zappa MA, Mozzi E, Antonini I, Boati P, Roviaro GC. Injection port and connecting tube complications after laparoscopic adjustable gastric banding. Obes Surg. 2010;20(4):410–14.
17. Trelles N, Gagner M. Sleeve gastrectomy. Oper Tech Gen Surg. 2007;9:123–31.
18. Lee CW, Kelly JJ, Wassef WY. Complications of bariatric surgery. Curr Opin Gastroenterol. 2007;23:636–43.
19. Lalor PF, Tucker ON, Szomstein S, Rosenthal RJ. Complications after laparoscopic sleeve gastrectomy. Surg Obes Relat Dis. 2008;4:33–8.
20. Baltasar A, Serra C, Perez N, Bou R, Bengochea M, Ferri L. Laparoscopic sleeve gastrectomy: a multi-purpose bariatric operation. Obes Surg. 2005;15:1124–8.

21. Braghetto I, Korn O, Valladares H, Gutiérrez L, Csendes A, Debandi A, et al. Laparoscopic sleeve gastrectomy: surgical technique, indications and clinical results. Obes Surg. 2007;17:1442–50.
22. Yehoshua RT, Eidelman LA, Stein M, Fichman S, Mazor A, Chen J, et al. Laparoscopic sleeve gastrectomy—volume and pressure assessment. Obes Surg. 2008;18:1083–8.
23. Moy J, Pomp A, Dakin G, Parikh M, Gagner M. Laparoscopic sleeve gastrectomy for morbid obesity. Am J Surg. 2008;196:e56–9.
24. Cottam D, Qureshi FG, Mattar SG, Gianetta E, Traverso E, Friedman D, et al. Laparoscopic sleeve gastrectomy as an initial weight-loss procedure for high-risk patients with morbid obesity. Surg Endosc. 2006;20:859–63.
25. Rubin M, Yehoshua RT, Stein M, Lederfein D, Fichman S, Bernstine H, et al. Laparoscopic sleeve gastrectomy with minimal morbidity. Early results in 120 morbidly obese patients. Obes Surg. 2008;18:1567–70.
26. Dapri G, Cadiere GB, Himpens J. Laparoscopic seromyotomy for long stenosis Curr Probl Surg, February 2010 163 after sleeve gastrectomy with or without duodenal switch. Obes Surg. 2009;19:495–9.
27. Dapri G, Vaz C, Cadiere GB, Himpens J. A prospective randomized study comparing two different techniques for laparoscopic sleeve gastrectomy. Obes Surg. 2007;17:1435–41.
28. Carucci LR, Turner MA, Conklin RC, DeMaria EJ, Kellum JM, Sugerman HJ. Roux-en-Y gastric bypass surgery for morbid obesity: evaluation of postoperative extraluminal leaks with upper gastrointestinal series. Radiology. 2006;238:119–27.
29. Schneider BE, Villegas L, Blackburn GL, Mun EC, Critchlow JF, Jones DB. Laparoscopic gastric bypass surgery: outcomes. J Laparoendosc Adv Surg Tech A. 2003;13:247–55.
30. Pitt T, Brethauer S, Schauer P. Obesity surgery: patients safety and best practices. Vol CH 40. Woodbury: Cine-Med, Inc.; 2008.
31. Gonzalez R, Murr MM. Anastomotic leaks following gastric bypass surgery. In: Jones DB, Rosenthal R, editors. Weight loss surgery: a multidisciplinary approach. Edgemont: Matrix Medical Communications; 2008. p. 369–70.
32. Thodiyil PA, Yenumula P, Rogula T, Gorecki P, Fahoum B, Gourash W, et al. Selective nonoperative management of leaks after gastric bypass: lessons learned from 2675 consecutive patients. Ann Surg. 2008;248:782–92.
33. Higa KD, Boone KB, Ho T. Complications of the laparoscopic Roux-en-Y gastric bypass: 1,040 patients—what have we learned? Obes Surg. 2000;10:509–13.
34. Dallal RM, Bailey LA. Ulcer disease after gastric bypass surgery. Surg Obes Relat Dis. 2006;2:455–9.
35. DeMaria EJ, Sugerman HJ, Kellum JM, Meador JG, Wolfe LG. Results of 281 consecutive total laparoscopic Roux-en-Y gastric bypasses to treat morbid obesity. Ann Surg. 2002;235:640–5, discussion 645–7.
36. Gumbs AA, Duffy AJ, Bell RL. Incidence and management of marginal ulceration after laparoscopic Roux-Y gastric bypass. Surg Obes Relat Dis. 2006;2:460–3.
37. Capella RF, Iannace VA, Capella JF. Bowel obstruction after open and laparoscopic gastric bypass surgery for morbid obesity. J Am Coll Surg. 2006;203:328–35.
38. Blachar A, Federle MP, Pealer KM, Ikramuddin S, Schauer PR. Gastrointestinal complications of laparoscopic Roux-en-Y gastric bypass surgery: clinical and imaging findings. Radiology. 2002;223:625–32.
39. Schauer PR, Ikramuddin S, Gourash W, Ramanathan R, Luketich J. Outcomes after laparoscopic Roux-en-Y gastric bypass for morbid obesity. Ann Surg. 2000;232:515–29.
40. Nguyen NT, Huerta S, Gelfand D, Stevens CM, Jim J. Bowel obstruction after laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2004;14:190–6.
41. Hwang RF, Swartz DE, Felix EL. Causes of small bowel obstruction after laparoscopic gastric bypass. Surg Endosc. 2004;18:1631–5.
42. Lauter DM. Treatment of nonadhesive bowel obstruction following gastric bypass. Am J Surg. 2005;189:532–5, discussion 535.
43. Kasotakis G, Sudan R. Retrograde intussusception after Roux-en-Y gastric bypass for morbid obesity. Obes Surg. 2009;19:381–4.
44. Goverman J, Greenwald M, Gellman L, Gadaleta D. Antiperistaltic (retrograde) intussusception after Roux-en-Y gastric bypass. Am Surg. 2004;70:67–70.
45. Efthimiou E, Court O, Christou N. Small bowel obstruction due to retrograde intussusception after laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2009;19:378–80.
46. Edwards MA, Grinbaum R, Ellsmere J, Jones DB, Schneider BE. Intussusception after Roux-en-Y gastric bypass for morbid obesity: case report and literature review of rare complication. Surg Obes Relat Dis. 2006;2:483–9.
47. Zainabadi K, Ramanathan R. Intussusception after laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2007;17:1619–23.
48. Simper SC, Erzinger JM, McKinlay RD, Smith SC. Retrograde (reverse) jejunal intussusception might not be such a rare problem: a single group's experience of 23 cases. Surg Obes Relat Dis. 2008;4:77–83.

Radiology in the Acute Bariatric Patient

2

Dustin R. Roberie and Thomas F. Murphy

Introduction

Obesity prevalence within the US adult population was calculated at 39.8% during 2015–2016 [1]. Furthermore, these data demonstrate a continuing upward trend from 30.5% in the year 2000. It is probable that obesity-related healthcare concerns will be increasingly commonplace.

The history of modern surgical management of obesity began in 1954 when Dr. Kremen et al. evaluated the role of intestinal absorption in dogs, subsequently leading to the practice of jejunoileal bypass [2]. This early technique proved successful for weight loss, though many patients experienced a host of complications related to malabsorption. In some cases, bacterial overgrowth within the excluded small bowel segment would culminate in liver failure. Ultimately, reversal of the procedure was sometimes required. This first attempt at weight loss surgery led to development of new techniques seeking to minimize complications.

Today a variety of surgical techniques are employed by bariatric surgeons relying upon various means of mechanical caloric restriction combined with the secondary effects of decreased absorption and hunger satisfaction. This chapter aims to provide a brief overview of the role radiology plays in the postsurgical complications of the most commonly performed bariatric procedures.

Abdominal Imaging

Imaging of the bariatric patient necessitates a multimodality approach with selection of specific diagnostic imaging studies determined by a variety of clinical factors. In the immediate postsurgical patient, there is concern for anastomotic leak. Patients not within the immediate postoperative period are more likely to develop complications as a result of their altered anatomy or surgical failure. These complications come in the form of bowel obstruction secondary to anastomotic stricture or internal hernia, gastrogastric fistula formation, or marginal ulcers at the gastrojejunal anastomosis.

Abdominal Radiographs

Evaluation of the acute abdomen often begins with plain abdominal radiographs, which may aid in the detection of bowel obstruction or perforation. Since abdominal radiographs are insensitive for most complications related to bariatric procedures, normal radiographs should not delay further workup.

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Upper GI

For evaluation of anastomotic leak or stricture, especially in the perioperative period, fluoroscopic upper gastrointestinal series (UGI) is the classic study of choice as it allows for dynamic assessment of the surgical anatomy. The specific imaging protocol for this procedure varies based upon the clinical question and time since surgery. If the patient is recently postoperative and there is suspicion for anastomotic leak, water-soluble contrast is substituted for barium. Water-soluble contrast avoids the risk of barium peritonitis should a leak be present. For this procedure, initial scout abdominal radiographs are obtained. The patient then consumes a small volume (<100cc) of contrast in the upright position, while the radiologist obtains fluoroscopic images in multiple projections. Prone and supine images are also obtained in multiple projections to visualize the surgical anatomy. After the fluoroscopic portion of the examination, overhead abdominal radiographs, which provide full coverage of the abdomen, should be obtained. Full abdominal coverage is imperative, as leaked intraperitoneal contrast material typically spreads in the peritoneal cavity to the dependent portions of the abdomen; a small field of view radiographs may exclude these collections.

Computed Tomography

Acutely, computed tomography (CT) is performed more often than UGI, as it is more readily available and more likely to provide an explanation for acute abdominal pain. Imaging protocols for abdomen and pelvis CT in post-bariatric surgery patients vary with the institution and the clinical question. For primary CT investigation of anastomotic leak, the patient is given at least 100 mL water-soluble contrast orally and then immediately scanned in order to best visualize the upper abdominal surgical anatomy and detect a leak. It is important to note that oral contrast used for CT is diluted, with an iodine concentration 2 orders of magnitude less than IV contrast. Should the patient drink undiluted contrast, the resultant artifacts may ruin the diagnostic value of the CT scan; therefore, properly diluted oral contrast should be obtained from the CT technologist. If the patient has a remote history of RYGB and presents with symptoms suggesting bowel obstruction, appendicitis, diverticulitis, or other acute abdominal process, then a larger volume of oral contrast (at least 500 mL) should be consumed, and CT of the abdomen and pelvis should be performed after only a 1-hour delay to allow better bowel opacification. In either case, IV contrast, unless contraindicated by allergy or renal failure, is helpful and should also be used. The use of CT to diagnose acute pulmonary embolism is discussed below.

MRI and Ultrasound

There is no role for routine use of MRI or ultrasound in the acute bariatric patient. Neither modality reliably shows extraluminal leakage of contrast material, which is an abnormal finding of utmost importance. MRI and ultrasound are insensitive for the detection of bariatric surgical complications when compared to fluoroscopy and CT.

Surgical Procedures and Complications

Imaging of the bariatric patient requires knowledge of normal postsurgical anatomy. The different operations have distinctive radiographic manifestations. Some complications, such as intestinal leak and obstruction, are generic; others may be specific to particular procedures.

Roux-en-Y Gastric Bypass

Initially developed in the 1960s and gradually modified to its current form, Roux-en-Y gastric bypass (RYGB) has, up until very recently, been the most frequently performed bariatric procedure [3]. Given the historic prevalence, patients who have undergone RYGB are most commonly encountered.

Roux-en-Y gastric bypass entails partitioning the fundus to make a small gastric pouch, separated from a much larger excluded component of the stomach or "gastric remnant." The jejunum is divided distal to the ligament of Treitz, and the distal limb (variously called Roux, alimentary, or efferent limb) is brought cephalad and anastomosed to the gastric pouch. The proximal limb of divided jejunum (called either the biliopancreatic or afferent limb) is anastomosed to the small intestine 75–150 cm distal to the gastrojejunostomy.

Complications of RYGB

Imaging of complications post-RYGB is directed based upon a number of clinical presentation and time since surgery, with early and late complications varying in incidence.

Leak

Anastomotic leaks are one of the most feared complications in the perioperative patient with some studies quoting a rate of 1.9% [4]. Detection of a leak is of paramount clinical importance, as delayed diagnosis can have catastrophic consequences leading to peritonitis, sepsis, and eventually death. There are also medicolegal concerns, with leaks comprising a vast majority of malpractice claims [5].

Anastomotic leaks are most likely to occur at the gastrojejunal anastomosis where the distal portion of the gastric pouch joins the jejunal Roux limb [6]. Less frequently, leaks may also occur at the distal jejunojejunal anastomosis where the biliopancreatic limb joins the jejunum [6].

On UGI this will appear fluoroscopically as extraluminal linear arcs of enteric contrast extending separate from the gastric pouch or contrast accumulation adjacent to the anastomosis without luminal conformity or gradual clearing. Overhead abdominal radiographs may also reveal curvilinear pockets of contrast layering dependently within the peritoneal cavity (Fig. 2.1).

Evaluation of anastomotic leak on abdominal CT will demonstrate similar radiographic signs compared with UGI, but with greater anatomic detail. While the presence of a leak is confirmed by identifying extraluminal contrast, CT can be helpful in determining the location based on the higher contrast density in the vicinity of the leak. CT may also aid in detection of associated complications, such as intra-abdominal abscess formation (Figs. 2.2 and 2.3).

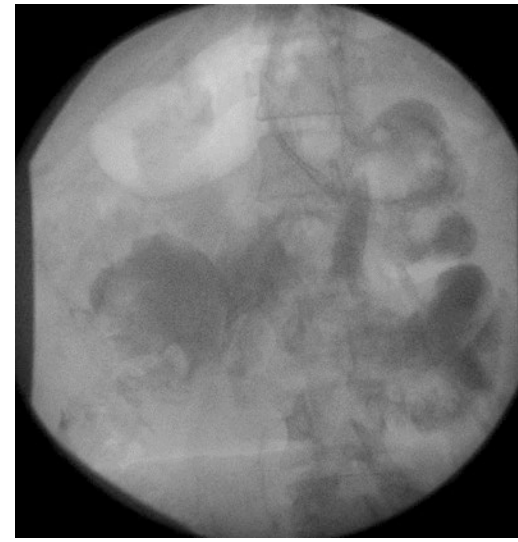


Fig. 2.1 UGI image demonstrating intraperitoneal contrast leak from the jejunum with amorphous radiodensity in the left upper abdomen

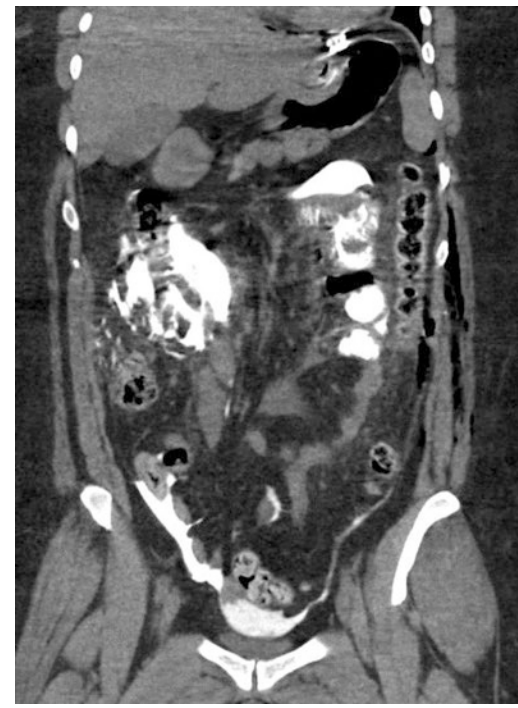


Fig. 2.2 CT from same patient demonstrating enteral contrast in the peritoneal cavity

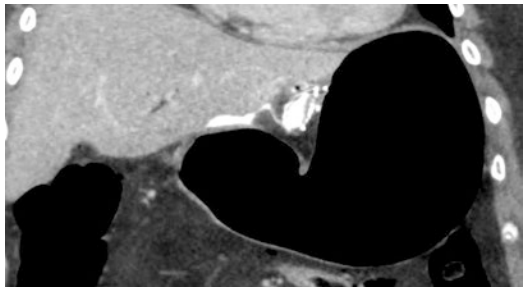


Fig. 2.3 Coronal CT image post RYGB demonstrating anastomotic leak

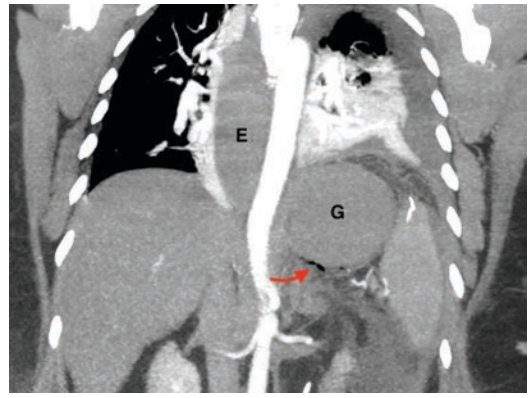


Fig. 2.4 Coronal CT pulmonary angiogram image from a recently post-RNYGB patient. CT demonstrates severe distension of the gastric pouch (G) with consequent gastric wall pneumatosis (arrow) in addition to massive esophageal distension (E) of refluxed enteric contrast. Findings proved secondary to gastric outlet obstruction at the gastrojejunal anastomosis with subsequent development of aspiration pneumonia

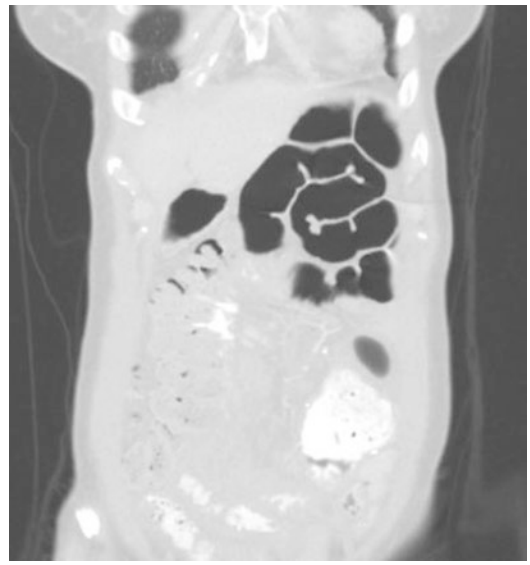


Fig. 2.5 Coronal CT image in lung window of a remotely post-RNYGB patient. CT demonstrates dilated loops of air-filled small bowel within the left upper abdomen secondary to internal hernia

Bowel Obstruction

Small bowel obstruction is another complication of Roux-en-Y gastric bypass, occurring in up to 4% of patients [7]. Causes for small bowel obstruction are variable and can be placed into two main categories. Early obstructions in the perioperative period are more likely secondary to technical complications with the Roux limb and may require revision [8]. Whereas, later complications are more likely the result of internal hernias, Roux limb compression, or formation of adhesions [7] (Fig. 2.4).

Internal hernias can be both congenital and iatrogenic due to any abdominal surgery. Internal hernias occurring following gastric bypass may occur through a surgical defect in the transverse mesocolon if the Roux limb has a retrocolic passage, at the enteroenterostomy, or posterior to the Roux limb within Petersen's space [9]. Clinical diagnosis of internal hernia can be challenging, owing to vague symptoms. Radiographic diagnosis of an internal hernia can also be troublesome, as detection of the mesenteric defect relies upon the presence of secondary signs. The most useful signs of internal hernia are visualization of small bowel loops outside of their expected location. Swirling of the mesenteric fat and vessels on CT, in addition to a "mushroom" shape of the mesenteric root, is also a useful sign for internal hernia [9] (Figs. 2.5 and 2.6).

A less common complication of gastric bypass is the development of a bezoar in the gastric pouch. Most commonly, phytobezoars (bezoars composed of plant-derived material) can form in the gastric pouch as a consequence of diminished mechanical digestion. Under normal physiologic circumstances, the muscular wall of the gastric body helps grind food into a fine paste for nutrient absorption. If this ability is impaired, fibrous plant material is at greater risk of forming an indigestible and immobile mass (Fig. 2.7).

Often, the bezoar will remain within the gastric pouch where it may contribute to symptoms of

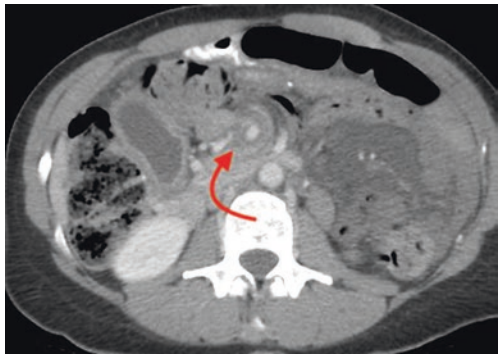


Fig. 2.6 Axial CT image from same patient demonstrating swirling of the mesenteric vasculature

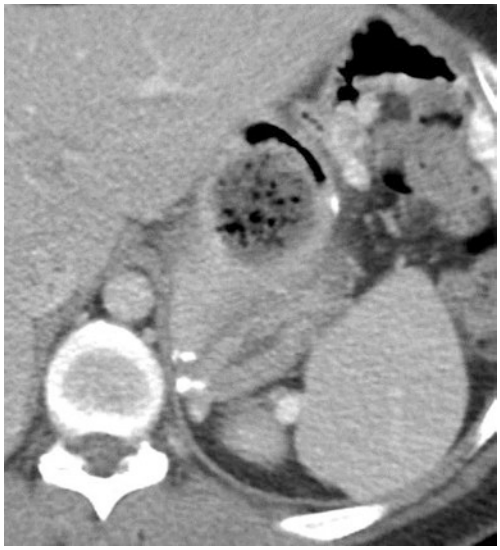


Fig. 2.7 Axial CT image from a post-RYGB patient with a bezoar in the gastric pouch

gastric outlet obstruction such as nausea or vomiting [10]. Small bowel obstruction may occur should the bezoar pass distally into the Roux limb.

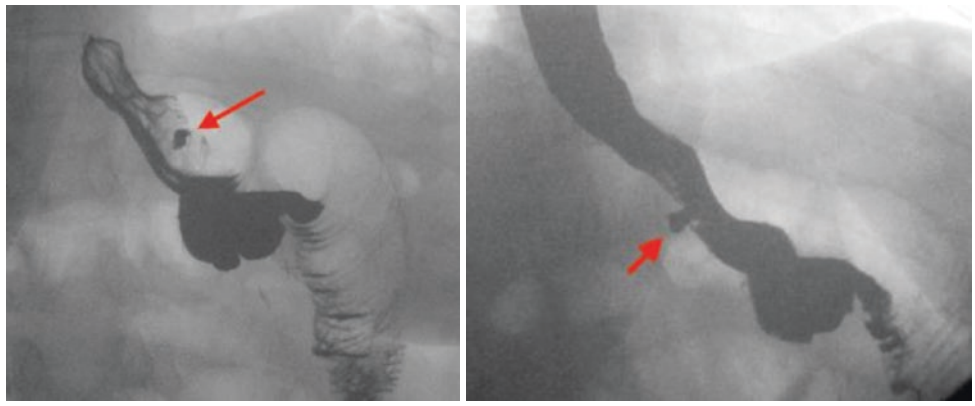
On CT, a bezoar will appear as a rounded heterogeneous and nonenhancing intraluminal mass with mottled internal foci of air. A bezoar with gas bubbles should not be confused with an abscess, which will be extraluminal, and demonstrate an enhancing rim with internal fluid density, in addition to air.

Marginal Ulcer

Marginal ulceration following Roux-en-Y gastric bypass varies widely with reported incidence reaching as high as 16% [11]. Smoking and diabetes have been described as risk factors for ulcer formation, in addition to large gastric pouch size and prior history of peptic ulcer disease [12]. Some studies also implicate nonsteroidal anti-inflammatory drugs (NSAIDs) as an associated risk factor [13].

Marginal ulcers most commonly arise at the gastrojejunal anastomosis or more distally within the jejunum [14]. Following gastric bypass, the jejunum is exposed to acidic secretions from the gastric pouch while lacking the buffering ability of bicarbonate production which normally occurs within the duodenum (Figs. 2.8 and 2.9).

Radiographically, ulcers will be seen as mucosal pits on UGI, with internal pooling of contrast when viewed from the appropriate dependent projection. Similarly, CT will demonstrate a variably sized mucosal contour defect with pooling of luminal contrast.



Figs. 2.8 and 2.9 UGI images post-RYGB demonstrating a posterior gastric pouch ulcer (arrows). Enteric contrast can be seen pooling within the mucosal defect

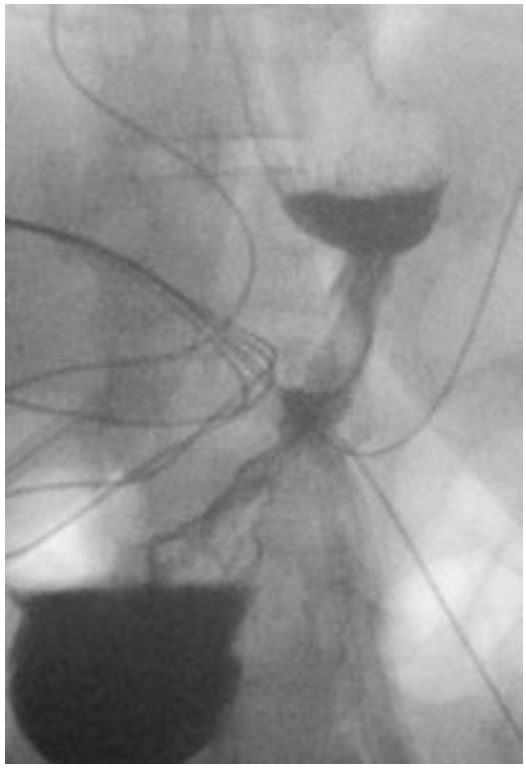


Fig. 2.10 UGI image demonstrating normal anatomic appearance following sleeve gastrectomy

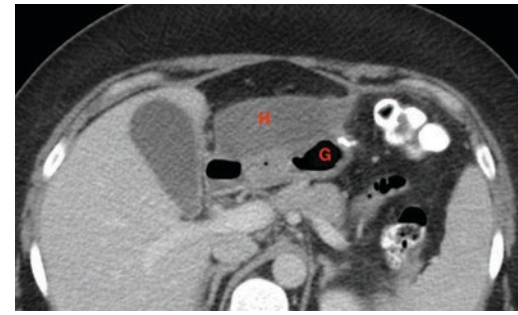


Fig. 2.11 Axial CT image post sleeve gastrectomy demonstrating a hematoma (H) anterior to the gastric lumen (G)

Sleeve Gastrectomy

An alternative to gastric bypass is the sleeve gastrectomy which was initially performed in association with biliopancreatic diversion and duodenal switch procedures in 1988 and first performed laparoscopically in 1999 [15]. According to procedure data published in 2016, incidence of sleeve gastrectomy has sharply increased in recent years, now surpassing Roux-en-Y gastric bypass as the most commonly performed bariatric procedure encompassing 58% of bariatric procedures in 2016 [3] (Fig. 2.10).

For this technique, the stomach is divided along the greater curvature with resection of a longitudinal portion of the gastric fundus and body. The result is a stomach with a tubular appearance.

In the early postoperative period, hemorrhage is a serious acute complication of sleeve gastrectomy with reported incidence between 1% and 6% [16]. Intermediate to high density intraabdominal fluid exhibiting a mean Hounsfield unit density higher than water density fluid which should have an average density close to 0 HU (Fig. 2.11).

Extraluminal leak is another serious acute complication of sleeve gastrectomy. Leaks may occur at any point along the surgical staple line. On UGI, extraluminal extravasation of water-soluble contrast media will be seen typically within the vicinity of the leak or layering dependently if discovered on post-fluoroscopic overhead radiographs. Abdominal CT may demonstrate thin linear projections of extravasated extraluminal contrast. CT imaging can aid in detection of other complications, such as abscess formation (Figs. 2.12 and 2.13).

Laparoscopic Adjustable Gastric Band

The least prevalent option of the three most commonly encountered bariatric procedures is the adjustable gastric band. The gastric band functions to limit gastric volume through inflation of a laparoscopically placed band encircling the proximal stomach. Similar to gastric bypass, this effectively creates a gastric pouch. The size of the pouch can be adjusted through the addition or removal of saline from within the gastric band, by way of a subcutaneous access port (Fig. 2.14a, b).

Complications of gastric banding can be categorized as those occurring early or late following surgery. Early complications include misplacement of the band or gastric perforation as a result of surgical trauma [17]. Surgical misplacement is rare but may result in development

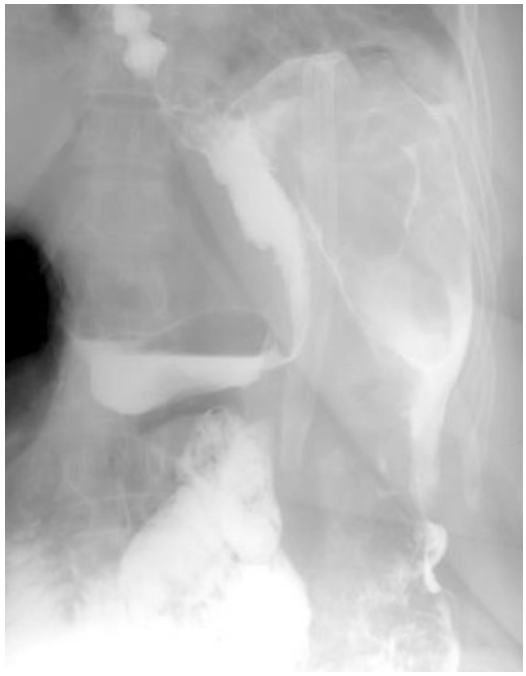


Fig. 2.12 UGI image demonstrating leak along the proximal gastric staple line following sleeve gastrectomy with contrast pooling along the left abdominal wall

of gastric outlet obstruction if the band is placed around the lower portion of the stomach [17] (Figs. 2.15 and 2.16).

Late complications of gastric banding include migration of the band over time, termed band slippage. Or, complications may also arise due to gradual failure of the hardware components

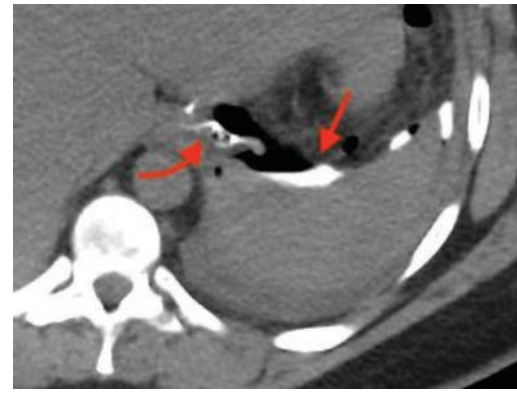


Fig. 2.13 Axial CT image from the same patient demonstrating site of gastric staple line leak near the gastroesophageal junction

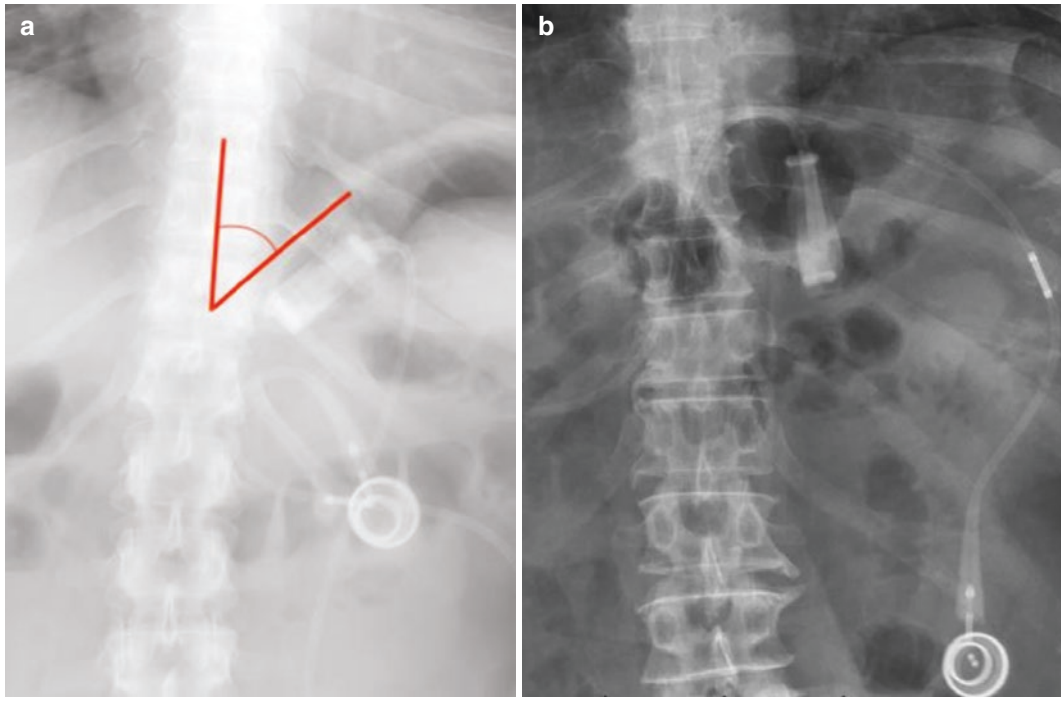
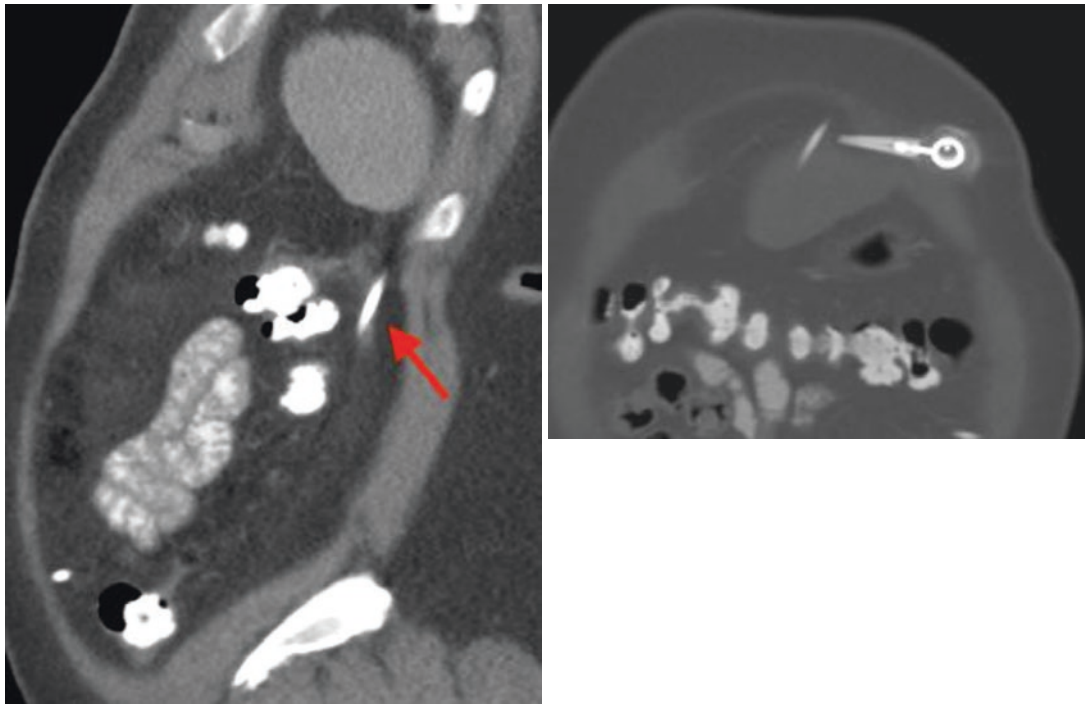


Fig. 2.14 (**a**) Frontal abdominal radiograph demonstrating normal gastric band orientation. (**b**) Frontal abdominal radiograph demonstrating abnormal acute angulation of the gastric band indicating band slippage



Figs. 2.15 and 2.16 Sagittal and coronal CT images demonstrating fractured gastric band tubing (arrow)

themselves, such as in the case of fractured port tubing.

Initial imaging evaluation for gastric band complications involves conventional radiographs of the abdomen. Abdominal radiographs allow for gross visual assessment of hardware integrity. Discontinuity of the port tubing should be readily identifiable on plain films, as is malpositioning of the band or access port. Normal angulation of the gastric band, relative to a vertical line drawn through the vertebral column, is between 4° and 58°, a measurement known as the phi angle [17]. An abnormal phi angle may be the first indication of gastric band malposition and can be confirmed by UGI or CT if clinically warranted.

Pulmonary Embolism

Patients undergoing bariatric procedures are also at increased risk for development of pulmonary venous thromboembolism (PE) with incidence varying between 0.2% and 1.3% at 30 days following surgery [18]. The classic chief complaint is that of acute dyspnea with pleuritic chest pain, often in addition to tachycardia. Multiple evidence-based models exist for the purposes of risk stratification and may help dictate the necessity for further imaging.

Given their often acute presentation, imaging of patients with suspected PE frequently begins with PA and lateral chest radiographs in order to rule out other readily identifiable causes for chest pain such as pneumonia or pneumothorax. The classic plain film radiographic signs of PE are Westermark's sign or presence of a Hampton's hump. Westermark's sign refers to a peripheral wedge-shaped segment of relative oligemia compared with other pulmonary segments as a result of decreased pulmonary perfusion. Hampton's hump refers to the presence of pulmonary infarcts manifested as peripheral wedge-shaped opacities. However, neither of these signs are a sensitive indicator for PE (Fig. 2.17).

CT pulmonary angiography (CTPA) is the study of choice in diagnosing PE as result of its ready availability, high sensitivity, and specificity, as well as its demonstration of anatomic detail. CTPA technique requires rapid IV injection of contrast material, a typical rate is 5 mL/s. A timing

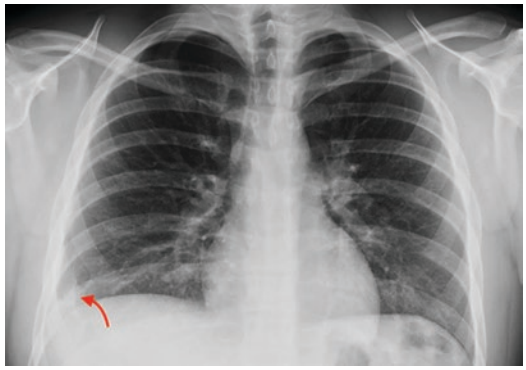


Fig. 2.17 Frontal chest radiograph demonstrating asymmetric blunting of the right costophrenic angle (arrow) subsequently revealed to represent pulmonary infarct on CTPA

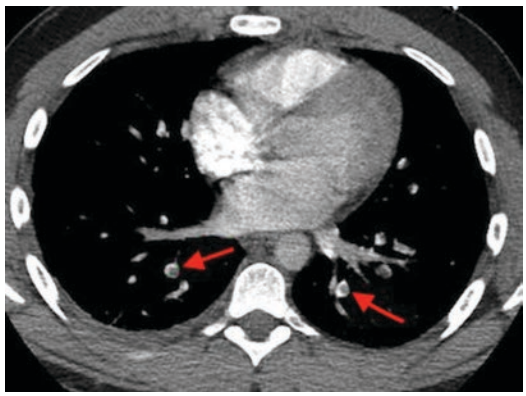


Fig. 2.18 Axial CT pulmonary angiogram image demonstrating extensive bilateral pulmonary emboli (arrows)

bolus, and bolus tracking software, helps to ensure optimal opacification of the pulmonary arteries.

On CT angiography, acute emboli will appear as low-density central filling defects within the pulmonary arterial system. These findings are best appreciated in a soft tissue window, similar to one used for evaluating the mediastinum. Care should be taken not to misidentify non-opacified pulmonary veins as extensive PE (Fig. 2.18).

Aside from detection of pulmonary embolus, CTPA allows for recognition of right heart strain through the presence of leftward bowing of the interventricular septum. Under normal physiologic conditions, pressures are greater within the left ventricle causing slight rightward septal deviation. In the setting of right heart strain, elevated right ventricular pressure results in the opposite effect. Similarly, passive hepatic congestion of intravenous contrast may be seen within the hepatic veins and inferior vena cava, as a consequence of heart strain.

In the immediate postoperative period, a bariatric surgery patient presenting with tachycardia and respiratory distress should have both a CTPA to exclude pulmonary embolism and abdominal CT to rule out a leak. In patients who have a contraindication to iodinated contrast material, ventilation/perfusion scintigraphy (V/Q scan) is an alternative imaging method to exclude pulmonary embolism.

Conclusion

Understanding the capability of imaging studies to reveal the surgically altered anatomy is key to recognizing complications of bariatric surgery. This knowledge, in conjunction with clinical factors such as symptomatology and time since surgery, can assist in the prompt diagnosis and effective management of postsurgical complications.

References

1. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity among adults and youth: United States, 2015–2016. NCHS data brief, no 288. Hyattsville, MD: National Center for Health Statistics; 2017.
2. Kremen AJ, Linner JH, Nelson CH. An experimental evaluation of the nutritional importance of proximal and distal small intestine. Ann Surg. 1954;140(3):439.
3. Estimate of Bariatric Surgery Numbers, 2011–2016. (n.d.). Retrieved April 10, 2018, from https://asmbs.org/resources/estimate-of-bariatric-surgery-numbers.
4. Zellmer JD, Mathiason MA, Kallies KJ, Kothari SN. Is laparoscopic sleeve gastrectomy a lower risk bariatric procedure compared with laparoscopic Roux-en-Y gastric bypass? A meta-analysis. Am J Surg. 2014;208(6):903–10. https://doi.org/10.1016/j.amjsurg.2014.08.002.
5. Cottam D, Lord J, Dallal RM, Wolfe B, Higa K, Mccauley K, Schauer P. Medicolegal analysis of 100 malpractice claims against bariatric surgeons. Surg Obes Relat Dis. 2007;3(1):60–6. https://doi.org/10.1016/j.soard.2006.10.008.
6. Marshall JS. Roux-en-Y gastric bypass leak complications. Arch Surg. 2003;138(5):520. https://doi.org/10.1001/archsurg.138.5.520.

7. Husain S. Small-bowel obstruction after laparoscopic Roux-en-Y gastric bypass. Arch Surg. 2007;142(10):988. https://doi.org/10.1001/archsurg.142.10.988.
8. Shimizu H, Maia M, Schauer PR, Kroh M, Brethauer SA. Surgical management of early small bowel obstruction after laparoscopic Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2013;9(5):718–24.
9. Lockhart ME, Tessler FN, Canon CL, Smith JK, Larrison MC, Fineberg NS, et al. Internal hernia after gastric bypass: sensitivity and specificity of seven CT signs with surgical correlation and controls. Am J Roentgenol. 2007;188(3):745–50. https://doi.org/10.2214/ajr.06.0541.
10. Eng K, Kay M. Gastrointestinal bezoars: history and current treatment paradigms. Gastroenterol Hepatol (NY). 2012;8(11):776–8.
11. Adduci AJ, Phillips CH, Harvin H. Prospective diagnosis of marginal ulceration following Roux-en-Y gastric bypass with computed tomography. Radiol Case Rep. 2015;10(2):1063. https://doi.org/10.2484/rcr.v10i2.1063.
12. Sverdén E, Mattsson F, Sondén A, Leinsköld T, Tao W, Lu Y, Lagergren J. Risk factors for marginal ulcer after gastric bypass surgery for obesity. Ann Surg. 2016;263(4):733–7. https://doi.org/10.1097/sla.0000000000001300.
13. Coblijn UK, Lagarde SM, Castro SM, Kuiken SD, Wagensveld BA. Symptomatic marginal ulcer disease after Roux-en-Y gastric bypass: incidence, risk factors and management. Obes Surg. 2014;25(5):805–11. https://doi.org/10.1007/s11695-014-1482-9.
14. Azagury D, Dayyeh BA, Greenwalt I, Thompson C. Marginal ulceration after Roux-en-Y gastric bypass surgery: characteristics, risk factors, treatment, and outcomes. Endoscopy. 2011;43(11):950–4. https://doi.org/10.1055/s-0030-1256951.
15. Gumbs AA, Gagner M, Dakin G, et al. Obes Surg. 2007;17:962. https://doi.org/10.1007/s11695-007-9151-x.
16. Sarkhosh K, Birch DW, Sharma A, Karmali S. Complications associated with laparoscopic sleeve gastrectomy for morbid obesity: a surgeon's guide. Can J Surg. 2013;56(5):347–52. https://doi.org/10.1503/cjs.033511.
17. Mehanna MJ, Birjawi G, Moukaddam HA, Khoury G, Hussein M, Al-Kutoubi A. Complications of adjustable gastric banding, a radiological pictorial review. Am J Roentgenol. 2006;186(2):522–34. https://doi.org/10.2214/ajr.04.0655.
18. Froehling DA, Daniels PR, Mauck KF, Collazo-Clavell ML, Ashrani AA, Sarr MG, et al. Incidence of venous thromboembolism after bariatric surgery: a population-based cohort study. Obes Surg. 2013;23(11):1874–9. https://doi.org/10.1007/s11695-013-1073-1.

3 Interventional Endoscopy: Endoluminal Therapy – Stenting, Clipping, and Suctioning

Brian Hodgens and Racquel S. Bueno

Introduction

As the global obesity epidemic rages on, the bariatric surgeon remains an integral part of its solution. Bariatric surgery is the most effective therapeutic option for the treatment of morbid obesity [1]. The minimally invasive bariatric surgeon first stepped to the forefront with the shift from open to laparoscopic surgical approaches. Compared to open surgery, laparoscopic bariatric surgery decreased wound infection rates, lengths of stay, postoperative pain, and overall mortality [2]. Ongoing refinement of effective surgical pathways continued to drastically lower morbidity and mortality [3]. This improved safety profile increased the number of procedures performed worldwide. In the United States alone, the number of procedures approached 216,000 in 2016 [3].

Increasing procedures translated into an obvious increase in the incidence of postoperative bariatric complications. The bariatric surgeon has, out of necessity, once again stepped up to meet the challenges of managing the obligatory rise in complication occurrences. The bariatric endoscopist has an expanded arsenal available as a wide array of endoscopic options has emerged. In the appropriate setting, these lower morbidity procedures offer non-operative alternatives, provide primary definitive management, function as a bridge to more definitive operative management, and provide the opportunity for patient optimization in the interim. The following is a description of the role of endoscopic therapies for bariatric surgery complications.

Leaks

A leak is the most dreaded and morbid complication in bariatric surgery. Leaks can occur either at the anastomoses, along the gastric remnant or gastric pouch staple lines for the Roux-en-Y gastric bypass (RYGB) patient, or along the gastric staple line for sleeve gastrectomy (SG) patients. Overall leak rates for primary operative events vary between 1% and 5% for RYGB and 0 and 8% for SG. The leak rates for revisional surgery are substantially higher at ~13% [4, 5]. The technical and epidemiological factors predictive of a leak remain debatable. Recent studies, however, support that the type of anastomosis (stapled vs. hand-sewn) does not affect leaks rates [6]. Moreover, the use of staple line reinforcement is

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protective [7], and the use of buttressing is deleterious [8]. Several studies have demonstrated that male sex, age > 55, diabetes mellitus (DM), sleep apnea, revisional surgery, and super obesity (BMI > 50) are associated with higher leak rates [9].

Timely diagnosis of a leak remains challenging given the lack of specificity in its clinical presentation in the morbidly obese patient. Objective diagnosis is often quite difficult, if not impossible, as contrasted imaging series and CT scans are often negative despite the presence of a leak [10]. The bariatric surgeon must be ever vigilant as symptoms of abdominal pain, nausea, and emesis are not uncommon after bariatric surgery. A high index of suspicion is essential for prompt diagnosis as sustained postoperative tachycardia may often be the only signal of an early complication. Vital sign abnormalities including tachycardia, fever, and tachypnea herald sepsis and, in these vexing situations, operative exploration should remain part of the diagnostic algorithm especially in the hemodynamically abnormal patient.

Presentation of a postoperative leak can occur over a range of days to weeks. Leaks presenting within 5–7 days after surgery are considered early leaks, while those presented after this early period are considered late [11, 12]. The timing of presentation offers insight into the potential etiology for failure and helps to guide the surgeon's management strategy. Leaks presenting within 48–72 hours of surgery are usually due to technical failure. Later presentations are more likely due to tissue ischemia related to tension, inadequate blood supply, and distal obstruction.

Prompt diagnosis is a major determinant of outcome. Early recognition with earlier initiation of therapy prevents ongoing progression of the local injury and increasing morbidity. Delays in therapy of more than 24 hours are associated with a significantly increased mortality rate [13]. Contrast media imaging studies, CT scan, and endoscopic evaluation in hemodynamically stable patients are useful tools in the diagnostic workup.

For RYGB, up to 68% of leaks occur at the gastrojejunal anastomosis (GJA), 10% at the gastric pouch, 7% at the jejunojejunal anastomosis (JJA), 4% at the remnant stomach, or (14%) at a combination of these [11]. SG leaks occur along the gastric staple line with more than 75% occurring along the proximal third of the stomach near the cardiac notch [14]. SG leaks are most commonly due to increased pressure within the lumen due to narrowing at the incisura, followed by tissue ischemia due to ligation of the short gastric vessels.

Hemodynamically unstable patients presenting with hypotension, tachycardia, and a suspected leak mandate operative exploration, drainage, repair, and initiation of nutritional support regardless of the timing of the presentation. Stable patients presenting early after surgery (within 48–72 hours) with suggestion of technical failure are also best managed with early operative intervention for drainage, control, and possible repair of the leak.

Hemodynamically stable patients with small, controlled anastomotic leaks (<2 cm) can be safely managed non-operatively with medical management, bowel rest, nutritional support, percutaneous drainage, and broad-spectrum antibiotics [10]. While often effective, this approach may require intensive care unit admissions, prolonged hospital stays, and extensive resource use. Even with early control using a conservative approach, patients may still require reoperation for definitive therapy.

Ultimately, patient presentation dictates the plan of care: unstable patients require surgery; stable patients may be safely managed non-operatively. For those patients in between, a wide variety of options exist, and the plan of care is not standardized. Interventional endoscopy is emerging as a useful option for prompt diagnosis and initiation of therapy for those patients in the middle – the hemodynamically stable patient with a controllable leak.

Early endoscopic evaluation is not only safe [15], it is essential for providing accurate defect localization and thorough interrogation of the defect characteristics. An important first step involves endoscopic debridement of necrotic tissues and irrigation and drainage of the suppuration. After this preparation a thorough endo-

scopic assessment of the area can take place as well as endoscopic drain placement within the extraluminal abscess cavity. Endoscopic evaluation should include localization of the defect noted as distance from the incisors, defect orientation relative to adjacent structures, defect diameter, and extraluminal cavity dimensions if possible. These details assist with formulating the therapeutic strategy and plan. Additionally, endoscopic preparation of the site prior to endoscopic therapy improves luminal control with subsequent sepsis control and progression toward overall healing and leak resolution.

Stenting

Endoscopic stenting and internal drainage for containment and coverage of the leak allow for sepsis control and early nutritional support with enteral feeding. Improved nutrition and resolution of the systemic burden contribute to primary healing and sealing of the leak. Even if a complete seal is not achieved, control of the leak at least provides a stable bridge for patient optimization in preparation for definitive operative management with improved outcomes.

Endoscopic stenting can be considered for leak management at the RYGB gastrojejunal anastomosis and for leaks along the SG gastric staple line. Endoscopic stenting is an appropriate therapeutic option in stable patients with a leak controlled by adequate external drainage. Stenting encourages healing and sealing of the leak site by providing coverage of the defect and isolation of the area of injury. Additionally, the stent exerts an outward axial force that decreases intraluminal pressure down the length of the stent, also promoting overall healing.

The stents of choice are self-expanding stents available in either plastic or metal. Plastic stents, once popular in the endoscopic management of esophageal pathology and perforation, are not well suited for post-bariatric patients due to their high axial force and high migration rates. Self-expandable metal stents (SEMS), however, are ideally suited for post-bariatric complications. SEMS are made of nitinol, which provides the advantage of combining flexibility while maintaining stent shape and integrity. SEMS exerts a lower axial force than plastic stents, making them more tolerable for the patient. To prevent tissue ingrowth into the stent, SEMS are either fully covered or partially covered. Fully covered (FC) stents are covered along the entire length with silicone or polyurethane, while partially covered (PC) stents leave an uncovered gap of 1–2 cm at both ends. FC stents will cover the leak site and are easy to remove, but they have a high rate of migration. PC stents allow for some tissue ingrowth, fixing the stent in place and ensuring diversion of luminal contents from the leak (Fig. 3.1). Removal of PC stents, however, is more difficult and prone to complications.

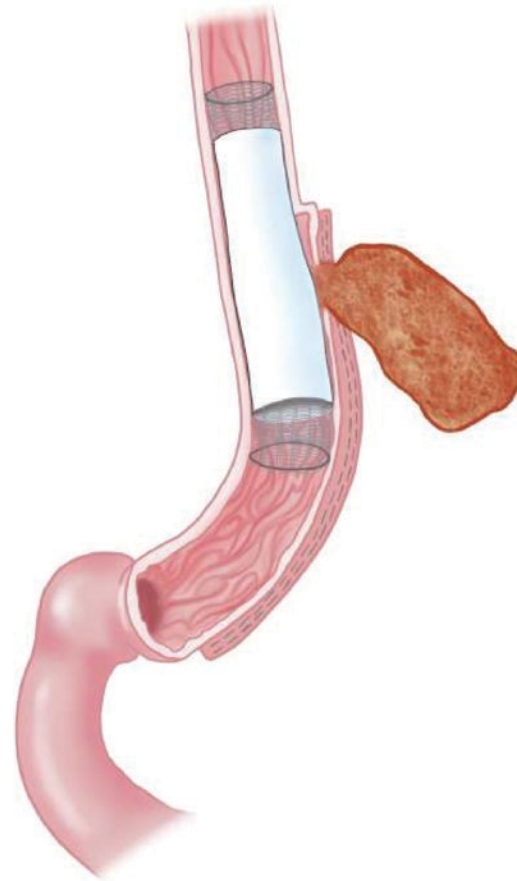

Fig. 3.1 Depicting partially covered stenting of a sleeve gastrectomy leak

Bariatric-specific stents have been recently developed and provide a promising alternative to standard linear stents. These newer stents are fully covered and specifically contoured to the anatomy of a postoperative RYGB or SG patient. They also attempt to decrease the axial force of the stent, making them less prone to migration. Their larger diameter, however, can increase pain and nausea and is thus not always well tolerated.

Endoscopic management of postoperative bariatric complications requires appropriate patient preparation. Enlisting anesthesia support for the administration, monitoring, and management of anesthesia during the procedure is essential. General anesthesia is often necessary for these complex procedures to ensure safe airway management. Anticipate longer procedure times if debridement and drainage of the leak cavity are required. Stent choice also dictates procedural preparation. SEMS placement requires fluoroscopic support during the procedure for accurate localization of the leak site and thorough interrogation of its extent prior to stent placement. Moreover, fluoroscopy confirms stent positioning and ensures appropriate deployment. The smaller caliber through-the-scope stents do not allow for fluoroscopic visualization during the procedure to confirm final stent placement.

Nausea and pain should be anticipated after stent placement and appropriately managed. After 24–48 hours of clinical stability, a liquid diet can be initiated if a contrast imaging study confirms satisfactory stent position and control of the leak site. Early initiation of oral nutrition, starting with liquids and semisolids, represents the greatest benefit of early endoscopic stenting of bariatric complications as improved nutrition promotes leak resolution.

The duration of endoscopic stent therapy varies. Recent reports suggest that stent therapy lengths between 4 and 6 weeks suffice; however longer treatment durations are sometimes required to ensure complete closure of the defect. Increasing the treatment timeline, however, needs to be balanced with the increased risk for complications associated with longer durations [16].

Close outpatient follow-up is essential and should be established every 1–2 weeks. Routine imaging monitors the stent's position and allows for early identification and management of issues that may require repeat endoscopic intervention. Symptoms suggestive of a stent complication, such as increased pain, nausea, or poor oral tolerance, should prompt evaluation. Additionally, stent type and size should be considered when interrogating post-procedural complaints. Larger stent diameters, like those seen with bariatric-specific stents, have a higher incidence of pain and vomiting as well as deep ulceration at the stent borders causing bleeding, perforation, and post-inflammatory stricture [17].

Most series report that approximately 80% of endoscopically stented leaks clinically resolve [16–18]. A recent review article comparing leak resolution by stent type demonstrated success rates of 76–94% with PC stents, 77–100% with FC stents, and 73–100% for bariatric-specific stents [17]. Leak resolution can be correlated to leak size and time from surgery to stent placement. Larger leaks diagnosed later in the postoperative course have a lower rate of closure, often requiring a longer duration of treatment and need for repeated intervention.

These reassuring resolution rates make temporary endoscopic stents useful tools in early leak management. More importantly, even if complete clinical leak resolution is not primarily achieved, temporary stent therapy can provide a valuable window of time to optimize a patient prior to definitive repair.

While the reported endoscopic stenting success rates of 80–90% are impressive, there are serious drawbacks warranting consideration. Although complications uncommonly occur during stent placement, post-procedural issues are common. Stent migration rates of 34–60% are expected for FC stents, 18–27% for bariatric stents, and 6–15% for PC stents [17]. The high migration rates for FC stents may mean repeated intervention and the possibility of prolonging therapy duration [19, 20].

Complications due to the radial traction of the stent along the intestinal wall occur in ~20% of individuals. These include digestive wall trauma, mucosal ingrowth, mucosal friability, and resulting post-inflammatory strictures, which

are attributed to longer treatment durations and PC stents. The higher rate of post-inflammatory esophageal stricture associated with PC stents may require balloon dilation [18]. Mortality rates of less than 5% are expected and are usually due to the intense inflammatory processes causing erosion into adjacent structures resulting in aorto-esophageal, aorto-enteric, and tracheoesophageal fistulas. Most fatal events are noted upon stent removal; thus a thorough understanding of the relationship of the zone of damage with its surrounding structures is mandatory when determining the feasibility of this therapeutic option.

After the anticipated 4–6 weeks of stent therapy, removal typically requires the use of simple endoscopic forceps securely grasping the proximal end of the stent and withdrawal along with the endoscope. Longer therapeutic durations increase the time for tissue integration and mucosal trauma upon removal. Significant tissue ingrowth, particularly with PC stents, may necessitate stent removal with either argon beam ablation of the area of hyperplasia or utilization of the stent in stent technique. The stent-in-stent technique deploys a second FC stent inside the first stent. Over a few weeks, the increased pressure generated causes ischemia in the hyperplastic tissue, thus allowing easier removal of both stents.

The high success rates with relatively low morbidity of SEMS make it an effective tool in the management of leaks after bariatric surgery. Although complication rates are high, they are often not severe and are typically managed endoscopically and with less morbidity than re-operative events. Additionally, even with failure of defect closure, these procedures offer leak control and initiation of nutrition repletion allowing for reduction and ultimate resolution of the systemic burden, optimizing the patient for future definitive interventions.

Clipping

Another important tool available to the bariatric endoscopist is the unassuming endoscopic clip. Through-the-scope endoscopic clips have been available for nearly 40 years. Previously primarily used for hemorrhage control due to ulceration, Mallory-Weiss tears, diverticular bleeding, or high bleeding risk polypectomy sites, its role expanded in the 1990s as the bariatric surgeon's endoscopic experience increased. Improved clip technology further advanced its use as an adjunctive tool for securing stents, feeding tubes, fistula closure, sealing of the luminal entry site in experimental natural orifice transluminal endoscopic surgery (NOTES), and for the management of bariatric postoperative anastomotic leaks and perforations [21].

Earlier generations of endoscopic clips were reusable varieties that required manually reloading a disposable clip placed onto a hook at the end of a reusable metal cable that ran through a plastic sheath. Disposal preloaded versions are now more commonly used. Modern preloaded clips further expanded its application for more complex issues as ease of use offered the endoscopist increased speed, maneuverability, and control. Improvements including increasing jaw opening diameters (5–11 mm), eliminating the need for plastic sheathing, and adding the capacity for clip reopening prior to finally deployment allow for increased flexibility of use. The bariatric surgeon can now seriously consider use of the endoscopic clip as a viable adjunct or alternative endoscopic tool for expanded indications. The endoscopist must be aware, however, of the appropriate FDA-approved indications for the selected device.

Two-pronged clip options are the most commonly used. Three major options are available in the United States: Cook Medical Instinct (USA, 2011), Olympus Corporation QuickClip Pro (Japan, 2014), and Boston Scientific Corporation Resolution Clip 360 (USA, 2016). Indications for use include endoscopic marking, hemostasis, affixing jejunal feeding tubes to the bowel wall, as well as a supplementary closing method for GI tract luminal perforations <20 mm that can be treated conservatively. Small luminal defects may be closed with serial clip placement, reducing the defect size with each subsequent clip application, until the tissues are re-approximated (Fig. 3.2).

Accurate and secure placement is possible with the ~11 mm jaw spans that can be opened and closed up to five times prior to final clip

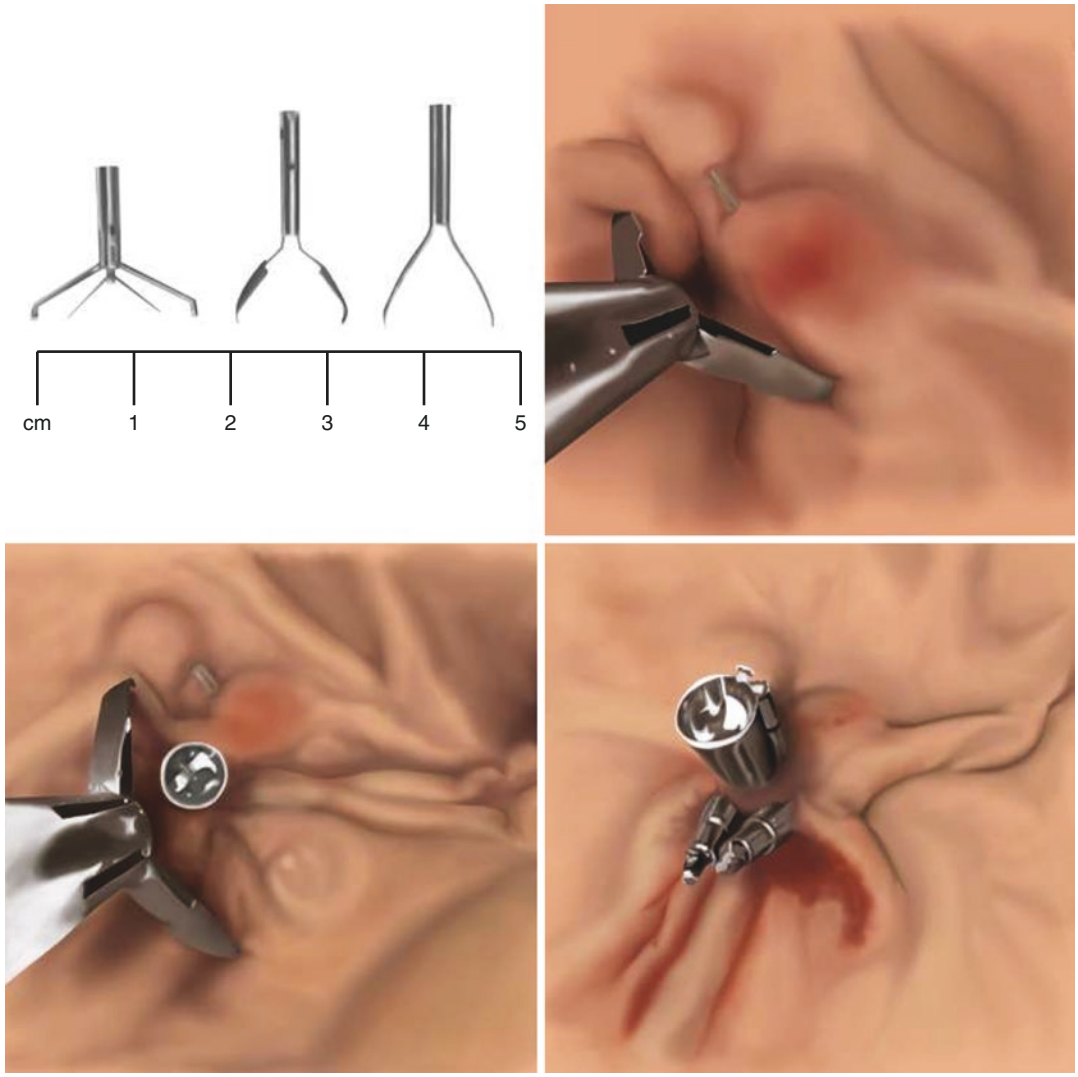

Fig. 3.2 Through the scope clip options for intraluminal control of bleeding/perforation

deployment. Today's endoscopist also benefits from the 360°, one to one positional rotating capacity and tactile feedback provided through the cable during manipulations available with these modern endoclips. Note that the capacity for full rotation and repeated opening and closing may be limited by the patient's anatomy, torque forces applied along the scope, and the unique conditions of the case.

Prior to committing to the final position, the endoscopist must confirm the clip's firm grasp of the tissues prior to complete closure to ensure maximum tissue capture. Once confirmed, the GI technician firmly squeezes for final clip deployment. The clip should unhook spontaneously from its inner cable. Once free from the clip, the catheter can be removed from the scope. If the clip remains attached to the cable, a gentle "jiggle" along the catheter encourages complete disengagement of the clip. Care should be taken not to remove the catheter until the clip is completed unhooked from the inner cable, otherwise tissue injury or clip dislodgement can result.

Two endoclips (QuikClip Pro [Olympus Corporation, Japan] and Instinct [Cook Medical, USA]) require a plastic over sheath. Clip deployment with these devices requires advancing the clip beyond the plastic over sheath to expose all portions of the clip's functioning mechanism. Advancement partially opens the clip as it is pushed forward. The clip is then "primed" by squeezing the trigger part way. This opens the clip to its maximum diameter. Once "primed" and fully opened, this clip can now be directed toward the target tissue. The GI technician needs to be aware that if the trigger is squeezed too far, the clip will start to irreversibly close, severely limiting its full function. With the clip properly "primed" in its fully opened position, the desired deployment site is targeted and squarely placed between the clip jaws with endoscopic maneuvering. If needed, clip rotation at the catheter or by the technician is done prior pressing the clip firmly against the target tissue. Once the clip is in position, the GI technician then squeezes the trigger all the way until a "click" is heard and felt. This completes the deployment cycle, and the clip can no longer be opened. The clip is released from the catheter in a similar fashion to that described above.

Studies comparing the various clip options have not identified dramatic differences between them. It is more important to be familiar with the selected device and to ensure appropriate patient selection and indication for use. Remember that the through-the-scope clips will have limited efficacy in primary leak closure if the defect is too large relative to the maximum clip opening width and if poor tissue quality precludes durable apposition of healthy tissue. Additionally, discussion with the GI technician team prior to use of a specific clip ensures the team's familiarity with the selected device and the overall success of the procedure.

Over-the-scope clips (OTSC) have shown promise as a more effective option for leak seal. These clips are larger and have been used to close leak defects up to 3 cm with good result. Small, clean defects are best suited for clip placement as a stand-alone therapy for closure. Larger defects with friable tissue are better approached with stenting in addition to clips. Leak closure rates of ~ 80% have been reported when a combination of endoscopic procedures, either concurrently or in series, is utilized. Clip placement for leak closure is often combined with stenting and fibrin glue application [22–24]. While earlier studies primarily looked at clipping leaks from LSG, more recent data has confirmed the utility of clipping for RYGB surgery as well.

The OTSC system (Ovesco) is assembled prior to insertion of the endoscope. The clip comes loaded onto a cap that is placed over the tip of the scope. A string connected to the clip is pulled through the working port of the scope and into the endoscopists' hand. The scope is placed over the visualized defect, and suction is used to bring the tissue into the cap, while the endoscopist pulls the string, and the clip is deployed. Clips and caps both have different sizes, and selection is based on the specific characteristics and dimensions of the defect.

An essential tenet for success in endoscopic therapeutic modalities is meticulous preparation of the target tissue. Adequate drainage of the leak cavity and debridement of necrotic tissue if present is imperative prior to attempts at endoscopic closure. Debridement and freshening of the edges of the leak cavity with the argon plasma coagulation prior to clip placement encourage local inflammation, incite wound healing, enhance scarring, and improve wound closure.

All of the options discussed are more effective when key concepts that significantly improve accurate and secure clip placement are carefully considered. First and foremost, effective clip deployment is best achieved when the distance between the scope and the target tissue is minimized. It's best to keep the clip tip to within 2–4 cm from the scope tip to improve accuracy, ensure appropriate deployment, and prevent bowing or bending of the catheter. Increasing the exposed catheter length decreases the translational force to the tissue, decreasing overall accuracy and control. Additionally, keeping the catheter perpendicular to the target tissue minimizes a tangential approach, which improves accuracy, maximizes the amount of tissue captured, and ensures proper clip deployment. If a

retroflexed position is needed, advancing the catheter out of the scope before retroflexion eases navigation beyond the extreme angulation at the scope tip. Most importantly, have a clear and confirmed strategic plan before exposing the clip. Extraneous maneuvering of the scope with an open clip can cause luminal damage or dislodge the clip from its catheter prematurely.

Suctioning

Intraluminal techniques, such as stenting, provide leak coverage and prevent growth, but often ignore and isolate the associated extraluminal cavity. Cavity isolation can lead to abscess formation and ongoing systemic sepsis. Access to these cavities, even with radiographic guidance, can be difficult. Although endoscopic stent placement is an option and procedural risks are low, as stated before, post-stent complications other than migration can be expected in up to 22% of patients [19, 25].

An emerging alternative is endoscopic vacuum-assisted closure (Endo VAC) therapy. Endo VAC therapy was first reported in 2008 for the treatment of anastomotic leaks after anterior resection of the rectum [26]. Its use has since expanded to the management of upper gastrointestinal leaks and bariatric surgery. High success rates of 60–80% with relatively lower morbidity have been reported confirming Endo VAC as a useful adjunct for leak and perforation management when conventional treatment options are unsuccessful or contraindicated. The minimally invasive nature of this therapy also contributes to its appeal.

The principles of therapy are based on the even distribution of continuous negative pressure suction by the open-pore polyurethane sponge attached to the tip of a drainage tube endoscopically positioned in the damaged zone of tissue (Fig. 3.3). The transnasal end of the tube is connected to the external vacuum system. Endoscopic assessment and preparation of the area confer the advantage of allowing potential sponge placement into the extraluminal cavity when feasible. The negative pressure

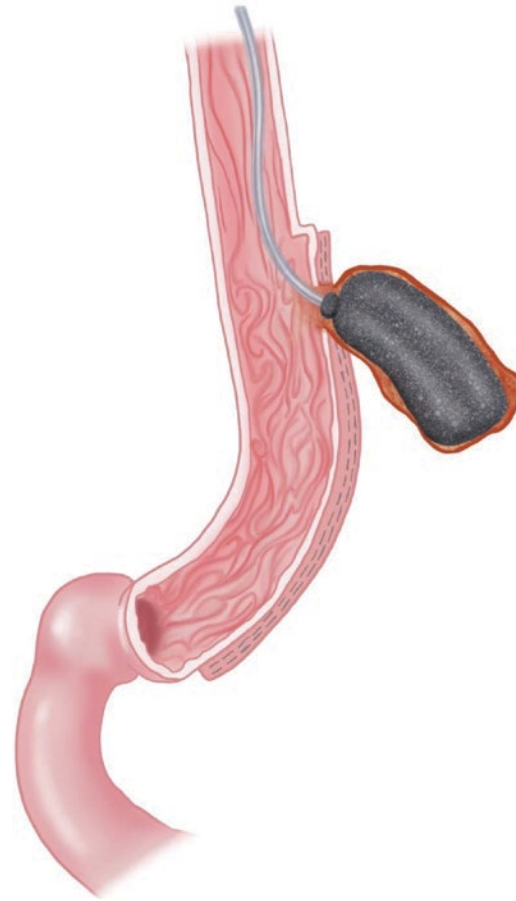

Fig. 3.3 Depicting Endo VAC therapy of a sleeve gastrectomy leak

mechanically clears intracavitary microorganisms and improves microcirculation that reduces interstitial edema. Collapse and closure of the extraluminal cavity occur as granulation tissue increases and re-epithelialization is initiated. After intracavitary closure as suggested by endoscopic evaluation or radiographic resolution, therapy continues with intraluminal placement of the polyurethane sponge, leading to primary defect closure. Alternatively, even if intracavitary sponge placement is not feasible, intraluminal sponge placement and external drainage of the cavity remain useful.

The initial Endo VAC procedure requires general anesthesia with the patient positioned supine. Endoscopic assessment is essential for appropriate sponge positioning. Thorough evaluation of

the luminal defect, its position from the incisors, orientation, and defect diameter as well as a similar assessment of the extraluminal cavity location and dimensions is essential. Gentle balloon dilation of the sinus tract improves access to and subsequent drainage of the extraluminal cavity. Placement of an endoscope overtube is sometimes necessary if a significant amount of preparatory intervention is required for this phase of the procedure. Preparation of the zone of therapy involves thorough irrigation and appropriate debridement of necrotic tissue.

Once endoscopic preparation and assessment is completed, a 12-French nasogastric tube (NGT) is placed transnasally and brought out through the mouth. The NGT may need to be trimmed to achieve the appropriate length. The sponge is tailored to fit the previously assessed leak cavity and secured to the tip of the NGT using 2-0 silk suture. The sponge should cover all of the NGT side holes. A looped suture is placed at the distal end of the apparatus to allow for guided placement using an endoscopic biopsy forceps.

A jaw lift maneuver opens the oropharyngeal area to allow for reintroduction of the gastroscope with the biopsy forceps within the therapeutic channel grasping the looped suture on the distal end of the sponge-tipped NGT. The sponge-tipped NGT is held alongside the gastroscope as the entire system is guided beyond the cricopharyngeal area. Once in the area of interest, the open-jawed forceps are used to push the sponge into the leak cavity. Once in position, continuous negative pressure at 100–125 mm Hg is applied prior to scope withdrawal. The pressure fixes the sponge in position, preventing dislodgement.

This apparatus is changed regularly, typically every 2–4 days, in order to prevent significant foam ingrowth into the wound cavity and for proper wound control. The suction must be interrupted when changing the Endo VAC tube apparatus. Gentle irrigation through the NGT with ~30–50 mL of sterile water also allows for ease of removal. Repeat endoscopic assessment allows for re-customization of the sponge if needed.

Procedure times of about 30–60 minutes should be initially expected. Procedure times are expected to decrease with subsequent treatment events as less time will be needed for endoscopic preparation and sponge customization. Preassembled Endo VAC sets for upper gastrointestinal leak and perforation management are also becoming more readily available commercially.

Treatment durations vary and depend on the wound response to therapy. Therapy should continue until the extraluminal cavity has completely collapsed and closed and the wound cavity is fully lined with granulation tissue. A recent series identified cavity characteristics associated with improved outcomes. Simple, contained, and relatively small cavity sizes of <8 cm in maximal dimension were more responsive to Endo VAC therapy. This group also noted an increased risk for procedure-associated complications in chronic, larger, loculated cavities. The chronicity of the inflammatory process and track fibrosis increased the risk of injury to adherent adjacent structures during Endo VAC tube changes and less responsiveness to therapy despite ongoing therapy [25, 27, 28].

Overall healing rates of 78–90% have been reported. Its minimally invasive approach demonstrated advantages over surgical revisions and primary SEMS management [25]. As previously discussed, differing endoscopic modalities can be employed in the same patient during different phases of the patient's treatment, depending on the specific need and situation. Endo VAC can easily be used in conjunction with other therapies, such as SEMS or endoclip placement, particularly after initial reduction of the extraluminal cavity by Endo VAC. The customizable and varied endoscopic treatment pathways nonetheless work toward minimizing morbidity and mortality and decreasing hospital lengths of stay. Of note, Endo VAC's promising primary healing rates and low morbidity demonstrate its potential to become a safe nonsurgical primary therapeutic approach to these complex and clinically challenging clinical problems [27, 28].

Endoscopic Internal Drainage (EID)

Another endoscopic technique that is gaining traction for leak management is internal drain-

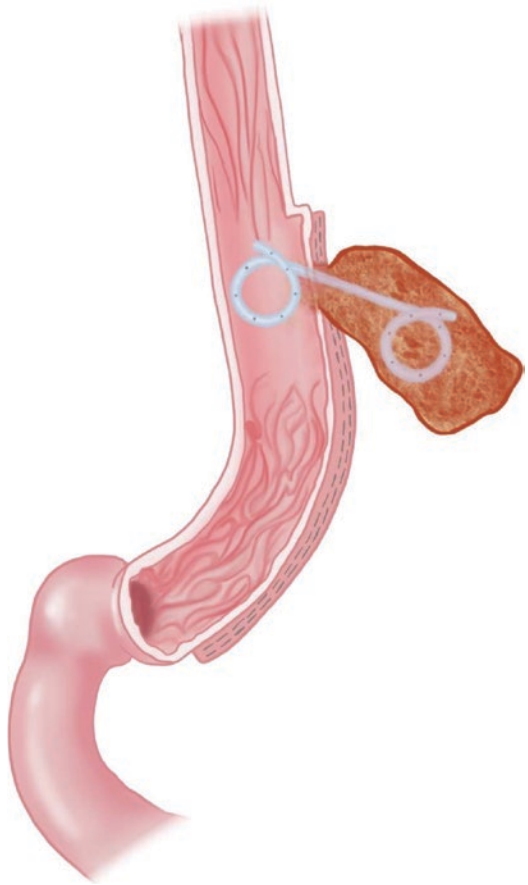

Fig. 3.4 Depicting endoscopic internal drainage of sleeve gastrectomy leak

age of the leak cavity using double pigtail plastic stents. A wire is endoscopically placed into the leak cavity, and one to three 7–10 Fr pigtail stents are inserted with one end in the cavity and the other in the natural lumen (Fig. 3.4). This encourages drainage of leak cavity contents into the natural lumen and also creates irritation by the plastic stents that stimulates epithelialization of the shrinking cavity [29, 30]. This helps to promote cavity closure as drainage continues. Internal drainage also allows for the removal of transcutaneous drains thereby avoiding fistula formation. There are few published studies on EID, but they show success rates of 86–100% and have fewer complications than stenting. One downside to EID is the need for longer treatment durations with average times until closure of 52 days [30] and a reliance on post pyloric enteral feeding. Data is also lacking on the optimal duration of therapy. Nevertheless, it is a safe and effective technique that is well tolerated and worthy of consideration in chronic leaks.

Bleeding

Bleeding complications associated with bariatric surgery can be described based on the temporal relationship of presentation to the operative event: intraoperative, the early postoperative period, and the late postoperative period. Endoscopic therapies can be applied for the management of either early or late bleeding presentations.

Early bleeding presents within 48 hours of the operative event. Early presentations can result from either intraluminal or intra-abdominal sources. Intra-abdominal bleeding can occur from any staple line created or adjacent organ injury and is best managed by urgent surgical intervention. Early bleeding occurs in 1–5% of bariatric patients after RYGB and 0–8% of SG patients [31].

For RYGB patients, intraluminal bleeding can occur at either anastomosis, but is most frequently seen at the GJ site. Bleeding can also occur from within the remnant stomach and the bypassed proximal gastrointestinal tract (Fig. 3.5). While rare, these scenarios must be considered in the RYGB patient presenting with gastrointestinal bleeding. Use of a double balloon enteroscopy or laparoscopic-assisted gastroduodenostomy may be necessary to access and interrogate the remnant stomach or bypassed intestinal tract as the source of bleeding.

Current literature supports the safe use of endoscopic therapies for the primary management of postoperative upper GI hemorrhage. Acceptable endoscopic therapies for hemorrhage control include sclerotherapy, surgical electricity, and clipping [32, 33]. Endoscopic clipping and sclerotherapy (Fig. 3.6) are the primary endoscopic methods employed, while monopolar or bipolar energy instruments for hemorrhage control are discouraged and should be used with caution. Use of electrosurgical modalities at the

Fig. 3.5 Depicting possible bleeding sites from Roux-en-Y gastric bypass

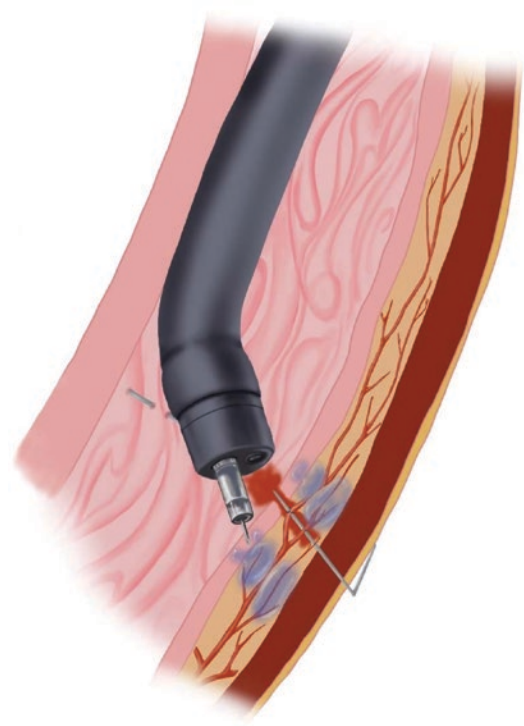

Fig. 3.6 Depicting endoscopic sclerotherapy of staple line bleeding

staple line invites the risk of thermal injury due to direct coupling with subsequent metal-to-metal arcing, resulting in injury that can lead to progressive tissue damage, ischemia, and possible necrosis with perforation.

Late bleeding is primarily due to an ulcerative processes. Patients often present with abdominal pain, nausea, emesis, and food intolerance in addition to clinical evidence of bleeding such as anemia. Endoscopic evaluation most commonly identifies the site of ulceration at the GJ anastomosis. Ulcers seen along the gastric side of the anastomosis (stomal ulcers) are typically due to ischemia secondary to technical factors of the operation. The etiological factors for ulcers seen on the jejunal side of the anastomosis (marginal ulcers) are not well understood. Possible risks for marginal ulcers include smoking, NSAID use, steroid use, alcohol use, acidic gastric secretions, and foreign bodies. For hemodynamically stable patients presenting with marginal ulceration and one or more of these risk factors, cessation or treatment of the underlying aggravating factor can be effective. Hemodynamically significant ulcerative bleeding can be safely and effectively managed with endoscopic clips, sclerotherapy, and electrosurgery. After initial hemorrhage control, all patients with marginal ulcers should be followed with regular endoscopic intervals, typically every 2 months, to monitor their response to therapy.

Helicobacter pylori association is controversial with some studies demonstrating higher rates of marginal ulcer formation in patients with existing *H. pylori* disease [34] and others showing no difference [35].

Foreign bodies near the operative sites can serve as a nidus for ulceration and irritation. The use of staples and permanent sutures, such as polyester, can cause local irritation, inflammation, and resulting erosions and ulceration in the area exposed to gastric secretions. These patients often present with chronic abdominal pain along with clinical evidence of bleeding. Endoscopic removal of the foreign body is an effective and safe treatment option [36].

Finally, in patients with ulcers refractory to treatment, a gastro-gastric (GG) fistula must be ruled out. These increase the direct jejunal acid exposure from the remnant stomach and can be difficult to identify. Contrasted studies and endoscopy are useful for evaluation and diagnosis of a GG fistula.

Stenosis/Stricture

Stricture or stenosis after bariatric surgery is a relatively common complication. Strictures are particularly common after RYGB, occurring in ~15% of patients, usually involving the GJ anastomosis. Technical error during anastomotic construction, ulceration due to ischemia or environmental factors, and prior endoscopic intervention for bleeding such as sclerotherapy are predisposing factors. Strictures are also the most common complication in the LSG population, occurring in ~4% of patients, with the area of the incisura being the most affected [37].

Patients typically present several weeks to months after surgery, but earlier presentations within 1 month of surgery can occur. Prospective studies evaluating the presence of GJ stenosis identified stenosis rates of 25–36% at 1 month, of which only one third are symptomatic [38]. Patients usually complain of dysphagia, nausea, emesis, and early satiety without abdominal pain. The acuity of the patient's presentation varies based on the degree of stenosis. Severe stenosis can severely limit the patient's capacity to maintain nutritional support, hydration, and saliva management. Appropriate clinical management including resuscitative efforts, repletion of electrolyte derangements, and nutritional support is essential for improving outcomes and response to therapies. Early endoscopic evaluation is essential in formulating a management strategy. Stenosis can be mild (7–9 mm), moderate (5–7 mm), and severe (<5 mm).

Retrospective reviews of symptomatic patients identified a 6–10% incidence of problematic strictures [39]. Symptomatic strictures are best treated endoscopically with through-the-scope (TTS) balloon dilators. The simplicity of TTS balloon dilation, requiring only a single intubation event of the esophagus, makes it the preferred method over bougienage. It is safe and effective with current data estimating acceptable perforation rates at 2–4%, including repeat dilations [38].

Bougienage with the serial oral advancement and passage of bougie dilators through the area of stricture is as effective as TTS balloon dilation with reported success rates approaching 100%. The lack of visualization during the bougie dilation event, however, makes this a less attractive option [40]. Regardless of technique, patients often require multiple dilation events prior to achieving durable results. Fortunately, these procedures are reasonably well tolerated, have minimal morbidity, and can produce lasting effects.

Compared to RYGB strictures, SG patients with stenosis are not as easily managed endoscopically. Balloon and bougie dilation are good options for treatment, but they are only successful 56% of the time. If durable resolution is not achieved after three dilations attempts, SG patients with symptomatic strictures should be considered for surgical intervention with conversion to Roux-en-Y gastric bypass [37]. Since revisional surgery is associated with significantly increased risk for perioperative morbidity, endoscopic interventions should be fully exhausted prior to considering reoperation.

Gastric Band Erosion

A relatively rare but serious complication of the adjustable gastric band is device erosion into the

stomach. This occurs in 1–2% of adjustable gastric band patients and occurs on average 3–4 years after band placement [41]. This complication sometimes presents with free gastric perforation requiring emergent surgical intervention, but the majority of patients present more insidiously with abdominal pain, nausea, and weight regain as the most common presenting symptoms. Port-site infections should also prompt investigation to rule out band erosion. Total endoscopic removal of the eroded band has been well documented and adopted by many bariatric surgeons. Complete endoscopic extraction has been shown to be effective and safe while avoiding a potentially major surgery. Success rates approach 90–95% in most series with low complication rates [42]. The best-described technique involves passing a guide wire around the band and re-grasping it to form a loop. A mechanical lithotripter is then used to cut the band with the looped guide wire. The band is disconnected from the subcutaneous port and removed transorally [42].

Conclusion

Today's bariatric endoscopist can choose from a wide variety of endoscopic therapies when managing postoperative bariatric surgical complications. These endoscopic alternatives or adjuncts offer less morbid and less invasive options to immediate reoperation. The surgeon is provided incredible flexibility to choose between concomitant applications and combinations of therapies, serial applications of the same therapy, or layering in different modalities across specialties. The art comes in selecting the appropriate modality, or combinations of modalities, along with its timing that allows for either clinical resolution or the luxury of time to strategize and plan for definitive surgical intervention. Either outcome is welcomed in these challenging situations. The availability of safe endoscopic options for managing challenging postoperative bariatric surgical complications undoubtedly strengthens the role of the bariatric surgeon as a part of the solution to the global obesity epidemic.

References

1. Sjöström L, Narbro K, Sjöström CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med. 2007;357(8):741–52. https://doi.org/10.1056/NEJMoa066254.
2. Buchwald H, Estok R, Fahrbach K, Banel D, Sledge I. Trends in mortality in bariatric surgery: a systematic review and meta-analysis. Surgery. 2007;142(4):621–32. https://doi.org/10.1016/j.surg.2007.07.018; discussion 632–635.
3. Phillips BT, Shikora SA. The history of metabolic and bariatric surgery: development of standards for patient safety and efficacy. Metabolism. 2018;79:97–107. https://doi.org/10.1016/j.metabol.2017.12.010.
4. Fernandez 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. https://doi.org/10.1007/s00464-003-8926-y.
5. Souto-Rodríguez R, Alvarez-Sánchez M-V. Endoluminal solutions to bariatric surgery complications: a review with a focus on technical aspects and results. World J Gastrointest Endosc. 2017;9(3):105–26. https://doi.org/10.4253/wjge.v9.i3.105.
6. Jiang H-P, Lin L-L, Jiang X, Qiao H-Q. Meta-analysis of hand-sewn versus mechanical gastrojejunal anastomosis during laparoscopic Roux-en-Y gastric bypass for morbid obesity. Int J Surg Lond Engl. 2016;32:150–7. https://doi.org/10.1016/j.ijsu.2016.04.024.
7. Shikora SA, Mahoney CB. Clinical benefit of gastric staple line reinforcement (SLR) in gastrointestinal surgery: a meta-analysis. Obes Surg. 2015;25(7):1133–41. https://doi.org/10.1007/s11695-015-1703-x.
8. Varban OA, Cassidy RB, Sheetz KH, et al. Technique or technology? Evaluating leaks after gastric bypass. Surg Obes Relat Dis. 2016;12(2):264–72. https://doi.org/10.1016/j.soard.2015.07.013.
9. 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(2):287–93. https://doi.org/10.1016/j.gie.2011.09.010.
10. Gonzalez R, Sarr MG, Smith CD, et al. Diagnosis and contemporary management of anastomotic leaks after gastric bypass for obesity. J Am Coll Surg. 2007;204(1):47–55. https://doi.org/10.1016/j.jamcollsurg.2006.09.023.
11. Jacobsen HJ, Nergard BJ, Leifsson BG, et al. Management of suspected anastomotic leak after bariatric laparoscopic Roux-en-y gastric bypass. Br J Surg. 2014;101(4):417–23. https://doi.org/10.1002/bjs.9388.
12. Rosenthal RJ, International Sleeve Gastrectomy Expert Panel, Diaz AA, et al. International sleeve gastrectomy expert panel consensus statement: best

practice guidelines based on experience of >12,000 cases. Surg Obes Relat Dis. 2012;8(1):8–19. https://doi.org/10.1016/j.soard.2011.10.019.
13. Biancari F, D'Andrea V, Paone R, et al. Current treatment and outcome of esophageal perforations in adults: systematic review and meta-analysis of 75 studies. World J Surg. 2013;37(5):1051–9. https://doi.org/10.1007/s00268-013-1951-7.
14. Sakran N, Goitein D, Raziel A, et al. Gastric leaks after sleeve gastrectomy: a multicenter experience with 2,834 patients. Surg Endosc. 2013;27(1):240–5. https://doi.org/10.1007/s00464-012-2426-x.
15. Sharma G, Ardila-Gatas J, Boules M, et al. Upper gastrointestinal endoscopy is safe and feasible in the early postoperative period after Roux-en-Y gastric bypass. Surgery. 2016;160(4):885–91. https://doi.org/10.1016/j.surg.2016.07.001.
16. El Hajj II, Imperiale TF, Rex DK, et al. Treatment of esophageal leaks, fistulae, and perforations with temporary stents: evaluation of efficacy, adverse events, and factors associated with successful outcomes. Gastrointest Endosc. 2014;79(4):589–98. https://doi.org/10.1016/j.gie.2013.08.039.
17. Shehab H. Enteral stents in the management of post-bariatric surgery leaks. Surg Obes Relat Dis. 2018;14(3):393–403. https://doi.org/10.1016/j.soard.2017.12.014.
18. Murino A, Arvanitakis M, Le Moine O, Blero D, Devière J, Eisendrath P. Effectiveness of endoscopic management using self-expandable metal stents in a large cohort of patients with post-bariatric leaks. Obes Surg. 2015;25(9):1569–76. https://doi.org/10.1007/s11695-015-1596-8.
19. Aryaie AH, Singer JL, Fayezizadeh M, Lash J, Marks JM. Efficacy of endoscopic management of leak after foregut surgery with endoscopic covered self-expanding metal stents (SEMS). Surg Endosc. 2017;31(2):612–7. https://doi.org/10.1007/s00464-016-5005-8.
20. Singer JL, Aryaie AH, Fayezizadeh M, Lash J, Marks JM. Predictive factors for the migration of endoscopic self-expanding metal stents placed in the foregut. Surg Innov. 2017;24(4):353–7. https://doi.org/10.1177/1553350617702026.
21. Romagnuolo J. Endoscopic clips: past, present and future. Can J Gastroenterol. 2009;23(3):158–60.
22. Keren D, Eyal O, Sroka G, et al. Over-the-scope clip (OTSC) system for sleeve gastrectomy leaks. Obes Surg. 2015;25(8):1358–63. https://doi.org/10.1007/s11695-014-1540-3.
23. Mercky P, Gonzalez J-M, Aimore Bonin E, et al. Usefulness of over-the-scope clipping system for closing digestive fistulas. Dig Endosc. 2015;27(1):18–24. https://doi.org/10.1111/den.12295.
24. Shehab H, Abdallah E, Gawdat K, Elattar I. Large bariatric-specific stents and over-the-scope clips in the management of post-bariatric surgery leaks. Obes Surg. 2018;28(1):15–24. https://doi.org/10.1007/s11695-017-2808-1.
25. Schmidt F, Mennigen R, Vowinkel T, et al. Endoscopic vacuum therapy (EVT)-a new concept for complication management in bariatric surgery. Obes Surg. 2017;27(9):2499–505. https://doi.org/10.1007/s11695-017-2783-6.
26. Weidenhagen R, Gruetzner KU, Wiecken T, Spelsberg F, Jauch K-W. Endoscopic vacuum-assisted closure of anastomotic leakage following anterior resection of the rectum: a new method. Surg Endosc. 2008;22(8):1818–25. https://doi.org/10.1007/s00464-007-9706-x.
27. Bludau M, Fuchs HF, Herbold T, et al. Results of endoscopic vacuum-assisted closure device for treatment of upper GI leaks. Surg Endosc. 2018;32(4):1906–14. https://doi.org/10.1007/s00464-017-5883-4.
28. Ooi G, Burton P, Packiyanathan A, et al. Indications and efficacy of endoscopic vacuum-assisted closure therapy for upper gastrointestinal perforations. ANZ J Surg. 2018;88(4):E257–63. https://doi.org/10.1111/ans.13837.
29. Bouchard S, Eisendrath P, Toussaint E, et al. Transfistulary endoscopic drainage for post-bariatric abdominal collections communicating with the upper gastrointestinal tract. Endoscopy. 2016;48(9):809–16. https://doi.org/10.1055/s-0042-108726.
30. Donatelli G, Dumont J-L, Cereatti F, et al. Treatment of leaks following sleeve gastrectomy by endoscopic internal drainage (EID). Obes Surg. 2015;25(7):1293–301. https://doi.org/10.1007/s11695-015-1675-x.
31. Khoursheed M, Al-Bader I, Mouzannar A, et al. Postoperative bleeding and leakage after sleeve gastrectomy: a single-center experience. Obes Surg. 2016;26(12):2944–51. https://doi.org/10.1007/s11695-016-2215-z.
32. Jamil LH, Krause KR, Chengelis DL, et al. Endoscopic management of early upper gastrointestinal hemorrhage following laparoscopic Roux-en-Y gastric bypass. Am J Gastroenterol. 2008;103(1):86–91. https://doi.org/10.1111/j.1572-0241.2007.01588.x.
33. Tang S-J, Rivas H, Tang L, Lara LF, Sreenarasimhaiah J, Rockey DC. Endoscopic hemostasis using endoclip in early gastrointestinal hemorrhage after gastric bypass surgery. Obes Surg. 2007;17(9):1261–7.
34. Rasmussen JJ, Fuller W, Ali MR. Marginal ulceration after laparoscopic gastric bypass: an analysis of predisposing factors in 260 patients. Surg Endosc. 2007;21(7):1090–4. https://doi.org/10.1007/s00464-007-9285-x.
35. Rawlins L, Rawlins MP, Brown CC, Schumacher DL. Effect of Helicobacter pylori on marginal ulcer and stomal stenosis after Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2013;9(5):760–4. https://doi.org/10.1016/j.soard.2012.06.012.
36. Ryou M, Mogabgab O, Lautz DB, Thompson CC. Endoscopic foreign body removal for treatment of chronic abdominal pain in patients after Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2010;6(5):526–31. https://doi.org/10.1016/j.soard.2010.02.035.
37. Deslauriers V, Beauchamp A, Garofalo F, et al. Endoscopic management of post-laparoscopic sleeve

gastrectomy stenosis. Surg Endosc. 2018;32(2):601–9. https://doi.org/10.1007/s00464-017-5709-4.

38. Go MR, Muscarella P, Needleman BJ, Cook CH, Melvin WS. Endoscopic management of stomal stenosis after Roux-en-Y gastric bypass. Surg Endosc. 2004;18(1):56–9. https://doi.org/10.1007/s00464-003-8919-x.
39. Ukleja A, Afonso BB, Pimentel R, Szomstein S, Rosenthal R. Outcome of endoscopic balloon dilation of strictures after laparoscopic gastric bypass. Surg Endosc. 2008;22(8):1746–50. https://doi.org/10.1007/s00464-008-9788-0.
40. Escalona A, Devaud N, Boza C, et al. Gastrojejunal anastomotic stricture after Roux-en-Y gastric bypass: ambulatory management with the Savary-Gilliard dilator. Surg Endosc. 2007;21(5):765–8. https://doi.org/10.1007/s00464-006-9134-3.
41. Quadri P, Gonzalez-Heredia R, Masrur M, Sanchez-Johnsen L, Elli EF. Management of laparoscopic adjustable gastric band erosion. Surg Endosc. 2017;31(4):1505–12. https://doi.org/10.1007/s00464-016-5183-4.
42. Neto MPG, 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(4):423–7. https://doi.org/10.1016/j.soard.2009.09.016.

4 Acute Nonsurgical Complications of Weight Loss Surgery

Freeman J. Condon and Robert Lim

Epidemiology

Weight loss surgery is recognized as a durable, effective, and safe treatment for obesity and its comorbid conditions, including type 2 diabetes mellitus [1]. The increasing incidence of obesity in the United States combined with the increased acceptance of WLS has generated explosive growth in the number of procedures performed. In 2008, 220,000 WLS operations were performed in the United States and Canada, a growth from 171,000 cases in 2005 [2, 3]. While bariatric surgery was classically reserved for adults, it is increasingly utilized in the adolescent population [4].

Many bariatric patients will have minor symptoms after surgery regardless of the procedure. This includes nausea, weakness, fatigue, dizziness, hair loss, abdominal pain, distention, constipation, diarrhea, early satiety, and a decreased appetite. Some of these are expected, but others could indicate larger problems. When these patients present acutely, the history of a bariatric procedure may cause providers to automatically consult a general surgeon. Given the number and diversity of patients having undergone WLS, physicians of all specialties must have a working knowledge of the postoperative complications of these operations.

Nutritional Derangements

Deficiencies in essential nutrients are most commonly encountered in those procedures with a malabsorptive component such as the Roux-en-Y gastric bypass (RYGB), though deficits are still found in restrictive procedures such as sleeve gastrectomy [5]. Specific nutrient deficiencies found in the WLS cohort are those of B12, folate, iron, thiamine, calcium, protein, and the fat-soluble vitamins A/D/E/K. Daily supplementation and close follow-up is the number one preventive strategy guarding against these complications. A 2-year postoperative biochemical assessment of nutrition status has demonstrated strong prediction of future micronutrient deficiencies [6].

Vitamin B12 and Folate

The gastric pouch of the RYGB is relatively lacking in gastric parietal cells. As the first step in B12 metabolism requires cleavage of the nutrient from carrier proteins in a low pH environment,

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patients with bypass anatomy are at risk for poor bioavailability for ingested B12 [7]. The cleaved B12 vitamin then attaches to intrinsic factor usually found in the antrum of the stomach. By bypassing the antrum, the availability of intrinsic factor is low, which means that the B12 that is freed in the gastric pouch is poorly bound for future absorption in the small bowel [8].

Folate absorption takes place within the small bowel and is therefore less susceptible to deficiency as a result of operations on the stomach. That said, the body does not maintain long-term storage of folate, and poor dietary intake can result in deficiency. To compound the problem, up to half of WLS patients are already deficient in folate preoperatively [9]. Women of reproductive age and their obstetricians must pay special attention to folate supplementation as standard multivitamin doses are insufficient to support healthy neural tube formation in utero [10].

Vitamins B12 and folate are necessary for erythrogenesis and nerve myelination. WLS patients with deficiencies in these nutrients therefore present with megaloblastic anemia, neuropathy, glossitis, and stomatitis. While the most common neurologic sequela of B12 deficiency is the distal paresthetic neuropathy of subacute combined degeneration, other neuropsychiatric findings are broad and may be subtle including irritability, insomnia, and slowed mentation, among others [11].

Supplementation of B12 is well tolerated and can be achieved through daily oral tabs or subcutaneous monthly injections. In the case of folate, a daily multivitamin twice a day after RYGB is sufficient for the majority of patients, though women of childbearing age may require additional supplementation.

Thiamine (B1)

Thiamine absorption occurs primarily in the duodenum, so RYGB patients are at elevated risk of deficiency given their bypass anatomy. In all WLS patients, the highest risk of deficiency comes in the setting of prolonged vomiting from any cause [12]. The feared complication of thiamine deficiency is the development of Wernicke-Korsakoff syndrome, a debilitating constellation of neurologic sequelae that may be irreversible. While more classically associated with the malnutrition present in chronic alcoholics, increasing incidence of Wernicke's encephalopathy (WE) is reported in the WLS community [13]. Clinical signs of this entity are encephalopathy, lateral rectus gaze palsy, and ataxia. The WLS patient who presents with prolonged vomiting must not, therefore, be given parenteral glucose solutions as these accelerate the consumption of what little thiamine remains and can precipitate the progression from WE to Korsakoff syndrome, the effects of which are irreversible.

In the acute setting where thiamine deficiency is suspected, parenteral high-dose repletion is required, and several protocols exist for this purpose. Thiamine deficiency is prevented with daily oral supplementation. Though standard multivitamins contain thiamine in excess of the recommended daily value of ~1 mg, WLS patients require additional supplementation. A daily intake up to 12 mg has been suggested [14]. This may be achieved with an additional B-complex vitamin.

Calcium and Vitamin D

Vitamin D is a fat-soluble vitamin, and therefore absorption occurs primarily in the ileum. It also requires pancreatic enzymes and bile salts. The delayed mixture of chyme with these products that occurs in RYGB and biliopancreatic diversion-duodenal switch patients therefore increases risk of deficiency. Calcium absorption takes place in the duodenum and proximal jejunum primarily. Its transport is facilitated by an acidic environment as well as the presence of vitamin D. WLS patients therefore have compounded factors that decrease the gut's ability to absorb calcium. Ramifications of calcium deficiency are principally related to parathyroid hormone-mediated osteoclastic resorption of calcium from the bone. While it has been shown that WLS patients have decreased bone density many

years out from surgery, this has not translated into increased risk of pathologic fracture to date [15, 16]. 1200–1500 mg of calcium are recommended for most WLS patients to prevent altered calcium homeostasis [17]. Calcium carbonate requires a low pH environment for availability and is therefore suboptimal. Calcium citrate is favored [18]. Vitamin D (as D3) should be taken in doses of 3000 IU daily to ensure adequate calcium absorption [19].

Fat-Soluble Vitamins (A, E, K)

Vitamins A, E, and K as fat-soluble vitamins are absorbed in a similar manner to vitamin D as above. Deficiencies of these vitamins have theoretical implications in poor wound healing, easy bruisability, and poor visual acuity. In practice, night blindness has been occasionally reported, but other sequelae, if they occur, have not been well established [20]. In any case, standard multivitamins are sufficient for supplementation.

Iron

Iron absorption occurs in the duodenum primarily and requires acidic environment for activation to the ferrous state [21]. Its decreased absorption in WLS patients is therefore, like calcium, multifactorial. As in all cases of iron deficiency, this problem is exacerbated due to menstrual losses in pre-menopausal women. Deficient patients present with fatigue, exercise intolerance, and in severe cases, pica. The anemia present in these patients can result from either iron deficiency or B12 deficiency as above, and so findings of microcytosis and hypochromia are needed to confirm the diagnosis. Oral iron repletion over and above the quantities found in multivitamins is required, and combined supplementation with vitamin C increases the bioavailability of ingested iron [22]. In contrast, simultaneous calcium ingestion impairs iron absorption. While both iron and calcium supplementation are necessary, they must be temporally spaced to avoid antagonism.

Biliary Complications

Rapid weight loss, decreased biliary kinesis, and operative changes to hepatic branches of the vagus nerve all contribute to increased generation of cholelithiasis [23]. In the case of an obese patient with preoperative symptomatic cholelithiasis, there is broad agreement for the contemporaneous removal of the gallbladder at time of WLS [24]. Though prophylactic cholecystectomy has been performed for asymptomatic patients at the time of their weight loss procedure, this is far more controversial. Little benefit has been demonstrated for synchronous cholecystectomy in this population [25]. Better supported is the use of ursodiol for 6 months postoperatively to prevent stone development, which results in a 16-fold relative reduction in choleliths [26].

Given their altered anatomy, RYGB patients who develop choledocholithiasis can be particularly vexing to manage. The mainstay of treatment for common duct stones, peroral ERCP with sphincterotomy or stone retrieval is exceedingly difficult as the ampulla of Vater is no longer accessible through traditional enteroscopy. Right upper quadrant pain with biochemical suggestion of obstruction should therefore be interrogated using MRCP. If present, common duct stones can be accessed by double balloon enteroscopy, though this requires specialized equipment and skilled practitioner. Alternatively, laparoscopic transgastric ERCP, percutaneous transhepatic cholangiography, or surgical common bile duct exploration may be required.

Hypoglycemia

Hypoglycemia can occur in up to 10% of bariatric patients [27]. Patients will typically present with postprandial palpitations, dizziness, weakness, diaphoresis, and nausea. Some will present with neuroglycopenia (altered cognition, seizures, and loss of consciousness) which can cause traumatic accidents and social impairment [28]. True post-bariatric hypoglycemia usually starts 1 year after the procedure [29]. The diagnosis can be difficult

to make, but a postprandial reaction within 3 hours should make someone suspicious. Most of the time, the symptoms can be treated by dietary counseling and medications that block glucose absorption [29]. However, refractory and the most severe cases may require surgery to include G-tube placement into the gastric remnant after RYGB to stimulate the normal hormonal pathways for glucose control or reversal of the RYGB. Of note, though, outcomes from these procedures are variable [28]. A consult to an endocrinologist or certified bariatrician should be made to assist with the diagnosis and management.

Psychiatric Complications

A therapeutic mental health effect from WLS has been demonstrated. Studies document up to 70% remission in depression following surgery [30]. Also widely reported are increased rates of psychosocial well-being resulting from favorably affected body image [31]. That said, an alarming association with increased suicidality and self-injurious behavior has also been described [32]. The etiology for this rise and dangerous behavior has not been elaborated. It has been hypothesized, however, that failure of postoperative weight loss may play a role [33]. Additionally, in one study alcohol use disorder was more prevalent in the second postoperative year than preoperatively [34]. Taken together these findings suggest that psychiatric involvement in the WLS process must not be limited to the preoperative evaluation stage. Primary care and emergency providers must have a healthy suspicion for self-harm behaviors in the WLS population. Prompt referral and, where appropriate, hospitalization of patients in crisis must be pursued.

Conclusion

Weight loss surgery is a safe, effective treatment for severe obesity and its wide-ranging concomitant disorders. Many of its complications, such as leak and internal hernia, are squarely the purview of the surgeon. As demonstrated above, however, WLS also has several more insidious complications necessitating the involvement and awareness of medical practitioners of all specialties. Frequent longitudinal follow-up is effective at promptly catching and preventing many of these problems before they become crises. Surgical, primary care, nutrition, and psychiatric multidisciplinary follow-up are also strongly recommended.

References

1. Buchwald H, Estok R, Fahrbach K, Banel D, Jensen MD, Pories WJ, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med. 2009;122(3):248–56.
2. Buchwald H, Oien DM. Metabolic/bariatric surgery worldwide 2008. Obes Surg. 2009;19(12):1605.
3. Robinson MK. Surgical treatment of obesity--weighing the facts. N Engl J Med. 2009;361(5):520.
4. Lawson ML, Kirk S, Mitchell T, Chen MK, Loux TJ, Daniels SR, et al. One-year outcomes of Roux-en-Y gastric bypass for morbidly obese adolescents: a multicenter study from the Pediatric Bariatric Study Group. J Pediatr Surg. 2006;41(1):137–43.
5. Gehrer S, Kern B, Peters T, Christoffel-Courtin C, Peterli R. Fewer nutrient deficiencies after laparoscopic sleeve gastrectomy (LSG) than after laparoscopic Roux-Y-gastric bypass (LRYGB)—a prospective study. Obes Surg. 2010;20(4):447–53.
6. Dalcanale L, Oliveira CP, Faintuch J, Nogueira MA, Rondó P, Lima VM, et al. Long-term nutritional outcome after gastric bypass. Obes Surg. 2010;20(2):181–7.
7. Smith CD, Herkes SB, Behrns KE, Fairbanks VF, Kelly KA, Sarr MG. Gastric acid secretion and vitamin B12 absorption after vertical Roux-en-Y gastric bypass for morbid obesity. Ann Surg. 1993;218(1):91.
8. Marcuard SP, Sinar DR, Swanson MS, Silverman JF, Levine JS. Absence of luminal intrinsic factor after gastric bypass surgery for morbid obesity. Dig Dis Sci. 1989;34(8):1238–42.
9. Caudill MA. Folate bioavailability: implications for establishing dietary recommendations and optimizing status. Am J Clin Nutr. 2010;91(5):1455S–60S.
10. Shankar P, Boylan M, Sriram K. Micronutrient deficiencies after bariatric surgery. Nutrition. 2010;26(11–12):1031–7.
11. Stabler SP. Vitamin B12 deficiency. N Engl J Med. 2013;368(2):149–60.
12. Kaidar-Person O, Person B, Szomstein S, Rosenthal RJ. Nutritional deficiencies in morbidly obese patients: a new form of malnutrition? Obes Surg. 2008;18(7):870–6.
13. Aasheim ET. Wernicke encephalopathy after bariatric surgery: a systematic review. Ann Surg. 2008;248(5):714–20.

14. Rudnicki SA. Prevention and treatment of peripheral neuropathy after bariatric surgery. Curr Treat Options Neurol. 2010;12(1):29–36.
15. Lalmohamed A, de Vries F, Bazelier MT, Cooper A, Van Staa TP, Cooper C, Harvey NC. Risk of fracture after bariatric surgery in the United Kingdom: population based, retrospective cohort study. BMJ. 2012;345:e5085.
16. Scibora LM, Ikramuddin S, Buchwald H, Petit MA. Examining the link between bariatric surgery, bone loss, and osteoporosis: a review of bone density studies. Obes Surg. 2012;22(4):654–67.
17. Kellum JM, DeMaria EJ, Sugerman HJ. The surgical treatment of morbid obesity. Curr Probl Surg. 1998;35(9):791–858.
18. Alvarez-Leite JI. Nutrient deficiencies secondary to bariatric surgery. Curr Opin Clin Nutr Metab Care. 2004;7(5):569–75.
19. Del Valle HB, Yaktine AL, Taylor CL, Ross AC, editors. Dietary reference intakes for calcium and vitamin D. Washington, DC: National Academies Press; 2011.
20. Hatizifotis M, Dolan K, Newbury L, Fielding G. Symptomatic vitamin A deficiency following biliopancreatic diversion. Obes Surg. 2003;13(4):655–7.
21. Parrott J, Frank L, Rabena R, Craggs-Dino L, Isom KA, Greiman L. American Society for Metabolic and Bariatric Surgery integrated health nutritional guidelines for the surgical weight loss patient 2016 update: micronutrients. Surg Obes Relat Dis. 2017;13(5):727–41.
22. Rhode BM, Shustik C, Christou NV, MacLean LD. Iron absorption and therapy after gastric bypass. Obes Surg. 1999;9(1):17–21.
23. Shiffman ML, Sugerman HJ, Kellum JM, Moore EW. Changes in gallbladder bile composition following gallstone formation and weight reduction. Gastroenterology. 1992;103(1):214–21.
24. Villegas L, Schneider B, Provost D, Chang C, Scott D, Sims T, et al. Is routine cholecystectomy required during laparoscopic gastric bypass? Obes Surg. 2004;14(2):206–11.
25. Hamad GG, Ikramuddin S, Gourash WF, Schauer PR. Elective cholecystectomy during laparoscopic Roux-en-Y gastric bypass: is it worth the wait? Obes Surg. 2003;13(1):76–81.
26. Sugerman HJ, Brewer WH, Shiffman ML, Brolin RE, Fobi MA, Linner JH, et al. A multicenter, placebo-controlled, randomized, double-blind, prospective trial of prophylactic ursodiol for the prevention of gallstone formation following gastric-bypass-induced rapid weight loss. Am J Surg. 1995;169(1):91–7.
27. Goldfine AB, Patti ME. How common is hypoglycemia after gastric bypass? Obesity. 2016;24(6):1210–1.
28. Salehi M, Vella A, McLaughlin T, Patti ME. Hypoglycemia after gastric bypass; current concepts and controversies. J Clin Endocrinol Metab. 2018;103(8):2815–26.
29. Hanipah ZN, Punchai S, Birriel J, Lansang C, Kashyap SR, Brethauer SA, Schauer PR, Aminian A. Clinical features of symptomatic hypoglycemia observed after bariatric surgery. Surg Obes Relat Dis. 2018;14(9):1335–9.
30. Dawes AJ, Maggard-Gibbons M, Maher AR, Booth MJ, Miake-Lye I, Beroes JM, Shekelle PG. Mental health conditions among patients seeking and undergoing bariatric surgery: a meta-analysis. JAMA. 2016;315(2):150–63.
31. Sarwer DB, Wadden TA, Moore RH, Eisenberg MH, Raper SE, Williams NN. Changes in quality of life and body image after gastric bypass surgery. Surg Obes Relat Dis. 2010;6(6):608–14.
32. Adams TD, Gress RE, Smith SC, Halverson RC, Simper SC, Rosamond WD, et al. Long-term mortality after gastric bypass surgery. N Engl J Med. 2007;357(8):753–61.
33. van Hout GC, Boekestein P, Fortuin FA, Pelle AJ, van Heck GL. Psychosocial functioning following bariatric surgery. Obes Surg. 2006;16(6):787–94.
34. King WC, Chen JY, Mitchell JE, Kalarchian MA, Steffen KJ, Engel SG, et al. Prevalence of alcohol use disorders before and after bariatric surgery. JAMA. 2012;307(23):2516–25.

Part II

Acute Presentations of Anal and Rectal Cancers

5 Initial Presentation, Evaluation and Management of Acute Anorectal Malignancies

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Unfortunately, malignancies of the anorectum are rising in incidence (Fig. 5.1). Therefore, it is fairly common for providers to encounter them in their practice. If discovered by a primary care physician, patients are often referred to gastroenterology, surgery, and/or oncology either sequentially or simultaneously. It is important that surgeons are invested in the relationships with referring colleagues, to inform them about why surgeons prefer to see the patient early in the discovery of their diagnosis. Surgeons have a unique role in the care of rectal and anal cancers, as they are typically at the center of the care plan (Fig. 5.2). The responsibility which lies with surgeons is twofold: (1) determining if upfront resection is the best option and (2) tracking the response to multimodality therapy.

Additionally, the surgeon may be the patient's *only* provider that will perform and document the three-part exam of the anorectum: (1) external exam, (2) digital anorectal exam (DARE), and (3) anoscopy/sigmoidoscopy.

In terms of presentation in the urgent or emergent setting, it is actually *not* common for anorectal malignancies to present acutely. In general, these are slow-growing lesions, and when they originate in a location superior to the dentate line, they are usually insensate. The built-in physiology of the rectum allows for small distensions to be accommodated for with corresponding rectal wall relaxation. In other words, if there was sudden distension of the rectum, the patient would immediately feel it and perhaps perceive it as pain. But when there is slow growth of a tumor over time, the natural adaptive mechanisms of accommodation are triggered, and these lesions are usually not perceived at all. Instead, the patient will present with symptoms of difficult defecation. This can be characterized by tenesmus, fullness, pelvic pressure, or, more generally, constipation. It is critical to keep in mind that many patients also harbor tremendous embarrassment and sometimes even self-blame. Many attribute their changes in bowel habits to self-deprecating comments about their "bad diet," and the like.

Sometimes, if an external lesion is felt by the patient directly or suspected to be present (often patients will avoid touching or looking at their perineum, so they may not even realize), then that may trigger further embarrassment for the patient. They will often refer to their issue as "My hemorrhoids are flaring up again," and this kind of dismissal of their problem as something that is common in the general public. If patients down-play their issues, chronically, it can lead to delays in seeking medical attention. Ultimately, when they reach a point of intolerability, they

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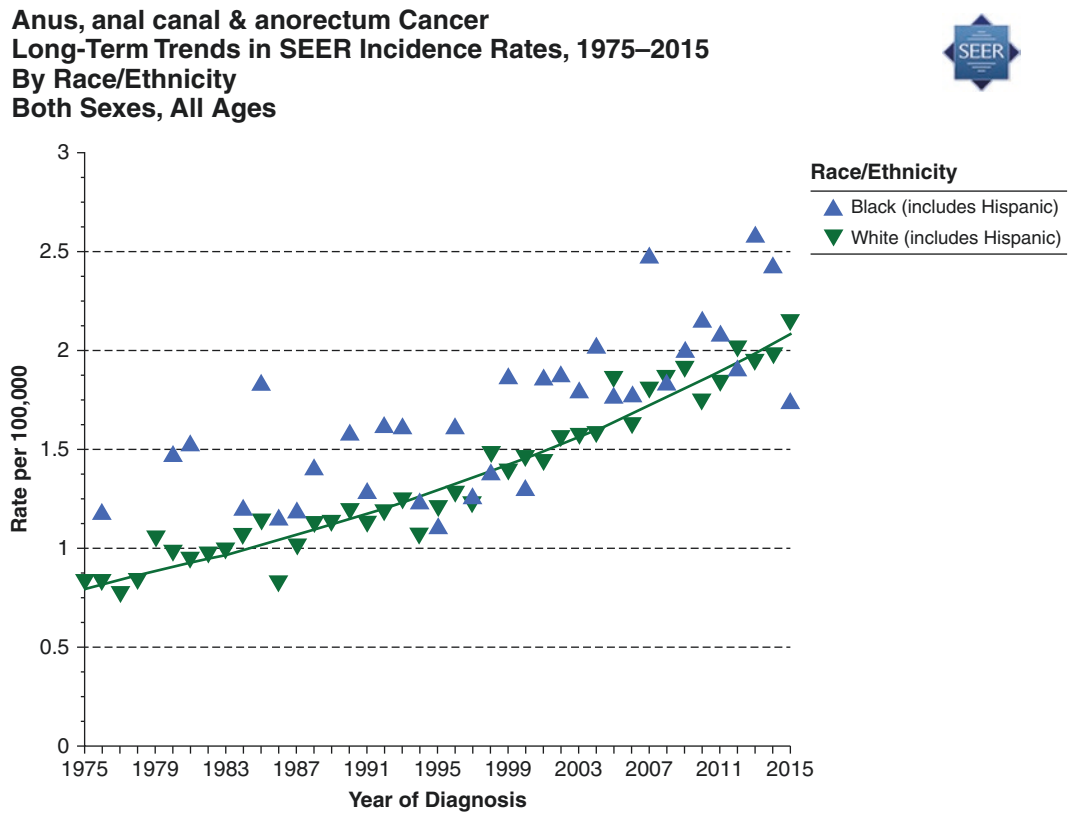

Fig. 5.1 Long-term incidence rates of cancers of the anus, anal canal, and anorectum. SEER incidence of anal cancer (triangle) over the past 20 years

may present to the urgent care setting or the emergency room setting with bleeding, discomfort, or a mass.

The Importance of Compassionate Care During the Active/Participatory Anorectal Exam

As providers, the acute part of the patient's presentation is this: *providers* need to be *acutely* sensitive to the patient's psychological state and fragility. It is of utmost importance that when an exam is performed, the patient feels cared for and reassured and that no comments about our observations (or surprise!) are made to the patient during the exam. Asking questions or giving instructions during the exam is a great way to avoid the natural tendency to say "Oh, my!" or "Wow!". Even if providers are amazed by what they see/feel upon turning the patient, they must refrain from making these kinds of side comments that would cause the patient further embarrassment or undue fear.

The following is a description of an active/participatory anorectal exam. The provider should examine patients in the left lateral Sim's position (Fig. 5.3). Start by resting the left hand on the patient's hip, so the patient won't be alarmed by the initial touch. Then, ask the patient to reach around and hold up their right gluteus. Having the patient's own hand present in that area is reassuring to them. At that point, the provider places their right hand on top of the patient's right hand, again, trying to prevent them from flinching and tensing. Ultimately, the provider needs to come down to the anal area and use their index finger and thumb in opposing directions to spread the external anal canal to see if there are any protrusions. The prone jackknife position (sometimes referred to as the knee-chest position) can cause tremendous suffering in patients who are already fearful of what may be discovered. This position can also detract from a good exam when Valsalva is needed.

The physical examination can be performed with the team member (nurse, student, or resident) and surgeon together. Usually, this will be the abdominal examination, digital rectal examination, anoscopy, and, if available, sigmoidoscopy. To explain why so many people are involved, say "It's good to have multiple sets of eyes on this so we don't miss anything" or "I'm going to need a hand with some of the instruments and your positioning so I have a few helpers." For male physicians, it is often good practice to have a female member of the team present during the pelvic and anorectal exams of women patients. A team-oriented physical examination also helps to sell the care team as a competent unit.

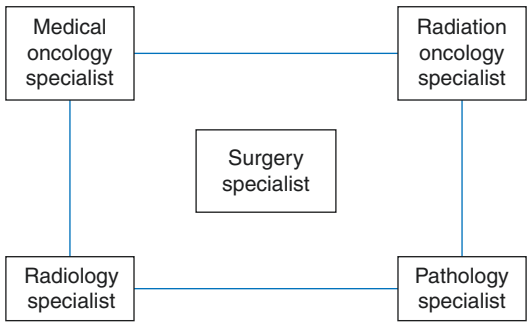

Fig. 5.2 Multidisciplinary team members who assess patients in need of rectal cancer treatment

Patients do not like to be exposed, so try to position the table so that the patient's head faces the door. Consider installing a curtain to be drawn in front of the exam room door. Patients feel vulnerable not being able to see what the care provider is about to do. Talk the patient through every part of the examination. Have them concentrate on motions of the muscles in the area. This actually helps them relax. For example, watch them squeeze the anal muscles. When the patient can elicit a squeeze on command, it is easier for them to then do the opposite motion (relax). Next, have them bear down against a cupped, gloved hand before performing any internal exams. Often, lesions will protrude past the anal canal when the patient bears down. Bearing down (Valsalva) is extremely difficult for a patient to do in the prone jackknife position, which is why the lateral Sim is preferable. If something prolapses, it gives you a sense of what to expect on digital.

About the digital exam: predict and verbalize what the patient may experience and give a warning that a finger is entering the anus or vagina. If a speculum or anoscope is an important part of the examination, then estimate and verbalize the size of the instrument relative to the provider's

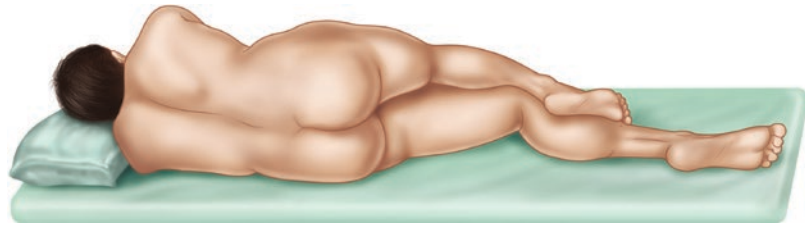

Fig. 5.3 Left lateral Sim's position

finger. Let the patient know that if they experience an urgency to defecate, it is a normal response. Remind them not to move if a cramp occurs.

If pain is elicited with the exam, perform the painful examination only once. If there is no perception of pain, the step may be repeated by another examiner, with the introduction "you are going to feel another finger now." Depending upon the working diagnosis, pain may be predicted with some manipulations. Some exams will not be painful. In any case, an effort to minimize pain will endear you to your patient. For example, lubricate the finger or instrument liberally and be gentle. If you see an obvious fissure (crack in the anoderm in the posterior or anterior midline), do not feel obligated to perform a digital rectal examination or anoscopy on the first visit.

Another tip: sometimes, asking the patient to push out against your finger not only relaxes the muscles but also gives the patient an action to focus on so that he or she won't immediately tense up when sensing your hand nearby.

Comprehensive Documentation of the Examination of the Patient with a Suspected Anorectal Malignancy

In addition to the abdominal exam, noting liver size, abdominal girth, pain, and masses, a groin exam must also be included and is best tracked if documented as a separate line item (i.e., under groin or lymphatics). In terms of timing of the exam, palpating for inguinal lymph nodes can usually be undertaken as part of the abdominal exam when the patient is in the standing and supine positions. Malignancies in the lower rectum and anus can frequently metastasize to these areas.

Table 5.1 lists a suggested order of the awake outpatient exam for suspected anorectal malignancy.

When a provider encounters a lesion, care should be taken to note its size, laterality, and location relative to the anal canal. Annotations should be easily *reproducible*. Colorectal surgical specialists prefer anatomical terms: anterior,

Table 5.1 Suggested order of the awake outpatient visit for suspected anorectal malignancy

Clinical component of visit	Documentation should detail
Focused history	Changes in Weight Constitution Stool habits or caliber Appetite Pelvic pressure or pain Presence of bleeding (related to defecation) Abdominal bloating Personal endoscopic history Family history, family endoscopic history
Clinical exam – part 1 (ok for patient to remain clothed)	Cervical nodes Heart/lung sounds Abdominal palpation Groin palpation
Clinical exam – part 2 (patient needs to be undressed from waist down)	Repeat abdominal exam, looking for scars Repeat groin exam, feeling for inguinal lymph nodes Anorectal exam (see Table 5.2) Administration of enema (if needed)
Anoscopic/office endoscopic exam	Anoscopy (see Table 5.2) Endoscopy, rigid vs. flexible (note distance, laterality)
Patient counseling (best if patient gets redressed and family is with patient)	Next steps Acquisition of tissue and imaging Multidisciplinary team meeting (tumor board presentation) Return to office for discussion of clinical plan

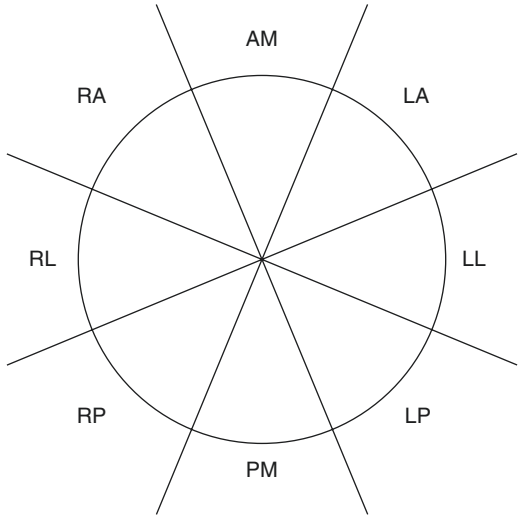

Fig. 5.4 Octants of the anorectal exam. A or AM anterior or anterior midline, LA left anterior, L or LL left or left lateral, LP left posterior, P or PM posterior or posterior midline, RP right posterior, R or RL right or right lateral, RA right anterior

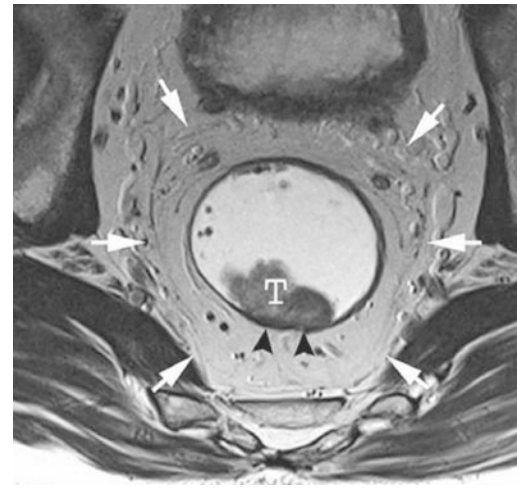

Fig. 5.5 High-resolution MRI image through polypoid rectal adenocarcinoma (labelled T) invading the submucosa but sparing the muscularis propria (T2 tumor). The dark signal along periphery of the rectum (black arrowheads) at the site of the tumor indicates that the tumor has not invaded the muscularis propria. The mesorectal fascia (white arrows) demarcates the mesorectal fat surrounding the rectum

posterior, left, and right. Further divide the anorectum into octants (Fig. 5.4). The "o'clock" designations are only helpful if the patient's position is clearly *and repeatedly* noted (i.e., prone jackknife, lateral decubitus – left or right), so therefore, they are vulnerable to confusion.

When conducting and documenting a lesion in a woman, estimate the size of the perineal body. A provider can get in the habit of doing this in a quick and reproducible way if they are familiar with their own finger's measurements. For example, if the distance from the tip of the thumb to the first knuckle is approximately 2.5 cm, it can be easily documented that a woman's perineal body is approximately 2 cm. When it is less than 2 cm, the provider may worry about and counsel her on having issues with compromise and thinning after chemoradiation. When palpating a lesion that is in the mid- or upper rectum, knowing the finger's measurements is also helpful for the reproducibility of the exam. Providers can annotate it and relate it to referring providers as such: "With my size-6-gloved index finger, I can feel the distalmost aspect of the lesion, but only on Valsalva." This may help guide the radiologist in their role of staging the patient. The best way to stage rectal cancers is by obtaining high-resolution magnetic resonance imaging (MRI) with modern phased array coil which uses specialized sequencing and planning. If oriented to depict surrounding structures relative to the tumor location, then the bowel wall layers can be more easily differentiated (Fig. 5.5). When a radiologist knows where to expect the tumor (based on your clinical description on the radiology order form [Fig. 5.6]), it can reduce healthcare costs.

Lastly, in the clinical documentation, give reference to the patient's resting anal tone and squeeze tone (absent, mild, moderate, strong). These components of the exam are critical to note in this initial evaluation because things may change after surgery or chemoradiation therapy. Table 5.2 lists the essential components of the documented clinical exam for a patient with a suspected anorectal malignancy.

Radiology Imaging Request Form

URGENCY __ Routine __ Emergent __ Sedated MRI MRN _____ Date _____

__ Suggested time frame: ___within a week, and prior to next GI tumor board_____

__ Do you need results read urgently? __ Patient to hand carry disk (CD)?

Patient Name _____ DOB _____ / _____ / _____

Phone Number _____ Can detailed message be left? __ Yes __ No

Patient Height _____ Patient Weight _____ LMP _____ / _____ / _____

Imaging Requested (please be specific):

1st Imaging Request	Diagnosis code (ICD)	History/Symptoms
CT Scan of chest, abdomen and thorax	C20 Rectal Cancer	Newly diagnosed Rectal CA in a smoker, please r/o distant mets
2nd Imaging Request	Diagnosis code (ICD)	History/Symptoms
MRI of pelvis Rectal cancer protocol	C20 Rectal Cancer	Anterior location, 8 cm from anal verge, ~ 3 cm in size, mobile mass relative to prostate
3rd Imaging Request	Diagnosis code (ICD)	History/Symptoms

Ordering Provider (First/Last/Title) _____

Clinic Name _____ Specialty _____

Clinic Contact _____ Tax ID Number _____

In the event a radiologist needs to relay results urgently, please provide an emergency/after-hours contact number:

Emergency Number _____ Daytime Number _____ Fax Number _____

Do results need to go to someone other than the ordering provider? If so, please complete the following information:

Provider Name _____ Clinic/Specialty _____

Phone Number _____ Fax Number _____

Is the patient scheduled? If yes, please provide location and date: _____

Important: Incomplete or illegible forms will be returned, resulting in a delay of scheduling for patient.

Routine Exams: Routine exams are generally processed within 48 hours. Patients will be contacted to schedule after that time.

Urgent Exams: If imaging study is needed within three business days, fax the quest form, notating "emergent." The order will be processed within 24 hours; the patient will be contacted to schedule the exam. PROVIDERS: If the patient has not been contacted within 24 hours after the fax has been sent, please contact the Radiology Appointing Center.

All MRI requests must be accompanied by a completed MRI Questionnaire.

Provider Signature: _____

Fig. 5.6 Sample radiology order form for MRI rectal cancer protocol

Table 5.2 Essential components of the anorectal clinical exam for a patient with a suspected anorectal malignancy

Documentation of anorectal exam	Questions to consider during the exam and to document
External exam	1. Quality of skin/hygiene 2. Presence of blood 3. Presence of extruding masses or fissure 4. Appearance of the anus at rest (some patients will have a patulous anus, meaning that the anus is open at rest, and the rectal vault is seen) 5. Action of muscles on command to squeeze 6. Sensitivity of external area to light touch 7. Valsalva against cupped hand. Does anything protrude or prolapse? If so, does the protrusion/prolapse reduce spontaneously?
Digital anorectal exam (DARE)	1. Finger dilation of the anus and lubrication of the anus in preparation for anoscopy 2. Resting tone, squeeze tone (weak, normal, strong) 3. Any masses/ulcers/polyps palpated? (note size, distance, and laterality) 4. Perform a DARE again during a Valsalva 5. Presence of blood on finger 6. Presence of impacted stool (if stool is present, administration of enema to aid anoscopy)
Anoscopy	1. Quality of rectal mucosa 2. Visibility of dentate line and anal transition zone 3. Accessibility of lesion (if lesion is present) to awake tissue acquisition (biopsy) 4. Documentation of size, distance, and laterality (if possible) 5. Presence and character of blood/mucous

The Role of Endoscopy at Initial Presentation

If a new lesion is discovered in the anorectum, the next part of the patient's work-up usually involves scheduling them for a colonoscopy and/or exam under anesthesia. However, proctoscopy can be performed in the office or in the urgent care setting as a same-encounter experience. In order for the provider to choose the next best step on the work-up algorithm (Fig. 5.7) and to distinguish between an anal lesion and a rectal lesion, it is useful to first focus on the patient's symptoms. Did the patient present with acute pain and are they in pain at present time? If so, their lesion is most likely encroaching on the anal canal, which is sensate (in some patients, disproportionally sensate). While an active/participatory external anal exam is essential for these patients in pain, the DARE, anoscopy, and proctoscopy should be avoided if moderate sedation cannot be easily provided in the setting of that encounter in real time.

If the patient is not in pain and no pain is elicited with the first three steps of the active/participatory anorectal exam ((1) external exam, (2) digital exam, (3) anoscopy), then an exam room-based proctoscopy can be considered.

Proctoscopic exam at initial presentation can be offered in two ways: rigid and flexible. They are discussed in detail in the next chapter.

Anal Exam Under Anesthesia

For a patient who presents with acute pain, uncontrolled bleeding, or obstruction and the cause of these issues is highly suspicious of an anorectal origin, an anal exam under anesthesia (EUA) should be booked.

When surgeons put some thought and preparation into their "preference card" or "pick sheet" (the documents that the operating room team uses to pick surgical instrumentation, supplies, positioning, and draping), it can greatly streamline the process of booking patients. The goals of the visit to the procedure room are:

1. Provide sedation (anesthesia).
2. Administer analgesia (this may result in the first time a patient experiences substantial pain relief).

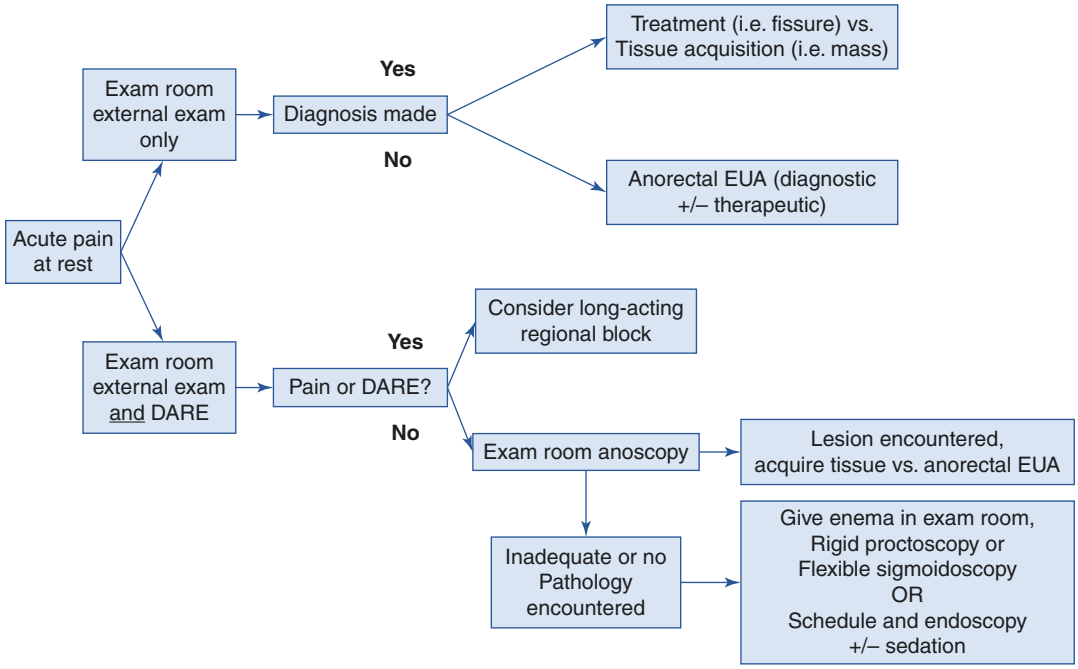

Fig. 5.7 Clinical decision-making algorithm based on presenting symptom (pain, bleeding, obstruction)

3. Obtain a more detailed exam, noting pertinent positives and negatives (which areas are spared).
4. Obtain tissue (if accessible).
5. Dilate and empty the rectal vault (if the patient is obstructed).

To meet these goals, very few instruments are actually necessary (Fig. 5.8).

Excellent exams can be achieved in the lithotomy or high lithotomy position. This positioning is less burdensome on the team in the operating room, allows the anesthesia colleague ample access to the airway, allows placement of an under-buttock collection bag (which is imperative in bleeding cases and in obstructed or near-obstructed cases needing dilation and evacuation), and, when minimal draping is used (clean, but not necessarily sterile), can provide for visual access by all of the team members. Streamlining an instrument set, avoiding sterile drapes, and using the proper waste containers (there is little for the use of biohazard red bags unless the items to be disposed of are soaked in blood) can greatly lessen the healthcare costs. As a general rule of thumb, in terms of relative sterility, what the institution is used to employing for cases performed in the endoscopy suite is acceptable for use in the operating room when doing an anal EUA.

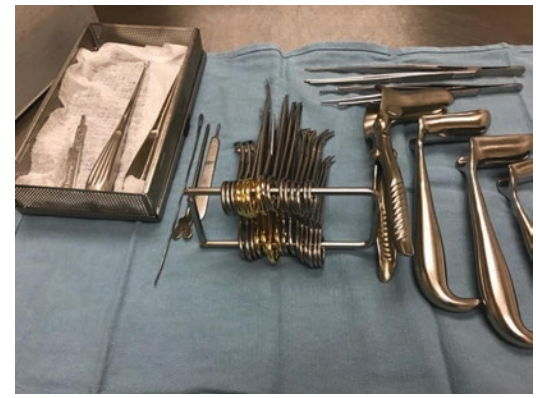

Fig. 5.8 Streamlined "anal minor set"

Antibiotics need not be given, and because these anal EUA cases are very short (usually no more than 30 minutes), using of sequential compression devices only on selective patients will help with ease of access to the anorectum.

Excellent lighting is critical. Invariably, the lamps in the procedure room are not able to focus

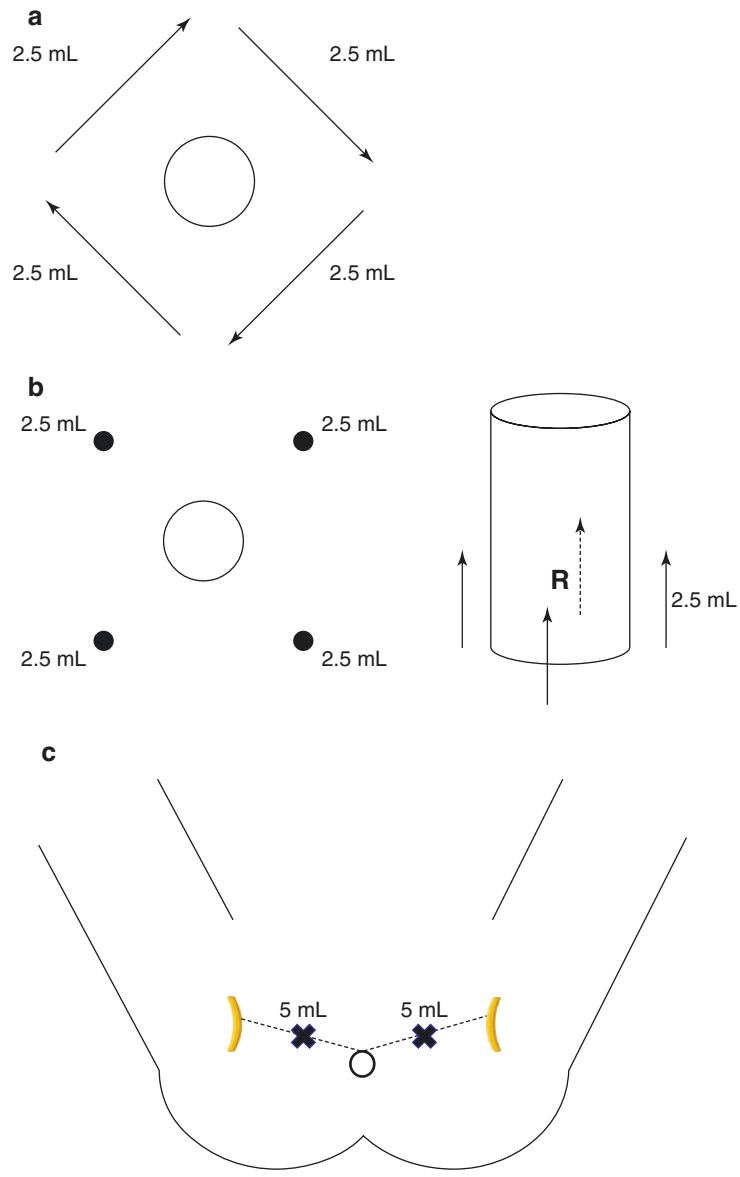

Fig. 5.9 Perianal and pudendal block. (**a**) Start with a superficial anal block using a total of 10 mL of injectate, evenly divided. (**b**) Inject the next 10 mL parallel to the rectum, starting the injection from at least four points. Inject on the way in and way out. (**c**) With the last 10 mL of injectate, divide it equally to do a 5 mL pudendal block on each side. Palpate the ischium, and find the halfway point between the ischium and the anterior aspect of the anus (labelled in this figure as X). Inject the 5 mL in a fan distribution at the location of the X

down narrowly enough to put light through the anal canal and into the rectum. Therefore, a headlamp should be worn or available. Lighted anoscopes can be helpful, though they require a capital investment by the institution. If a flexible endoscope is available, it can be held by an assistant to provide not only focused lighting but also a magnified view.

When the patient is to be positioned prone, many anesthesia providers will be more comfortable with endotracheal intubation prior to flipping the patient. However, when a patient is positioned in high lithotomy, the anesthesia provider may be comfortable with laryngeal mask ventilation. Patients in pain should receive general anesthesia. The goals of care enumerated above can be achieved without general anesthesia for those patients who have no pain on presentation. In those cases, conscious sedation is adequate.

To provide the patients who are in pain with longer term pain relief, consider giving a perianal and pudendal block (Fig. 5.9). This can be done with Marcaine injectate or with liposomal-bound bupivacaine products. In rare cases of pain,

inserting a catheter-directed infusion pump for slow delivery of local anesthesia may be necessary, but not if it will delay the next steps of their work-up and treatment (MRI, radiation, etc.). When the next step of the treatment course is radiation, the pain experienced by patients from a mass is usually greatly alleviated, even after the first dose.

For obstructing lesions, Hegar dilators can be used, keeping in mind that the contents on the other side of the dilator can be under pressure. The use of face masks and eye protection is of utmost importance to the providers involved. Dilation, at the minimum, should be performed to the level of a suction device. Those that have a straight or tapered tip (rather than a tulip tip) are preferred. Ideally, dilation and lavage should be done so that a pediatric endoscope (usually a pediatric gastroscope) can be inserted and a reasonable view can be obtained. In the acute setting, obstructed patients may have a large burden of solid stool proximal to the lesion. Administering Gastrografin solution as a lavage will help break up the inspissated stool. Proximal diversion of these patients is discussed in more depth in a subsequent chapter.

Patients who are acutely bleeding will only bleed further after tissue biopsy is performed, but the conundrum is that the tissue biopsy is critical in choosing the next step in the plan of care. The patient should be medically optimized prior to the biopsy. Is the patient anticoagulated or have a known diagnosis of a coagulation disorder? Can their condition be reversed temporarily? Is the platelet count sufficient? Is there a need for pre-biopsy transfusion of blood and/or blood products?

For patients who are acutely bleeding from a malignancy, if the next step in the treatment algorithm is radiation, initiating this will greatly slow the bleeding. Radiation causes an obliterative end arteritis that will aid in slowing or stopping the bleeding. Endoscopic techniques for bleeding rectal polyps will be detailed in the subsequent chapter.

Shuja et al. have described that radiation therapy can be initiated as a therapeutic option for gastrointestinal cancers that present with bleeding.

Tissue Diagnosis and Documentation of EUA

Anal cancer staging is based on size. Treatment is based in part on stage but also on proximity/involvement of the anal canal. Treatment of anal cancers which involve the canal differs from treatment of rectal cancer as anal cancer relies more heavily on non-operative management using the Nigro protocol. Treatment strategies of rectal cancers have evolved remarkably in the past decade and will be thoroughly discussed in subsequent chapters. Table 5.3 provides a quick reference for staging and subsequent treatment considerations.

Table 5.3 Staging for anal cancer versus rectal cancer

Cancer type	AJCC stage		TNM stage	Characteristics
Anal cancer	Stage 0		Tis N0 M0	Cancer limited to mucosa No LN involvement No metastasis to distant sites
	Stage 1		T1 N0 M0	<2 cm No LN involvement No metastasis to distant sites
	Stage 2	a	T2 N0 M0	2–5 cm No LN involvement No metastasis to distant sites
		b	T3 N0 M0	>5 cm + LN involvement No metastasis to distant sites
	Stage 3	a	T1–2 N1 M0	<5 cm + LN involvement No metastasis to distant sites

Table 5.3 (continued)

Cancer type	AJCC stage		TNM stage	Characteristics
		b	T4 N0 M0	Cancer of any size which has grown into nearby organ(s), such as the vagina, urethra, prostate gland, or bladder No LN involvement No metastasis to distant sites
		c	T3–4 N1 M0	<2 cm +/− Local organ ingrowth + LN involvement No metastasis to distant sites
	Stage 4		Any T Any N M1	A cancer of any size +/− Local organ ingrowth +/− LN involvement + Metastasis to distant organs such as the liver, brain, bone, or lungs
Rectal cancer	Stage 0		Tis N0 M0	Cancer limited to mucosa No LN involvement No metastasis to distant sites
	Stage 1		T1 or T2 N0 M0	Spread to the submucosa (T1) or Spread to muscularis propria (T2) No LN involvement No metastasis to distant sites
	Stage 2	a	T3 N0 M0	Spread to outermost layers of the colon/rectum but not through them No LN involvement No metastasis to distant sites
		b	T4a N0 M0	Spread through wall of the colon/rectum but not to nearby organs No LN involvement No metastasis to distant sites
		c	T4b N0 M0	Spread to nearby tissues or organs No LN involvement No metastasis to distant sites
	Stage 3	a	T1 or T2 N1 or N1c M0	Spread to the submucosa (T1) Spread to muscularis propria (T2) + 1–3 nearby LNs (N1) + Areas of fat near LNs (N1c) No metastasis to distant sites
			T1 N2a M0	Spread to the submucosa + 4–6 LNs No metastasis to distant sites
		b	T3 or T4a N1 or N1c M0	Spread to outermost layers of the colon/rectum (T3) or visceral peritoneum (T4a), not to nearby organs + 1–3 LNs (N1a/N1b) or areas of fat near LNs (N1c) No metastasis to distant sites
			T2 or T3 N2a M0	Spread to muscularis propria (T2) or Spread to outermost layers of the colon/rectum (T3) + 4–6 LNs No metastasis to distant sites
			T1 or T2 N2b M0	Spread to the submucosa (T1) or Spread to muscularis propria (T2) + >6 LNs No metastasis to distant sites
		c	T4a N2a M0	Spread through wall of the colon/rectum, not to nearby organs + 4–6 LNs No metastasis to distant sites

(continued)

Table 5.3 (continued)

Cancer type	AJCC stage		TNM stage	Characteristics
			T3a or T4a N2b M0	Spread to outermost layers of the colon/rectum (T3) Visceral peritoneum (T4a), not nearby organs + >6 LNs No metastasis to distant sites
			T4b N1 or N2 M0	Spread to nearby organs + LN or Areas of fat near LNs No metastasis to distant sites
	Stage 4	a	Any T Any N M1a	+/− Spread through wall of the colon/rectum +/− LN involvement Spread to one distant organ or distant LNs but not distant part of peritoneum
		b	Any T Any N M1b	+/− Spread through wall of the colon/rectum +/− LN involvement Spread to >1 distant organ but not distant part of peritoneum
		c	Any T Any N M1c	+/− Spread through wall of the colon/rectum +/− LN involvement Spread to distant part of peritoneum +/− distant organs

Adapted from American Joint Commission on Cancer

Conclusion

In summary, honesty, humility, and communication are the keys to success in establishing a trusting relationship with your patient at the first encounter. Examining the patient in the most comfortable position (left lateral Sim's) will allow them to relax and provide for a more thorough exam. Clear documentation using anatomic landmarks (as opposed to "o'clocks") is always preferred. If there is benefit from an anorectal exam under anesthesia in the operating room, the high lithotomy position, streamlined equipment set, and clean, but not necessarily sterile, bags and sheets to drape will help to conserve personpower and reduce the environmental impact. Lastly, approaching each situation from the patient's perspective is always the best practice.

Acknowledgment The authors gratefully acknowledge Mariah Conley for editorial assistance.

Suggested Reading

1. Abel GA, Shelton J, Johnson S, Elliss-Brookes L, Lyratzopoulos G. Cancer-specific variation in emergency presentation by sex, age and deprivation across 27 common and rarer cancers. Br J Cancer. 2015;112(s1):S129.
2. Baer C, Menon R, Bastawrous S, Bastawrous A. Emergency presentations of colorectal cancer. Surg Clin. 2017;97(3):529–45.
3. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Rural and urban differences in stage at diagnosis of colorectal and lung cancers. Br J Cancer. 2001;84(7):910.
4. Gralnek IM, Neeman Z, Strate LL. Acute lower gastrointestinal bleeding. N Engl J Med. 2017;376(11):1054–63.
5. Shuja M, et al. Bleeding in locally invasive pelvic malignancies: is hypofractionated radiation therapy a safe and effective non-invasive option for securing hemostasis? A single institution perspective. Cureus. 2018;10(2):e2137.
6. Steele SR, Hull TL, Read TE, Saclarides TJ, Senagore AJ, Whitlow CB, editors. The ASCRS textbook of colon and rectal surgery. Cham: Springer; 2016.
7. Watson AJ, Smith BB, Whitehead MR, Sykes PH, Frizelle FA. Malignant progression of anal intraepithelial neoplasia. ANZ J Surg. 2006;76(8):715–7.
8. Yellu M, Deeb A, Olowokure O. Overview of recent trends in the management of metastatic anal cancer. World J Oncol. 2015;6(1):311–5.
9. Zauber AG, Winawer SJ, O'Brien MJ, Lansdorp-Vogelaar I, van Ballegooijen M, Hankey BF, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med. 2012;366(8):687–96.

6 Endoscopic and Transanal Approaches for Acute Anal and Rectal Cancers

John McClellan and Anjali S. Kumar

Introduction

In 1977, Morson et al. first described techniques regarding local excision of early distal rectal cancers at St. Mark's Hospital in London [1]. Prior to this novel idea, the standard for treatment of anorectal malignancy included a total mesorectal excision (TME) to assure best oncologic outcomes. Although the 5-year recurrence rates for TME are low (2–8%) [2, 3], TME are associated with significant morbidity leading surgeons to question whether there is a role for less invasive procedures, with reduced morbidity and comparable outcomes. Transanal options are generally reserved for early-stage tumors which, by definition, are not likely to present acutely with obstruction or uncontrolled hemorrhage. Still, proper staging may determine that the tumor is in an early stage.

There are multiple current options for local excision of anal and rectal tumors. The tenets of these procedures include full thickness excision of the tumor with appropriate circumferential margins and deep excision to the perirectal fat. Techniques such as transanal, transsphincteric, and transcoccygeal excision have evolved into more modern techniques that utilize similar surgical resections via the transanal approach. Transanal options can use modern optics included in laparoscopic and robotic equipment for better visualization and articulated instrumentation. Examples are transanal endoscopic microsurgery (TEM) and transanal minimally invasive surgery (TAMIS). Additionally, endoscopic instrumentation is also evolving quickly. Procedures include endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), using endoscopic needle-knife technology. Platforms for natural orifice surgery, with superb visualization and articulating instrumentation, have been designed for delivery through long, flexible portals such as an endoscope. The use of all these techniques in early-stage rectal cancer has steadily increased in the United States within the past decade, and it is important for all modern surgeons to become aware of these contemporary options [4].

Although the focus of this chapter is on acute presentations of anal and rectal malignancies, the majority of the workup of these complicated pathologies is not usually performed in the acute setting. The procedures discussed, however, can be considered for use in acute issues such as bleeding and obstruction in select patients.

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Preoperative Workup

Before utilizing either endoscopic or transanal techniques, it is imperative to ensure proper patient selection. The preoperative evaluation of patients who may be candidates for local excision does not vary from any other patient with anorectal malignancies. All should undergo preoperative physical exam, laboratory, and well-established protocols for staging workup. Knowing that local excision spares the lymphatic drainage of the rectum, it is important that dedicated rectal imaging is available (rectal MRI and ultrasound as described later) to select patients with no evidence of and low risk of lymphatic spread. A combination of these adjuncts as well as the histopathologic characteristics of the tumor is needed before proceeding with resection.

Focused exam relies on the surgeon's digital rectal examination (DRE) to determine size, mobility, and distance of anorectal lesions from the anal verge. Tumors greater than 4 cm and those involving more than 40% of rectal circumference are technically difficult to excise locally and should be excluded [5]. The mobility of the lesion is equally important. Anorectal tumors under consideration for local excision should be freely mobile on DRE as those that fixed are highly predictive of advanced disease [6]. Traditionally, lesions present in the distal rectum (6–8 cm) are reachable with TAE. However, with newer techniques such as TEM and TAMIS, lesions as far proximal as 15 cm from the anal verge can now be adequately removed.

The laboratory workup of a patient with an anorectal adenocarcinoma includes a preoperative carcinoembryonic antigen (CEA) level and re-review of the original biopsy. Concerning features on histopathologic evaluation, as in most cancers, include poor differentiation, lymphovascular invasion, and tumor budding or sprouting. Any of these findings suggest advanced malignancy with associated higher rates of nodal metastasis. In these cases, local excision alone can be ruled out [7, 8].

Imaging is important adjunct to selecting patients who would benefit from local excision of a rectal tumor. All patients should undergo CT imaging of the chest, abdomen, and pelvis for staging purposes. However, CT alone is not sufficient in quantifying the depth of invasion of a rectal tumor, which correlates well with chances of lymph node metastasis [9, 10]. Both rectal MRI and transrectal US can be used to determine the extent of rectal wall invasion and mesorectal lymph node status. While MRI is more sensitive at evaluating lymph node involvement and higher chance of metastasis, transrectal US is considered a useful adjunct in distinguishing T1 from T2 tumors [11, 12].

Proctoscopy and colonoscopy are crucial in the workup of patient with a newly diagnosed rectal lesion. Proctoscopy allows the surgeon to assess the tumor size, distance, and relationship to the circumference of the rectum. This is especially useful in patients with more proximal lesions unable to be evaluated with DRE and anoscopy. It also may aid in biopsy or rebiopsy of the lesion. If the rectal lesion was found prior to endoscopy, it is important, if technically feasible, to perform a colonoscopy to rule out synchronous lesions. It is equally important that the area of concern is tattooed for future localization.

Treatment

The early options for local excision of rectal tumors include transanal, transcoccygeal, and transsphincteric. In addition to endoscopic methods, we will discuss the most common transanal procedures to excise rectal tumors. It is also important to note that these procedures can be used for multiple other pathologies to include biopsy of undiagnosed rectal masses, high-grade dysplasia, and unresectable polyps. Distal submucosal masses such as carcinoid tumors and gastrointestinal stromal tumors (GIST) may also be amenable to a transanal approach. The tenants of a transanal approach are the same for most lesions: full thickness excision of the entire specimen with at least 1 cm margin of benign tissue circumferentially.

The preoperative preparation for transanal excision (TAE) and transanal minimally invasive surgery (TAMIS) is similar. Full mechani-

cal bowel preparation versus rectal irrigation alone depends significantly on the bowel habits of the patient scheduled to undergo TAE. Patients with known history of constipation and straining should undergo full mechanical bowel preparation of the surgeon's preference to allow for proper visualization and also to avoid postoperative straining. In patients with normal bowel habits, single-dose enema therapy the night prior to the procedure will most likely suffice. However, in TAMIS, a more thorough bowel preparation is utilized. Typically, these patients have more proximal tumors, so a full mechanical and antibiotic bowel preparation is indicated for multiple reasons. First, this will minimize intraoperative contamination if peritoneal violation occurs during resection. Second, full preparation permits the surgeon to transition a more traditional resection and anastomosis if the lesion is deemed locally unresectable. Third, visualization is especially crucial for more proximal tumors, and proper bowel preparation is extremely beneficial. Options for mechanical bowel preparation will vary by practice, but a common preparation includes polyethylene glycol mixed with electrolyte sports drink along with antibiotics (neomycin and metronidazole). On table rectal irrigation is also helpful using a bulb syringe with warm irrigation.

Patients should receive a dose of preoperative antibiotics prior to incision (within 1 hour). Many of these procedures can be performed under local anesthesia and moderate sedation given their short duration. Most patients undergoing local excision of a rectal tumor will be positioned in high lithotomy, which should be adequate for most locations. However, anterior rectal lesions in high lithotomy are usually the most difficult to visualize. Prone jackknife positioning can be helpful in these situations placing the lesion in the most dependent location. Once positioning is secured to include taping apart of buttocks, perianal and pudendal nerve blocks can be utilized to relax the anal sphincter during the procedure and provide postoperative pain control. Headlamps are especially useful in TAE to maximize visualization.

Transanal Excision (TAE)

TAE utilizes anoscopes (Hill-Ferguson) (Fig. 6.1) and/or self-retaining retractors (Lone Star) with hooks to aid in visualization. The anus is serially dilated prior to placement of retraction. Once the lesion is identified, the circumferential margins are marked with monopolar surgical electricity. Some surgeons find that needle point monopolar energy and a combination of cut and coagulation settings reduce tissue retraction and distortion. An additional method that may be utilized to help bring the lesion into the field of view is placing distal sutures to help deliver the tissue into the working space. Once the margins are identified, surgical electricity and/or advanced energy devices are used to carry the dissection through the rectal wall to the level of the perirectal fat, which is visible once the tumor and surrounding benign tissue are lifted from the wound bed. Anterior lesions are at risk of vaginal perforation in females and prostate involvement in males. Special care should be taken in these specific situations during the full thickness resection. In the case of vaginal perforation, multilayer repair and/or Martius flap (biologic tissue interposition) can be performed at the time of the original resection.

Once the tumor is mobilized and removed from the rectum, it is oriented appropriately using straight pins and a corkboard (Fig. 6.2) and

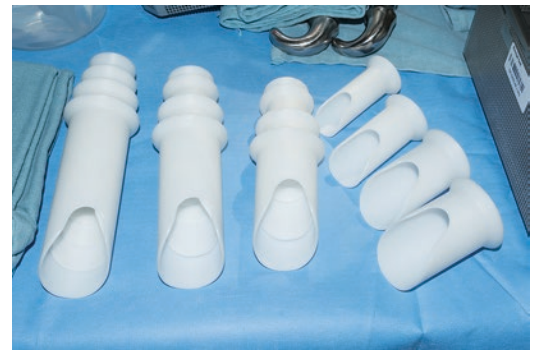

Fig. 6.1 Ferguson anoscope set (CSA-2000) by CS Surgical Inc. (Slidell, LA) provides varying lengths and diameters for access. The soft bevel allows for the lesion to fall into view for resection

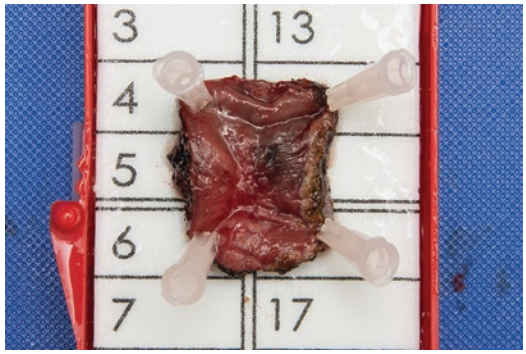

Fig. 6.2 After excision, the full-thickness specimen is pinned to a corkboard and oriented to the patient's anatomy and laterality on the pathology slip by using the numbers on the board (i.e., 4, right proximal; 14, left proximal; 6, right distal; 16, left distal). We show an example of an adenocarcinoma arising in a polyp that was incompletely excised by snare polypectomy. We did a TAE centering the tattoo and residual polyp and resecting it full thickness, en bloc with a 1 cm border of benign tissue around it

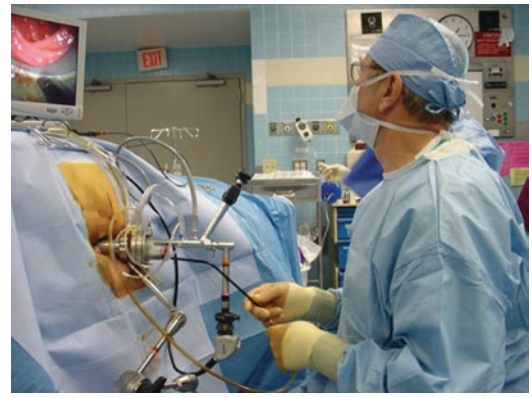

Fig. 6.3 The TEM proctoscope [Richard Wolff Medical Instruments – Vernon Hills, IL] allows for three-dimensional viewing via the operating microscope or for two-dimensional viewing via the fiber-optic video cable. The patient is placed in the left lateral decubitus position with his legs extended to allow for the operator (Dr. Lee E. Smith) to sit comfortably

passed off the table as specimen. After copious irrigation (depending on the size of the defect), the area can be closed with absorbable sutures. Smaller and more distal wounds can be left to heal by secondary intention. A proctoscope should then be employed to assess the patency of the lumen after closure.

Transanal Endoscopic Microsurgery (TEM)

TEM employs a rigid, beveled proctoscope. The procedure works best when the patients are positioned so that the lesion is in a dependent position, and the bevel of the proctoscope holds up the opposite bowel wall (Fig. 6.3). In this way, visualization is optimized.

Transanal Minimally Invasive Surgery (TAMIS)

In this nuanced procedure, the patient is first positioned in high lithotomy position, and TAMIS is usually utilized in more proximal lesions that cannot be reached via TAE (Fig. 6.4). TAMIS employs the use of a single-port access portal that is placed through the anus into the distal rectum,

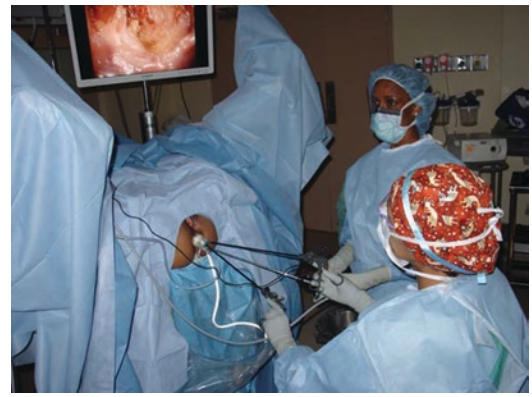

Fig. 6.4 TAMIS approach using a Olympus TriPort [Olympus Corporation of the Americas Center Valley, PA]. The patient is placed in lithotomy, and laparoscopic instrumentation is used by the operator (Dr. Anjali S. Kumar)

to allow laparoscopic instruments to be passed through sealed trocars. Carbon dioxide pneumoinsufflation is achieved with airtight seal on the ports allowing the rectum to expand and provide adequate visualization with a laparoscopic camera or flexible endoscope. The tenets of resection are similar to those in TAE. Using laparoscopic instruments and hook monopolar energy, the first step is to identify the lesion and mark 1 cm grossly benign margins circumferentially. Using a combination of cut and coagulation settings, the

tissue is taken full thickness through the rectal wall. Given the lack of retraction on the rectal wall, the specimen has a higher chance of curling. This can be avoided by not completing the full thickness dissection distally until the proximal margin is created and carried back laterally to the initial incision. Again, advanced energy devices can be considered for added hemostasis. Often a continuous flow of carbon dioxide is required to allow for procedural suctioning and to minimize rectal bellowing. The specimen can then be oriented appropriately to ensure correct margins are identified.

Once the specimen has been removed, the wound is irrigated with a laparoscopic suction-irrigator device. Care is taken to provide a watertight closure using absorbable suture. Some surgeons advocate for barbed absorbable suture that allows for easy approximation but often has to be completely removed if misthrows are made. It is also imperative to avoid narrowing the rectal lumen during this process. Once the wound is closed, a rigid and flexible proctoscope should be used to check for bowel lumen patency, adequacy of closure, and possible peritoneal violation.

If the patient is placed in lithotomy for TEM or TAMIS, there may be an opportunity to perform a pneumoinsufflation leak test by inserting laparoscopic instrumentation via the anterior abdominal wall (Fig. 6.5). End-tidal carbon dioxide monitoring should be checked frequently by the anesthesia team, and minute ventilation adjusted appropriately.

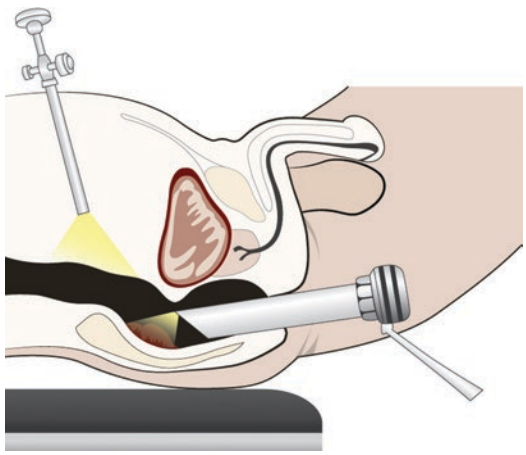

Fig. 6.5 Cartoon illustration of TEM instrumentation for a posterior rectal lesion with concurrent transabdominal laparoscopic instrumentation

Endoscopic Mucosal Resection (EMR)/ Endoscopic Submucosal Dissection (ESD)

Although performed primarily by therapeutic gastroenterologists, endoscopic mucosal resection and endoscopic submucosal dissection are additional procedures available for management of lesions confined to the mucosal and submucosal lesions throughout the gastrointestinal tract. Within the colon, these procedures are indicated for colorectal adenomatous lesions to early carcinomas. EMR is technically easier than ESD and is essentially a standard polypectomy using advanced devices. Both have broadened the opportunities available for endoscopic resection of colonic polyps that has expanded to even large, low risk polyps. Endoscopic resection is associated with quick recovery, decreased length of hospital stay, and lower costs [13]. This includes those with minimal submucosal invasion and no lymphovascular invasion, poor differentiation, tumor budding, or tumor free margin >1 mm [14]. Ultimately, the goals of resection are similar for EMR and ESD: complete tumor removal with negative microscopic margins (R0 margins).

Endoscopic mucosal resection is completed using a standard colonoscope and is best suited for flat or sessile polyps. The first step of the procedure is to completely visualize the lesion and delineate the margins or proposed resection before distorting the tissue. It is helpful to mark along the resected edges with monopolar energy as a guide. Once the resection is planned, the base of the polyp is injected with injectable solution (normal saline/sodium hyaluronate) into the submucosal space, elevating the lesion. This allows the operator to snare the polyp while protecting the deeper space and rectal/colonic wall. The polyp can be removed in en bloc or in piecemeal fashion. Piecemeal resection is typically only indicated in low risk polyps, given the significant risk of recurrence versus en bloc removal [13]. However, it is useful in large,

benign adenomas or in situations where carcinoma is present within the adenoma. It is important to note that the carcinomatous portion should never be cut into pieces and should be delivered entirely. Typically, en bloc resection is completed using standard snare and electrosurgical instrumentation. Variants of EMR include cap-assisted mucosectomy and ligation-assisted. As expected, the complications that are most often associated with EMR and ESD are bleeding and perforation.

ESD is an alternative to EMR that has been shown to have more reliable en bloc resection and lower recurrence rates than EMR [15]. However, ESD is also highly technical requiring advanced training and experience. Similar to EMR, the submucosal plane is developed with injectable fluid. ESD is performed using needle-type knife and electrosurgical energy to meticulously dissect the submucosal plane. This allows the operator to remove the specimen en bloc regardless of its size. Similar to EMR, there are multiple variants to ESD to include to a hybrid procedure to include the use of a snare.

Robotic Surgical Approaches

Development of single platform portals for robotic surgical instrumentation entry poses an intriguing opportunity for future development. Three-dimensional visualization combined with articulated instrumentation will give the operator added advantage [16].

Advanced Endoscopy

Argon plasma coagulation (APC) is an additional modality for use in patients for rectal bleeding. The majority of the literature describes APC for use in bleeding related to arteriovenous malformations (AVM) and radiation proctitis. A few reports cite success rate of 77–90% in bleeding AVMs making it a viable option especially after other options have failed [17, 18]. APC is also effective for treatment of hemorrhagic radiation proctitis where the rectal mucosal is friable and bleeding is often difficult to control without causing additional harm. Given the success of APC use in treatment of these challenging issues, it should be considered in acute anorectal bleeding.

Another endoscopic modality that may serve a role in acute rectal obstruction is colonic stenting. As with many of the previous procedures discussed, endoscopic stenting requires a practitioner trained in advanced endoscopy. Colorectal endoluminal stenting (CELS) was first described in 1991 for the treatment of colorectal neoplasms [19]. It's use has expanded for treatment of colorectal obstructions throughout the entirety of large bowel. A recent study evaluated the clinical use of self-expandable metal stents in malignant rectal obstruction to their use in left colonic obstruction and found that success rates were comparable [20]. Anorectal stenting of malignant obstruction should be considered as a reasonable option for acute obstruction.

Conclusion

As described, there are multiple endoscopic and surgical options available for the local treatment of early-stage anorectal malignancies. After appropriate workup of the tumor, there are many factors that must be considered before proceeding including stage, location, feasibility, and equipment available for resection. These principles should guide the modern acute care surgeon to select the most appropriate and personalized approach.

References

1. Morson BC, Bussey HJ, Samoorian S. Policy of local excision for early cancer of the colorectum. Gut. 1977;18(12):1045–50.
2. McCall JL, Cox MR, Wattchow DA. Analysis of local recurrence rates after surgery alone for rectal cancer. Int J Color Dis. 1995;10(3):126–32.
3. Enriquez-Navascues JM, Borda N, Lizerazu A, et al. Patterns of local recurrence in rectal cancer after a multidisciplinary approach. World J Gastroenterol. 2011;17(13):1674–84.
4. You YN, Baxter NN, Stewart A, Nelson H. Is the increasing rate of local excision for stage I rectal cancer in the United States justified?: a nationwide cohort study from the National Cancer Database. Ann Surg. 2007;245(5):726–33.

5. Brunner W, Widmann B, Marti L, Tarantino I, Schmied BM, Warschkow R. Predictors for regional lymph node metastasis in T1 rectal cancer: a population-based SEER analysis. Surg Endosc. 2016;30(10):4405–15.
6. Nicholls RJ, Galloway DJ, Mason AY, Boyle P. Clinical local staging of rectal cancer. Br J Surg. 1985;72(Suppl):S51–2.
7. Blumberg D, Paty PB, Guillem JG, et al. All patients with small intramural rectal cancers are at risk for lymph node metastasis. Dis Colon Rectum. 1999;42(7):881–5.
8. Kitajima K, Fujimori T, Fujii S, 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.
9. 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(2):200–6.
10. Landmann RG, Wong WD, Hoepfl J, et al. Limitations of early rectal cancer nodal staging may explain failure after local excision. Dis Colon Rectum. 2007;50(10):1520–5.
11. Kennedy E, Vella ET, Blair Macdonald D, Wong CS, McLeod R, Cancer Care Ontario Preoperative Assessment for Rectal Cancer Guideline Development G. Optimisation of preoperative assessment in patients diagnosed with rectal cancer. Clin Oncol (R Coll Radiol). 2015;27(4):225–45.
12. Kwok H, Bissett IP, Hill GL. Preoperative staging of rectal cancer. Int J Color Dis. 2000;15(1):9–20.
13. De Ceglie A, Hassan C, Mangiavillano B, et al. Endoscopic mucosal resection and endoscopic submucosal dissection for colorectal lesions: a systematic review. Crit Rev Oncol Hematol. 2016;104:138–55.
14. Tanaka S, Kashida H, Saito Y, et al. JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc. 2015;27(4):417–34.
15. Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy. 2015;47(9):829–54.
16. Marks J, Ng S, Mak T. Robotic transanal surgery (RTAS) with utilization of a next-generation single-port system: a cadaveric feasibility study. Tech Coloproctol. 2017;21(7):541–5.
17. Kwan V, Bourke MJ, Williams SJ, et al. Argon plasma coagulation in the management of symptomatic gastrointestinal vascular lesions: experience in 100 consecutive patients with long-term follow-up. Am J Gastroenterol. 2006;101:58–63.
18. Olmos JA, Marcolongo M, Pogorelsky V, et al. Long-term outcome of argon plasma ablation therapy for bleeding in 100 consecutive patients with colonic angiodysplasia. Dis Colon Rectum. 2006;49:1507–16.
19. Harris GJ, Senagore AJ, Lavery IC, Fazio VW. The management of neoplastic colorectal obstruction with colonic endolumenal stenting devices. Am J Surg. 2001;181(6):499–506.
20. Lee HJ, Hong SP, Cheon JH, Kim TI, Kim WH, Park SJ. Clinical Outcomes of self-expandable metal stents for malignant rectal obstruction. Dis Colon Rectum. 2018;61(1):43–50.

7 Abdominal and Perineal Operative Considerations for Acute Presentations of Anal and Rectal Malignancies

Joselin Anandam and John Abdelsayed

Rectal Cancer

Clinical Presentation

Colorectal cancer is the third most common cancer diagnosed and the third most common cause of cancer death in the United States. Per the American Cancer Society, approximately 43,030 new cases of rectal cancer will be diagnosed in 2018 [1]. Of those, approximately 20% of colorectal cancer will present acutely as a surgical emergency [2]. Of critical importance in the treatment algorithm for rectal cancer is the site of pathology. High rectal cancer, defined as rectal cancer from 10–15 cm from the anal verge and above the peritoneal reflection, should be managed differently than a mid- to low rectal cancer that presents acutely. Like all cancers, tissue diagnosis is important to establish a treatment plan.

Initial Management

The initial step for identification is physical exam and lower endoscopy. Digital rectal exam is of utmost importance in identifying the location of the lesion in the rectum (anterior versus posterior), the distance from the anal verge, and the tumor's location in relation to the anal sphincters (see Fig. 7.1). Rigid proctoscopy is a useful adjunct for visual identification of a lesion as well as affords the ability to sample any concerning masses. A rigid proctoscope can be easily performed in the office or the emergency department with adequate lighting, lubricant, and if needed a pre-procedural enema. Ideally a full colonoscopy should be performed when the patient is stable to identify location of the tumor and to rule out synchronous tumors. Approximately 3–5% of rectal cancers present with synchronous tumors that would alter the surgical approach [3]. Locoregional staging should be performed with magnetic resonance imaging of the pelvis (MR pelvis) or endorectal ultrasound to establish T staging and nodal involvement. Endorectal ultrasound often requires specialized expertise and is subject to operator technique; therefore MR pelvis is preferred at the authors' institution. After locoregional staging, evaluation with CT chest/abdomen/pelvis is obtained to evaluate for the presence of metastatic disease. Approximately 20–25% of rectal cancers present with evidence of metastatic disease (see Table 7.1).

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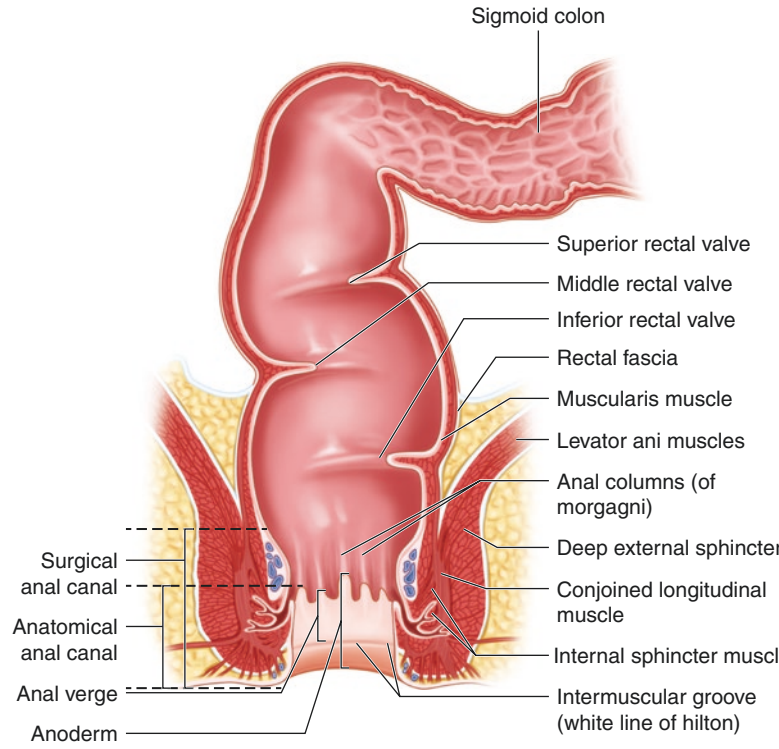

Fig. 7.1 Rectum and anus anatomy, coronal view

Stage II–III disease, if possible, should be referred for neoadjuvant chemoradiation. Following neoadjuvant therapy, referral back to a colorectal surgeon for resection is recommended. However, rectal cancer that acutely presents with bleeding causing hemodynamic instability, obstruction, perforation, or peritonitis is an indication for urgent operative intervention.

Management of acutely presenting rectal cancer should always begin with resuscitation. The main modalities of resuscitation often initiated in the emergency room are IV fluid administration, broad-spectrum antibiotics for sepsis, blood product transfusion as needed for anemia or coagulopathy, and identification of the cause of acute presentation. Lower endoscopy is an invaluable tool for the diagnosis and acute management of rectal cancer. The use of endoscopic management for bleeding and obstruction is presented in another chapter (See Chap. 11, Endolumenal Therapies for Bleeding and Obstructing Colorectal Malignancy).

Surgical Management

After diagnosis, localization, and staging of the offending pathology, surgical management should be individualized to patients who can tolerate an operation that adheres to oncologic principles. Patients presenting with an acute clinical obstruction with evidence of resectability on imaging are candidates for creation of a diverting ostomy as a bridge to neoadjuvant therapy prior to definitive resection [4]. However, surgeons should be aware that there can be a significant delay to neoadjuvant therapy and the subsequent definitive resection following creation of a decompressive ostomy compared to starting neoadjuvant therapy right away [5]. As such, surgeons should reserve a diverting ostomy only for those who are clinically obstructed (see Fig. 7.2).

If diversion is used, then referral to a colorectal surgeon should be considered for definitive resection. Additionally, evaluation by a tumor

Table 7.1 AJCC rectal cancer staging system from NCCN rectal cancer

(A) Definitions for T, N, M					
T	**Primary Tumor**	**M**	**Distant Metastasis**		
TX	Primary tumor cannot be assessed	**M0**	No distant metastasis by imaging, etc.; no evidence of tumor in distant sites or organs		
T0	No evidence of primary tumor				
Tis	Carcinoma *in situ,* intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae)	**M1**	Metastasis to one or more distant sites or organs or peritoneal metastasis is identified		
T1	Tumor invades the submucasa (through the muscularis mucosa but not into the muscularis propria)	M1a	Metastasis to one site or organ is identified without peritoneal metastasis		
T2	Tumor invades the muscularis propria	M1b	Metastasis to two or more sites or organs is identified without peritoneal metastasis		
T3	Tumor invades through the muscularis propria into the pericolorectal tissues	M1c	Metastasis to the peritoneal surface is identified alone or with other site or organ metastases		
T4	Tumor invades the visceral peritoneum or invades or adheres to adjacent organ or structure				
T4a	Tumor invades through the visceral peritoneum (including gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum)	**(B) AJCC Prognostic Stage Groups**			
			T	**N**	**M**
T4b	Tumor directly invades or is adheres to adjacent organs or structures	**Stage 0**	Tis	N0	M0
		Stage I	T1-T2	N0	M0
N	**Regional Lymph Nodes**	**Stage IIA**	T3	N0	M0
NX	Regional lymph nodes cannot be assessed	**Stage IIB**	T4a	N0	M0
N0	No regional lymph node metastasis	**Stage IIC**	T4b	N0	M0
N1	One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0. 2mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative	**Stage IIIA**	T1-T2	N1/N1C	M0
			T1	N2a	M0
N1a	One regional lymph node is positive	**Stage IIIB**	T3-T4a	N1/N1C	M0
N1b	Two or three regional lymph nodes are positive		T2-T3	N2a	M0
N1c	No regional lymph nodes are positive, but there are tumor deposits in the subserosa, mesentery, or nonperitonealized pericolic, or perirectal/mesorectal tissues		T1-T2	N2b	M0
		Stage IIIC	T4a	N2a	M0
N2	Four or more regional lymph nodes are positive		T3-T4a	N2b	M0
N2a	Four to six regional lymph nodes are positive		T4b	N1-N2	M0
N2b	Seven or more regional lymph nodes are positive	**Stage IVA**	Any T	Any N	M1a
		Stage IVB	Any T	Any N	M1b
		Stage IVC	Any T	Any N	M1c

board should also be considered for timing and appropriateness of neoadjuvant therapy. If during the acute setting of obstruction, bleeding, or perforation, resection and anastomosis is considered, the surgeon must remember the oncologic principles. During definitive resection, the surgical principles required for radical transabdominal resection of rectal cancer include complete resection of the tumor and a high-quality total mesorectal excision (TME) with preservation of

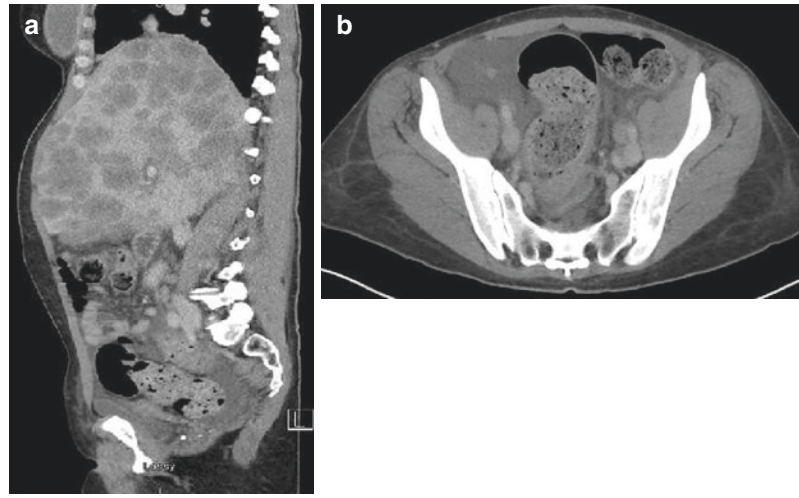

Fig. 7.2 CT images of obstructing high rectal tumor. (**a**) CT obstructing high rectal tumor with proximal colonic dilation, sagittal view. (**b**) CT obstructing high rectal tumor, axial view. The patient underwent endoscopic stenting but would eventually succumb to her metastatic disease [24]

the autonomic pelvic nerve plexuses and clear circumferential radial margin (CRM) [6]. The use of a defunctioning stoma for anastomotic protection should be considered in any anastomosis performed under tension, in the setting of hemodynamic instability, or gross contamination from a perforation. It should be strongly considered in cases of a low pelvic anastomosis and after neoadjuvant chemoradiation. Laparoscopic resection of rectal tumors is safe with noninferior oncologic outcomes including quality of TME, improved postoperative SSI, and length of stay [7, 8]. The operating surgeon should perform whichever operation he/she feels comfortable performing to achieve the best clinical outcomes.

For tumors of the upper rectum (10–15 cm from the anal verge), a low anterior resection with mesorectal excision extending 5 cm below the distal edge of the tumor is the operation of choice [9]. For an intra-abdominal perforation or chronic obstruction of a high rectal tumor, LAR with primary anastomosis and diverting loop ileostomy or if necessary a Hartmann's procedure should again be considered depending on the physiologic status of the patient.

For tumors of the middle rectum, a low anterior resection with total mesorectal excision is also indicated [10]. A clear distal bowel margin of at least 1 cm is required. A diverting stoma should again be considered in these cases.

For early-stage tumors of the lower rectum (T1, N0 or T2-3, N0) with a distance of >1 cm from the external anal sphincter, a LAR with TME and intersphincteric distal dissection with hand sewn coloanal anastomosis and diverting ileostomy can be considered [11]. However, for a tumor with the above characteristics and a coloanal anastomosis that would result in poor functional outcomes (i.e., a patient with existing fecal incontinence), an abdominoperineal resection is recommended.

For patients presenting with sepsis due to mid to low rectal tumors with proximal colonic perforation, with or without sphincter involvement, attempts at non-oncologic resectional management of the primary tumor can be considered in a damage control setting. Again, this would be control of the perforation with resection and an ostomy and mucous fistula. This damage control option can be considered in patients unable to tolerate a full resection or in an attempt to bridge to neoadjuvant chemoradiation for an attempt at sphincter preservation. For local sepsis from perforation of the rectal tumor in the pelvis, diverting ostomy with transrectal, transanal, or transperineal drainage should be considered. However, it should be noted again that all surgical options delay the timing to initiation of neoadjuvant therapy.

In cases of perforation of a high or mid rectal cancer, abdominal resection should be pursued to prevent worsening sepsis [12]. After initial

resuscitation with IV fluids and antibiotics, a Hartmann's procedure with resection of the tumor, mesorectum, and end colostomy and tagging of the distal rectal stump may be performed. Drain placement is recommended. Only in extremely rare selected patients with perforation and sepsis should a resection and primary anastomosis be considered. Drainage and proximal diversion with loop ileostomy would be strongly advised to protect and mitigate the consequences of an anastomotic leak if an anastomosis is performed.

The two types of diversionary stomas commonly employed are the loop ileostomy and loop colostomy. There is no clear answer to which is superior in terms of morbidity following resection. Ileostomies are associated with significantly less prolapse, septic complications, and reoperation rates compared to colostomies (see Fig. 7.3). However, colostomies have lower rates of dehydration, acute kidney injury, and resultant renal failure. Therefore, it is recommended that a loop ileostomy should be preferred and colostomy reserved for those who are at risk of dehydration [13]. Closure of the stoma can be performed 6–8 weeks following completion of any adjuvant therapy (see Table 7.2).

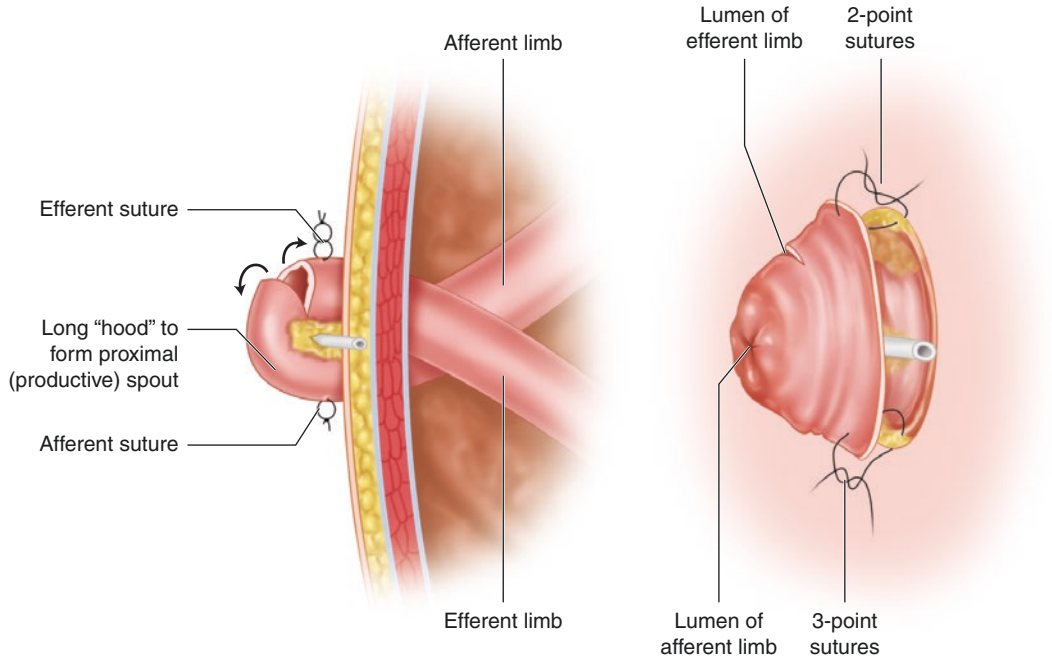

Fig. 7.3 Loop ileostomy creation

Table 7.2 Comparison of ileostomy vs colostomy

	Ileostomy	Colostomy
Stool consistency	Liquid	Semisolid
Regulation	None	Yes- if with regular frequency
Fluid requirements	Increased	No change
Creation	Usually simple	Difficulty dependent on location and mesenteric length
Complications	Dehydration, AKI, dermatitis, pouching difficulty, hernia	Prolapse/retraction, peristomal abscess, stricture, sepsis, hernia
Reversal	Usually local incision	Possible locally, sometimes laparotomy required

Special Circumstances

Perforation while undergoing neoadjuvant therapy

Given the age of most patients diagnosed with rectal cancer, there are a number of special circumstances to be discussed. Patients with previously diagnosed locally advanced rectal cancer often are undergoing or have previously undergone chemoradiation in anticipation of upcoming operative resection. Occasionally these patients will present with contained or free perforations. Given the vasculitis following pelvic radiation, anastomoses in this setting are extremely tenuous and should be protected with proximal intestinal diversion. If the patient has completed or is near completion of neoadjuvant therapy and is not septic, an attempt at primary anastomosis with proximal diversion is reasonable depending on the conditions in the pelvis. If the patient presents acutely septic, resection and proximal diversion with an end colostomy should be considered.

The Anticoagulated Patient

A second scenario is the anticoagulated patient who presents with melena or hematochezia due to a rectal tumor. Often these patients are treated under current protocols of lower gastrointestinal bleeding which consists of temporarily holding and reversing anticoagulation medication. In the rare patient that anticoagulation cannot be stopped (i.e., recent cardiac stent placement on dual antiplatelet therapy), an exam under anesthesia with attempt to locally control bleeding can be considered. Use of local hemostatic adjuncts can be an invaluable tool to assist in bleeding control with surgical electricity use, manual compression, and hemostatic products such as Surgicel (mechanical oxidized cellulose hemostat), Combat Gauze (hemostatic procoagulant Kaolin-based dressing), Floseal (liquid bovine thrombin-fibrinogen adhesive), or Tisseel (liquid fibrinogen-thrombin adhesive) [14]. These products can be used locally without concern for systemic absorption. For patients who are not candidates for resection who present with excessive lower GI bleeding, consideration for angiogram and internal iliac branch embolization should be considered.

Abscess Formation

Another complex situation is the patient who presents with chronic or acute abscesses or pelvic sepsis due to perforation. All attempts at source control should be made with drainage, diversion, and resection in an attempt to bridge the patient to neoadjuvant chemotherapy +/− radiation for local control. These infections will undoubtedly delay the initiation of rectal cancer therapy and should be managed aggressively. Initial attempts at management with antibiotics and noninvasive drain placement via interventional radiology or endoscopically should be considered as first-line options. Operative washouts, if necessary, should be performed with a liberal use of surgical drain placement making it rare for a patient to require multiple operative washouts. This again would help to prevent further delays to neoadjuvant therapy.

Anal Cancer

Clinical Presentation

Anal cancer represents a small percentage of cancers of the GI tract. Per the American Cancer Society from 2018, the estimated incidence of anal cancer in the United States is 8580 new cases with resultant estimated deaths of approximately 1160 [15]. Risk factors associated with anal cancer include the presence of precancerous anal lesions such as high-grade anal intraepithelial neoplasms (AIN), chronic immunosuppression, HIV, and smoking. Knowledge of the anatomy of the anal canal assists in diagnosis and management of the various types of anal neoplasms. The surgical anal canal can be divided into two unequal areas by the dentate line: an upper zone lined with columnar epithelium supplied by the superior rectal artery and a lower zone lined with squamous epithelium supplied by the inferior rectal artery. The short segment area between the two is termed the anal transition zone. Neoplasms of the anal canal include squamous cell cancer, anal adenocarcinoma, neuroendocrine tumors, and anal melanoma (see Fig. 7.4).

Anal cancers usually present with bleeding (45%) or palpation/sensation of a perianal mass

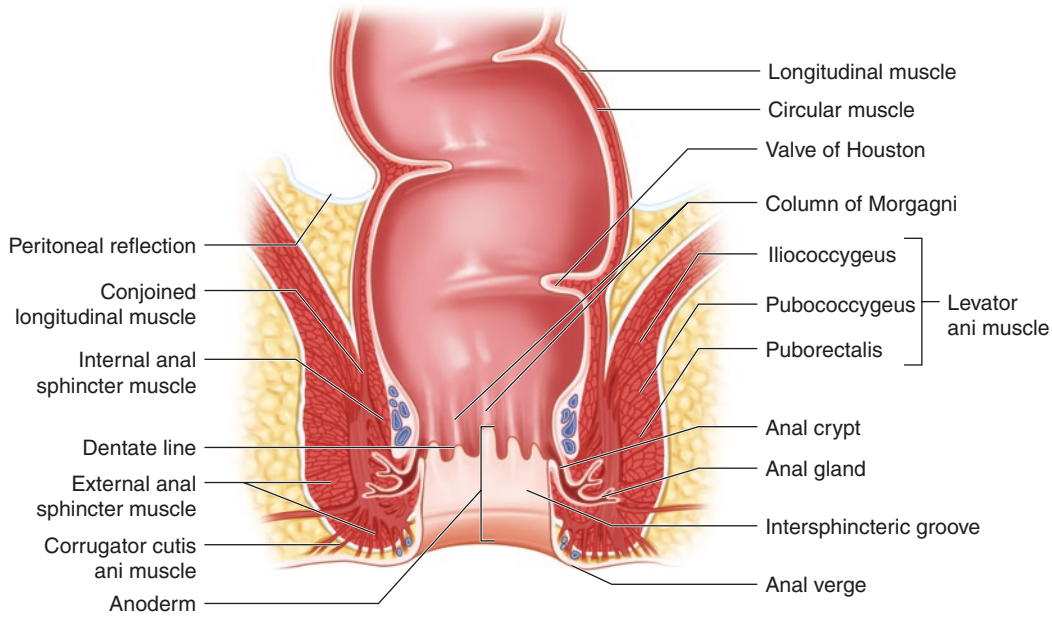

Fig. 7.4 Anal canal anatomy, coronal view

(30%); however up to one third may be asymptomatic. Other complaints include discomfort while sitting, change in bowel habits, discharge, fecal incontinence (from sphincter infiltration), anal abscess, fissures, fistula, or very rarely obstruction. Diagnosis should be confirmed by visual inspection using an anoscope and pathologic biopsy when suspected. If neoplasm is confirmed, staging is performed with a digital rectal exam and a CT chest/abdomen/pelvis or combination PET/CT depending on local availability and expertise [16, 17].

Initial Management

Initial management of an acute presentation of anal cancer should include resuscitation and accurate diagnosis. Often with large masses, clinical evidence of neoplasm may be visually obvious, but multiple biopsy specimens should be obtained to confirm histologic diagnosis. Resuscitation with IV fluids for hypovolemia or dehydration should always be performed, especially when the patient presents with obstruction and sequestration of fluid. Rarely a patient will present with symptomatic anemia and should be transfused to a minimal hemoglobin safe for anesthesia (usually up to 7 g/dL at the author's institution) or cessation of symptoms. Workup for and full reversal of any existing anticoagulation should also be initiated prior to any intervention. It is uncommon for anal cancer to cause an acute drop in hemoglobin, and given the usual age at presentation, concomitant diagnoses for alternate causes of anemia should be in the differential diagnosis and evaluated. A complete history including any previous colonoscopies should be elicited from the patient during initial workup [18].

Indications for Surgical Management

Emergent presentation requiring urgent surgical management of anal cancer is rare. Indications for surgical management include patients who present acutely with bleeding, obstruction, or those with a symptomatic anal mass without diagnosis. The surgical approach differs depending on the clinical presentation. For a slowly bleeding anal cancer without hemodynamic instability, prompt initiation of external beam radiation via radiation oncology is recommended, often with concurrent

chemotherapy. For bleeding causing hemodynamic instability, various surgical approaches are available as damage control.

Surgical Approach

Perineal Approach

A perineal approach with the patient in high lithotomy or prone jackknife position affords the surgeon adequate positioning for full evaluation of the anal canal (see Fig. 7.5). For the acutely bleeding mass without other endoluminal sources, a prompt exam under anesthesia and anorectal exam should be performed. Attempts to incompletely resect the bleeding mass can be performed with the goal of bleeding cessation rather than a complete R0 resection. Strict avoidance of any injury to the rectum should be maintained to avoid further complicating the situation. Use of previously listed local hemostatic adjuncts can be an invaluable tool to assist in bleeding

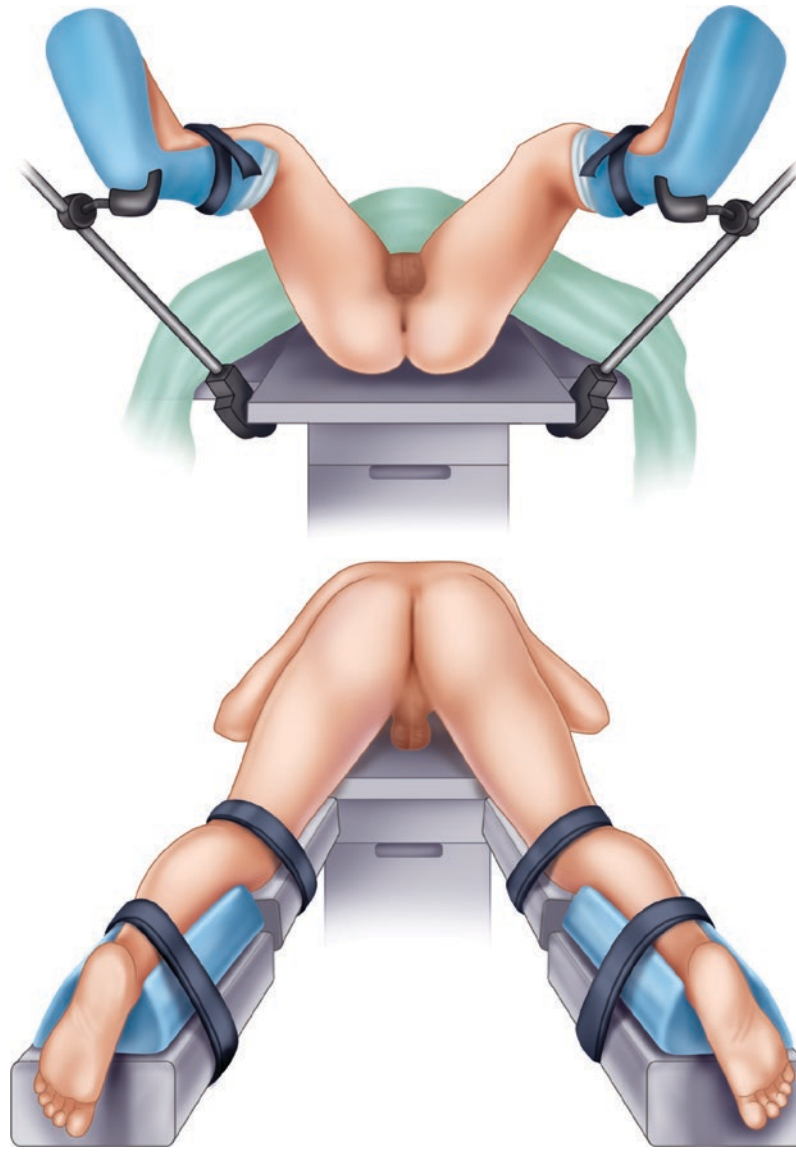

Fig. 7.5 Illustrations of prone jackknife and high lithotomy positioning

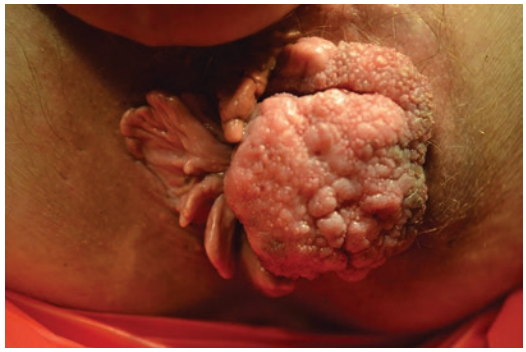

Fig. 7.6 Fungating anal cancer with notable extension outside the anal verge. (Anandam [24, 25])

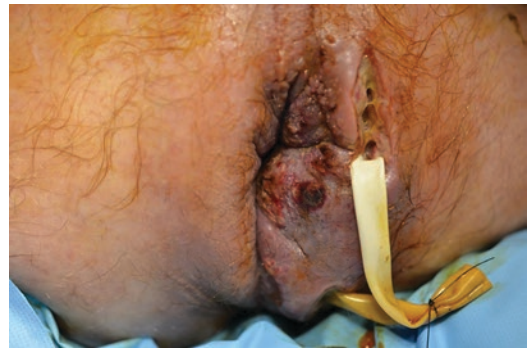

Fig. 7.7 Anal cancer with associated abscess and Penrose drain placement. (Anandam [26])

control. Complications of acute perineal debulking include the potential for abscess and fistula formation as well as a nonhealing wound which could delay definitive chemoradiation therapy for the patient.

Tumors outside the anal canal that present acutely with lifestyle limiting pain may be amenable to debulking if below the dentate line (see Fig. 7.6). Wide local excision with at least 1 cm margin should be performed and can alleviate the patient's acute symptoms. However, long-term oncologic benefit will depend on disease-free resection margins and adjunctive therapy with chemotherapy and radiation [19]. Though initial improvement in pain can be achieved, complications of abscess and fistula are common. A similar delay to definitive therapy and a deforming and unacceptable scar can result.

Anal tumors can also present with perianal abscess or fistulas. If the patient has an abscess, aggressive management with incision and drainage and postoperative antibiotics should be employed, bridging to eventual standard management with chemoradiation [20]. If suspicion of cancer exists without a tissue diagnosis, then a concurrent biopsy should be performed for histologic diagnosis. For supralevator abscesses associated with superior extension of an anal cancer, transabdominal or transgluteal drainage should be considered in addition to transrectal drainage. Antibiotics should cover skin flora as well as enteric bacteria (see Fig. 7.7).

Abdominal Approach

In addition to a perineal approach, an abdominal approach may be indicated in acute anal cancer presentations that present with obstruction or fecal incontinence. Fecal incontinence is due to infiltration of the external sphincters by the tumor. The diversion is done to better control the fecal stream.

Diversion

Creation of a diverting loop ileostomy and loop colostomy are common treatment options to divert the intestinal stream and prevent perforation. Either can be performed laparoscopically or via an open technique to relieve an impending complete obstruction. A loop colostomy allows for proximal diversion and distal decompression via the efferent limb and can be performed at any part of the colon that will reach the abdominal wall without tension. The more distal the colostomy creation site, the more water can be absorbed, and solid stool will be extruded mimicking the natural function of the colon. Though an end colostomy may be appropriate in some circumstances, caution should be used when creating an end colostomy in the setting of a distal anal obstructing tumor for fear of creating a closed loop rectal obstruction. Diverting end colostomies, however, are more prone to prolapse as well as more difficult in terms of eventual closure through a peristomal incision should that be warranted in the future.

Though technically easier to create, a diverting loop ileostomy can be associated with peristomal dermatitis, pouching difficulties, dehydration, electrolyte disturbances, and even acute kidney injury due to high output. Similar to an end colostomy, caution should be warranted in the creation of an end ileostomy in a patient with a distal obstruction and a patent ileocecal valve. A meta-analysis of randomized controlled trials comparing diverting loop ileostomies and colostomies shows no difference between the two groups in terms of stoma complications or in time to ostomy closure [21].

Abdominoperineal Approach

For recurrent or persistent anal canal cancer following definitive chemoradiation therapy, consideration for an abdominoperineal resection should be discussed as salvage therapy [22]. Here again, consideration should be given for referral to a colorectal surgeon if the acute surgeon is not comfortable or familiar with this procedure. Consideration should be given to an APR if the patient has developed a recurrence following chemoradiation, is unable to tolerate initial definitive chemoradiation therapy, has developed intolerable fecal incontinence or lifestyle limiting anal pain, or has persistent disease months after chemoradiation [23]. In the acute setting of bleeding or obstruction, a damage control operation should be considered prior to definitive resection and permanent stoma. Following damage control procedures and bridging to definitive therapy, evaluation of the patient for a larger resection such as an abdominoperineal resection can be performed.

Conclusions

Acute presentations for anal and rectal cancers are fortunately not common, but they certainly may be seen by any general surgeon taking call. For rectal diseases, it is important to recognize the location of the disease in the rectum because this will dictate the type of surgery that is required. If the patient can be stabilized and neoadjuvant therapy can be initiated, this may relieve the symptoms allowing the opportunity for a more definitive cure afterward. If they cannot and a surgical decompression or hemorrhage control is needed, this will likely delay the start of chemoradiation therapy. For anal cancers, acute presentations can be controlled with local resection versus a diverting ostomy with/without hemorrhage control and drainage of associated abscesses if needed. Most anal cancers can be treated with chemoradiation therapy only. Surgery is reserved for those who fail chemoradiation therapy, who cannot tolerate chemoradiation therapy, or who have a complication while undergoing chemoradiation therapy. Patients at risk of dehydration and kidney disease should be considered for a colostomy as opposed to an ileostomy.

References

1. Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER cancer statistics review, 1975–2013. Bethesda: National Cancer Institute. http://seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER data submission, posted to the SEER web site, April 2016.
2. Cuffy M, et al. Colorectal cancer presenting as surgical emergencies. Surg Oncol. 2004;13(2–3):149–57.
3. Van Leersum NJ, et al. Synchronous colorectal carcinoma. Dis Colon Rectum. 2014;57(4):460–6. https://doi.org/10.1097/dcr.0000000000000068.
4. Anderson BJ, Hill EG, Sweeney RE, Wahlquist AE, Marshall DT, Staveley O'Carroll KF, Cole DJ, Camp ER. The impact of surgical diversion before neoadjuvant therapy for rectal cancer. Am Surg. 2015;81(5):444–9.
5. Patel JA, Fleshman JW, Hunt SR, Safar B, Birnbaum EH, Lin AY, Mutch MG. Is an elective diverting colostomy warranted in patients with an endoscopically obstructing rectal cancer before neoadjuvant chemotherapy? Dis Colon Rectum. 2012;55(3):249–55.
6. Heald R, Ryall R. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet. 1986;327(8496):1479–82.
7. Guillou PJ, Quirke P, Thorpe H, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet. 2005;365:1718–26.
8. Trastulli S, Cirocchi R, Listorti C, et al. Laparoscopic vs open resection for rectal cancer:a meta-analysis of randomized clinical trials. Color Dis. 2012;14:e277–96.

9. Monson JR, Weiser MR. Practice parameters for the management of rectal cancer (Revised). Dis Colon Rectum. 2013;48(3):535–50. https://doi.org/10.1007/s10350-004-0937-9.
10. Scott N, Jackson P, Al-Jaberi T, Dixon MF, Quirke P, Finan PJ. Total mesorectal excision and local recurrence: a study of tumour spread in the mesorectum distal to rectal cancer. Br J Surg. 1995;82:1031–3.
11. Kuvshinoff B, Maghfoor I, Miedema B, et al. Distal margin requirements after preoperative chemoradiotherapy for distal rectal carcinomas: are < or = 1 cm distal margins sufficient? Ann Surg Oncol. 2001;8:163–9. 77.
12. Slanetz CA Jr. The effect of inadvertent intraoperative perforation on survival and recurrence in colorectal cancer. Dis Colon Rectum. 1984;27:792–7.
13. Rondelli F, Reboldi P, Rulli A, et al. Loop ileostomy versus loop colostomy for fecal diversion after colorectal or coloanal anastomosis:a meta-analysis. Int J Color Dis. 2009;24:479–88.
14. Chiara O, et al. A systematic review on the use of topical hemostats in trauma and emergency surgery. BMC Surg. 2018;18(1):68.
15. American Cancer Society. Cancer facts & figures 2018. Atlanta: American Cancer Society; 2018.
16. Otto SD, Lee L, Buhr HJ, Frericks B, Höcht S, Kroesen AJ. Staging anal cancer: prospective comparison of transanal endoscopic ultrasound and magnetic resonance imaging. Gastrointest Surg. 2009;13:1292–8.
17. Krengli M, Milia ME, Turri L, et al. FDG-PET/CT imaging for staging and target volume delineation in conformal radiotherapy of anal carcinoma. Radiat Oncol. 2010;5:10.
18. Wasvary HJ, Barkel DC, Klein SN. Is total colonic evaluation for anal cancer necessary? Am Surg. 2000;66:592–4.
19. Gordon PH, et al. Current status: perianal and anal canal neoplasms. Dis Colon Rectum. 1990;33:799–808.
20. Gaertner WB, Hagerman GF, Finne CO, Alavi K, Jessurun J, Rothenberger DA, Madoff RD. Fistula-associated anal adenocarcinoma: good results with aggressive therapy. Dis Colon Rectum. 2008;51(7):1061–7.
21. Guenaga KF, et al. Ileostomy or colostomy for temporary decompression of colorectal anastomosis. Cochrane Database Syst Rev. 2007;(1):CD004647.
22. Renehan AG, Saunders MP, Schofield PF, O'Dwyer ST. Patterns of local disease failure and outcome after salvage surgery in patients with anal cancer. Br J Surg. 2005;92:605–14.
23. Mariani P, Ghanneme A, De la Rochefordière A, Girodet J, Falcou MC, Salmon RJ. Abdominoperineal resection for anal cancer. Dis Colon Rectum. 2008;51:1495–501.
24. Anandam J. CT image of obstructing high rectal tumor. [Photograph]. Dallas: University of Texas Southwestern; 2018.
25. Anandam J. Fungating anal cancer. [Photograph]. Dallas: University of Texas Southwestern; 2018.
26. Anandam J. Anal cancer with associated abscess. [Photograph]. Dallas: University of Texas Southwestern; 2018.

8 The Role of Radiology in Obstructing or Bleeding Anal and Rectal Cancers

Thomas F. Murphy

Introduction

Over 40,000 new cases of anorectal malignancy are diagnosed each year in the United States, with rectal cancer 7 times more common than anal cancer. Recommended imaging studies for initial staging include CT scan of the chest, abdomen, and pelvis, endorectal ultrasound, pelvic MRI, and PET/CT; recommendations vary depending on tumor histology, size, and organizational guidelines [1]. In a minority of these cases, the patient presents emergently due to a complication. This chapter considers imaging methods that are available to assist the diagnosis and management of patients who present with bowel obstruction or hemorrhage caused by anorectal malignancies. Several of the most commonly employed tests and their appropriate use in the emergency setting are described. As obstruction and bleeding are not usually encountered together, they will be discussed separately.

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Obstruction and Malignancy

Malignancy is the most common cause of large bowel obstruction (LBO) in adults, accounting for up to 60% of cases [2]. The clinical presentation of abdominal pain, constipation or obstipation, and abdominal distention is typically insidious, unlike the common presentation of small bowel obstruction. The goals of imaging in this situation are to confirm or exclude obstruction, determine the level of blockage and the cause, to reveal the extent of disease, and to search for complications.

Abdominal Radiography

When LBO is suspected, the most common initial imaging study is abdominal radiography. This should include both supine and upright abdominal radiographs, which can detect LBO (Fig. 8.1), and help exclude small bowel obstruction (SBO) and pneumoperitoneum. A left lateral decubitus view can be done in lieu of an upright view in a patient unable to stand. The colon is considered to be dilated if its diameter exceeds 6 cm in the transverse, descending and sigmoid portions; the normal cecum can be significantly larger [3]. The sensitivity of abdominal radiographs for LBO is 84%, specificity only 72%; ileus or pseudo-obstruction can also cause a dilated colon [4]. Radiography may also be useful in reveal-

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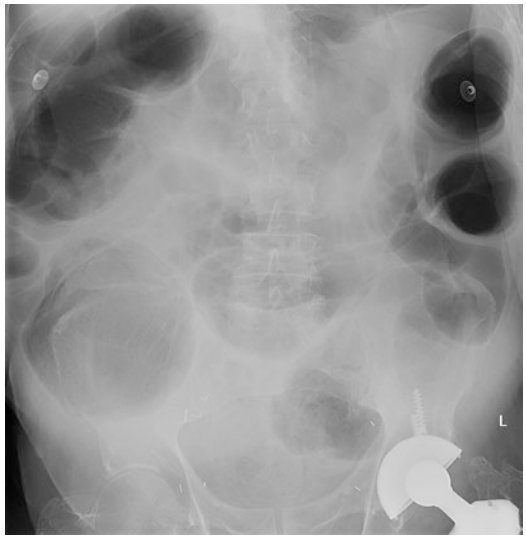

Fig. 8.1 An 87-year-old male with constipation. Supine abdominal radiograph shows dilated colon secondary to obstructing rectal cancer

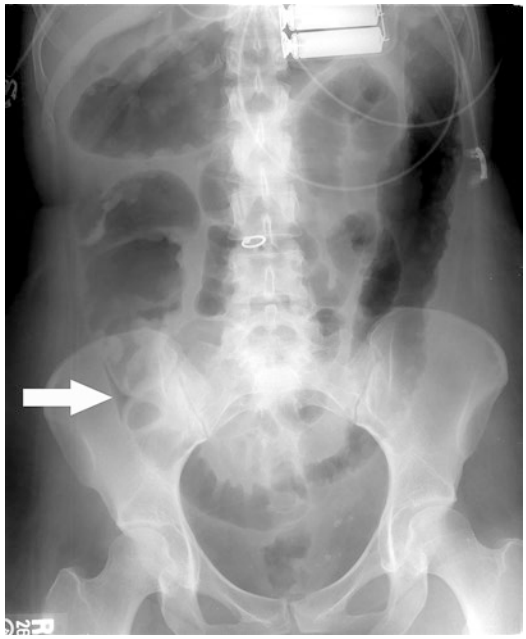

Fig. 8.2 A 29-year-old female with ulcerative colitis and abdominal pain. Supine abdominal radiograph shows triangular collection of peritoneal gas in right lower quadrant (arrow) due to colon perforation

ing complications of LBO, such as pneumatosis intestinalis, portal venous gas, and perforation manifested as pneumoperitoneum (Fig. 8.2). Upright views are more sensitive for the detection of pneumoperitoneum and can detect as little 1 ml of air in the peritoneal cavity [5].

Computed Tomography (CT)

Multidetector CT is the preferred method for diagnosing the cause of LBO. It can show the level of obstruction and can reveal intraluminal as well as mural and extraluminal disease. Metastatic disease, both local and regional, can be assessed. Inflammation, ischemia, and bowel perforation can also be diagnosed. A dilated colon with a transition point of luminal constriction allows the diagnosis of LBO by CT (Fig. 8.3) [6]. The sensitivity of CT for the diagnosis of LBO is 96%, specificity of 93% [7]. CT is useful to evaluate patients who have been treated for LBO by diagnosing postoperative complications. Colonic stents may be used to palliate obstructing rectal cancers; in these cases CT can demonstrate stent position (Fig. 8.4) and reveal complications such as migration, perforation, and tumor ingrowth [8].

Technical options for performing CT depend on the situation. Intravenous contrast is highly recommended, as this improves delineation of anatomic structures and helps in revealing a mass, ischemia, and inflammation. Contraindications to the use of iodinated intravenous contrast include iodine allergy (not to be confused with shellfish allergy) and renal insufficiency [9]. Oral contrast is helpful to show intraluminal features of the bowel, but the prolonged time needed for its consumption and passage distally may render it impractical in an emergency. In selected cases, rectal contrast may help to prove luminal obstruction. Multiplanar reformations (MPRs) are routinely performed and help to demonstrate pathologic anatomy. In the acute setting, a grasp of the extent of the patient's disease is helpful to

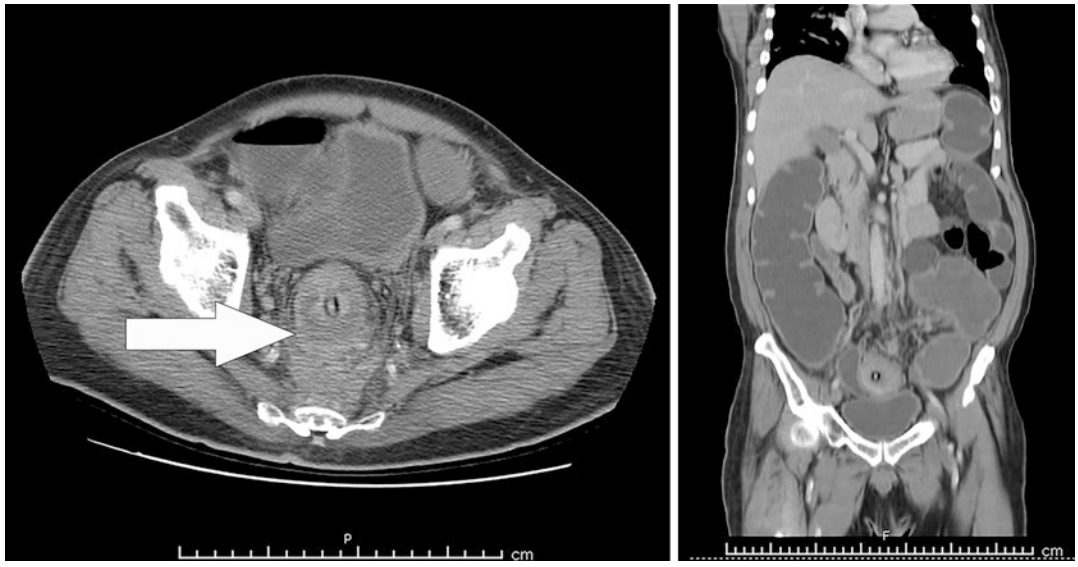

Fig. 8.3 A 51-year-old male with abdominal pain and distention. Axial and coronal images from contrast-enhanced CT reveal rectal cancer (arrow) causing colon obstruction. A decompression tube is seen in the rectal lumen

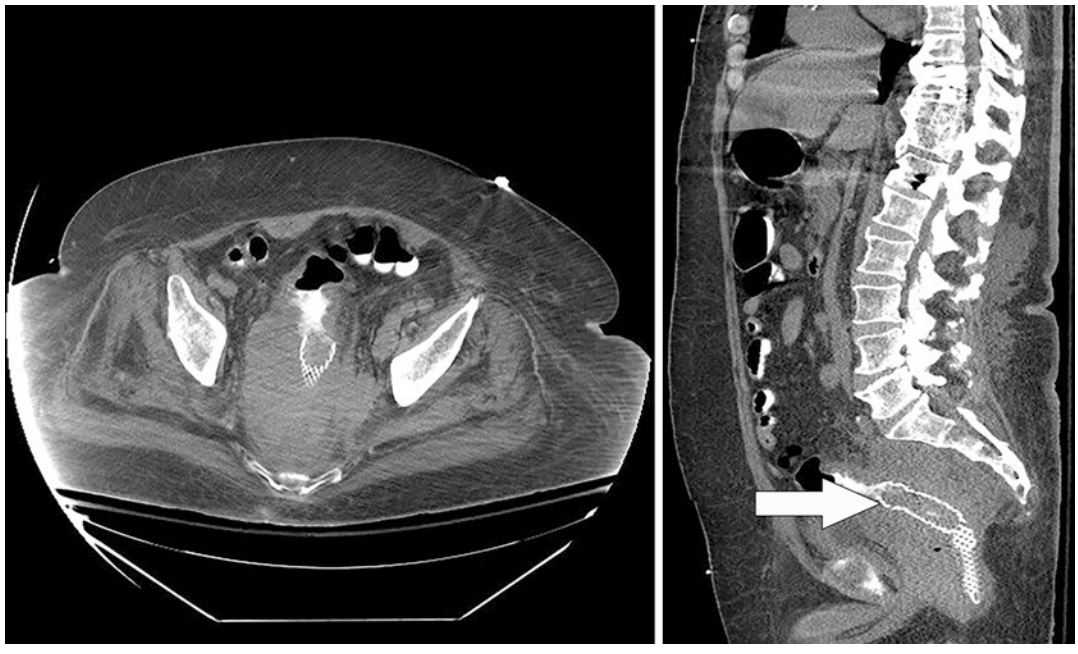

Fig. 8.4 A 67-year-old male with obstructing rectal cancer, palliated by rectal stent (arrow), as seen on contrast-enhanced CT

inform the choice of treatment. CT of the chest, abdomen, and pelvis with intravenous and oral contrast can be done to stage the malignancy.

Contrast Enema

A contrast enema is less commonly performed than CT. It is still a useful diagnostic tool to distinguish mechanical LBO from pseudo-obstruction and may be helpful to prove the diagnosis of colonic volvulus (Fig. 8.5). The retrograde passage of contrast material from the rectum to the ileocecal valve disproves colonic obstruction. Water-soluble iodinated contrast material (similar to that used for intravenous injection) should be used in preference to barium. Its advantages include absorbability by the peritoneum in the event of perforation and decreased artifact if CT is performed afterward [7]. Hence the term "barium enema" in the emergency context is misleading and should be avoided. A scout radiograph of the abdomen should be done before the enema, so that preexistent calcifications and other radiopaque intra-abdominal objects will not be confused with the contrast material. After a digital rectal exam, a flexible catheter is inserted into the rectum, and contrast material is allowed to flow retrograde by gravity, monitored by fluoroscopy [10]. Inflow of contrast is terminated when the cecum is opacified, a point of obstruction is reached, or extraluminal contrast material (indicating colon perforation) is seen. The study is documented as the radiologist captures fluoroscopic images and the technologist performs overhead radiographs; "overheads" are useful for showing the entire abdomen and allowing measurements.

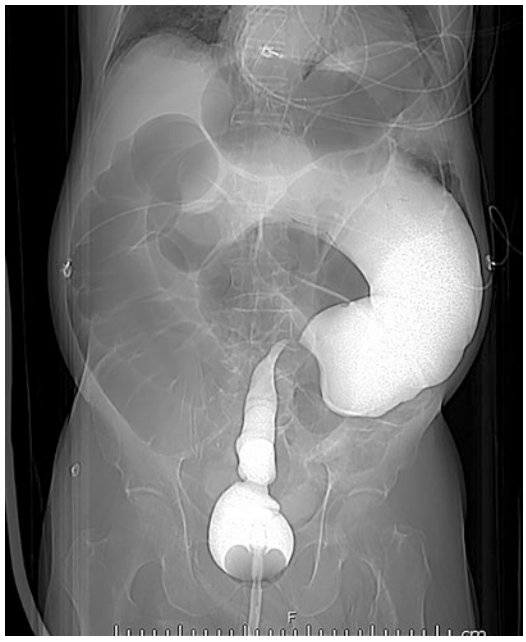

Fig. 8.5 An 82-year-old male with constipation and abdominal pain. Radiograph from contrast enema shows smooth luminal tapering with a twisted appearance of the sigmoid colon, typical of sigmoid volvulus

Magnetic Resonance Imaging (MRI)

MRI is not commonly used to evaluate LBO; however, it is the preferred technique for local staging of rectal cancer. It can assess tumor location, size, relation to anal sphincter, extramural spread, peritoneal, and lymph node involvement (Fig. 8.6). The examination can be performed using either 1.5 or 3 Tesla scanners. Neither endorectal coils, bowel preparation, nor endoluminal contrast is necessary. Intravenous contrast

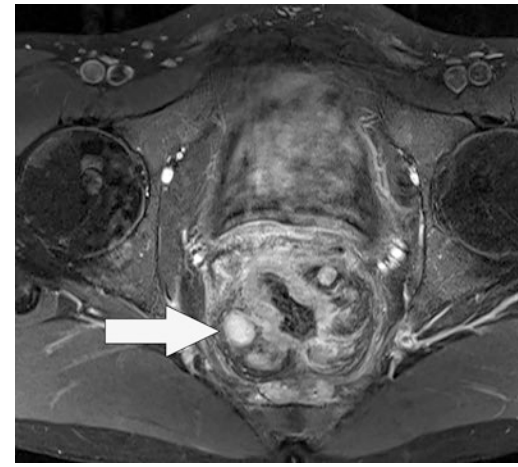

Fig. 8.6 A 29-year-old male T4 N2 rectal cancer. Gadolinium-enhanced axial T1 fat-suppressed MRI shows rectal wall thickening with spiculations extending into the mesorectal fat and enlarged mesorectal lymph nodes (arrow)

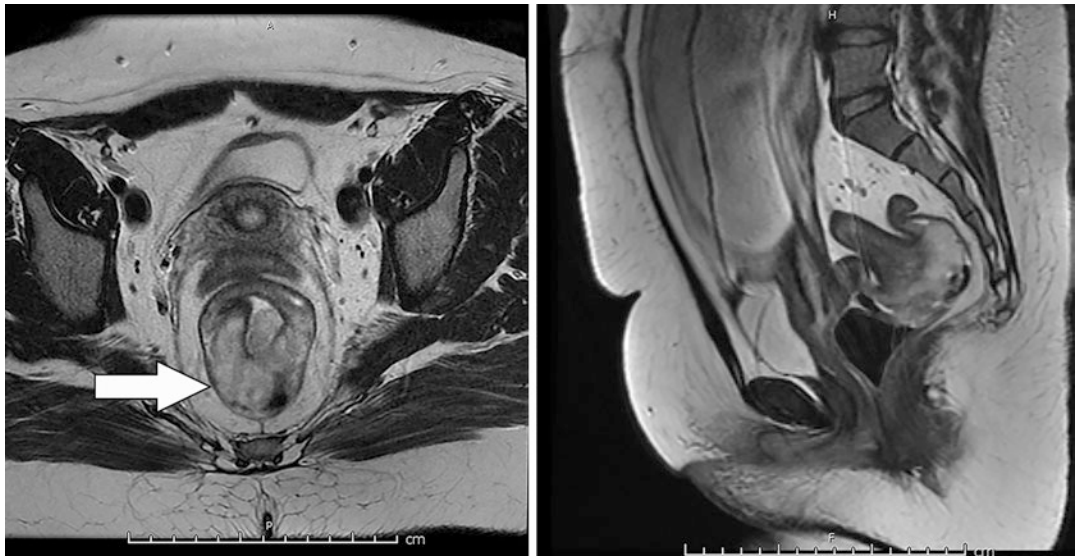

Fig. 8.7 A 22-year-old pregnant female with mass noted on obstetric ultrasound. T2 axial and sagittal MRI shows telescoping of rectum, typical of intussusception, caused by carcinoma of rectum (arrow)

and diffusion weighted imaging may improve tumor detection. T2-weighted imaging is crucial and should be done in sagittal, axial, and coronal planes.

T2-weighted imaging is more sensitive in distinguishing diseased from normal tissue and helps determine the extent of local invasion. High-resolution 3-mm-thick sections should also be done perpendicular to the tumor's long axis, as seen on the sagittal views [11]. A unique role for MRI is the imaging of pregnant patients with acute abdominal pain (Fig. 8.7), where CT is contraindicated due to concern for fetal exposure to ionizing radiation [12]. Disadvantages to the use of MRI include lack of availability in the emergency setting and patient safety issues related to cardiac pacemakers and other ferromagnetic implanted medical devices.

Bleeding from Anorectal Malignancies

Malignancy is a relatively uncommon etiology of rectal bleeding, accounting for less than 10% of cases [13]. The most common causes are colonic diverticula and angiodysplasia, while ischemic colitis, inflammatory bowel disease, and rectal varices are also in the differential diagnosis. Colonoscopy is the appropriate first diagnostic maneuver to diagnose the cause, and potentially treat, rectal bleeding [14]. In the emergency situation, the limitations of colonoscopy include poor visualization of the mucosa due to lack of colon preparation and blood filling the lumen and hemodynamic instability. CT angiography and radionuclide scintigraphy are diagnostic imaging tests which can supplement or be used instead of colonoscopy. Catheter angiography has a lower sensitivity to detect bleeding and is more appropriate as a therapeutic tool. The goals of imaging are detecting active bleeding, localizing the site, and diagnosing the cause, with the aim of guiding surgery and/or therapeutic angiography.

CT Angiography (CTA)

CT angiography can detect bleeding rates as low as 0.35 mL/min, superior to catheter angiography and slightly less sensitive than nuclear medicine [15]. CTA sensitivity for acute hemorrhage is as high as 92%. CTA technique requires the rapid injection of intravenous contrast at a rate

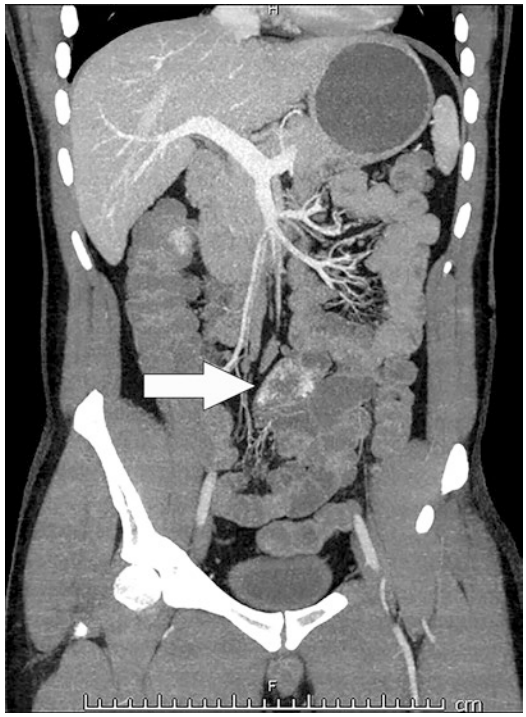

Fig. 8.8 A 28-year-old male with hematochezia. CT angiogram shows small bowel luminal enhancement (arrow) consistent with active bleeding. At surgery, a Meckel diverticulum with heterotopic gastric mucosa was found

of 4–6 ml/s. No oral contrast should be used, as it obscures hemorrhage in the bowel lumen. A scan before injecting contrast is useful to show opaque-ingested material, medications, suture, and surgical clips which could be mistaken for sites of bleeding. After contrast injection, scanning is performed in both arterial and venous phases. Increasing density with the bowel lumen from one phase to the next (noncontrast, arterial, venous) is proof of active bleeding (Fig. 8.8) [16]. Images are reconstructed with thin (1–2 mm) slices in axial, coronal, and sagittal planes. Maximum intensity projections (MIPs) are also created in multiple planes. MIPs increase the conspicuity of small areas of increased density, thus are helpful in showing subtle foci of contrast spillage into the bowel lumen, or small angiodysplasias and arteriovenous malformations. Volume rendering (VR), which assigns colors to voxels based on their attenuation, is useful for revealing

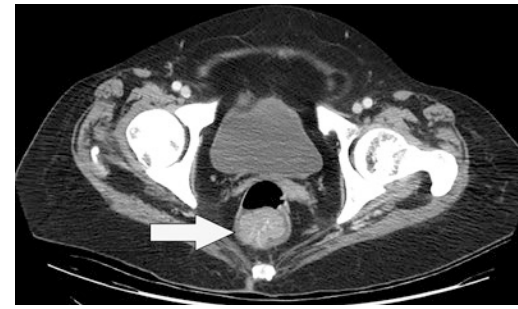

Fig. 8.9 A 58-year-old female with metastatic breast cancer and abnormal pelvic finding on PET/CT. CT angiogram shows enhancing vessel in pedunculated rectal mass (arrow) which proved to be a villous adenoma

bowel wall edema, hyperemia, and thickening [17]. Beyond the detection of bleeding, CTA can show local tumor size and morphology (Fig. 8.9), lymph node involvement, distant metastasis, and complications such as bowel obstruction, perforation, and abscess. The limitations of CTA include the hazards of iodinated intravenous contrast, renal failure, and allergy to iodine. The dose of ionizing radiation is a concern in younger and pregnant patients.

Scintigraphy

Scintigraphy for gastrointestinal bleeding typically uses the patient's own erythrocytes, labelled with 99 m technetium. Various labelling methods are available, the most efficient being the in vitro method in which blood is withdrawn from the patient; RBCs are labelled with 99mTc and then reinjected [18]. This results in tagging of the entire circulating RBC pool, which can be imaged using a gamma camera. Dynamic images are acquired, from 1 to 20 seconds per image. The duration of imaging is long enough to allow detection of intermittent bleeding, from 1 to 4 hours. Diagnosis of a gastrointestinal bleed requires that four criteria be met: a focus of extravascular activity should start in a previously normal area, activity should increase in intensity over time, activity should move in either antegrade or retrograde fashion, and activity should conform to the bowel (Fig. 8.10) [19]. Bleeding rates as

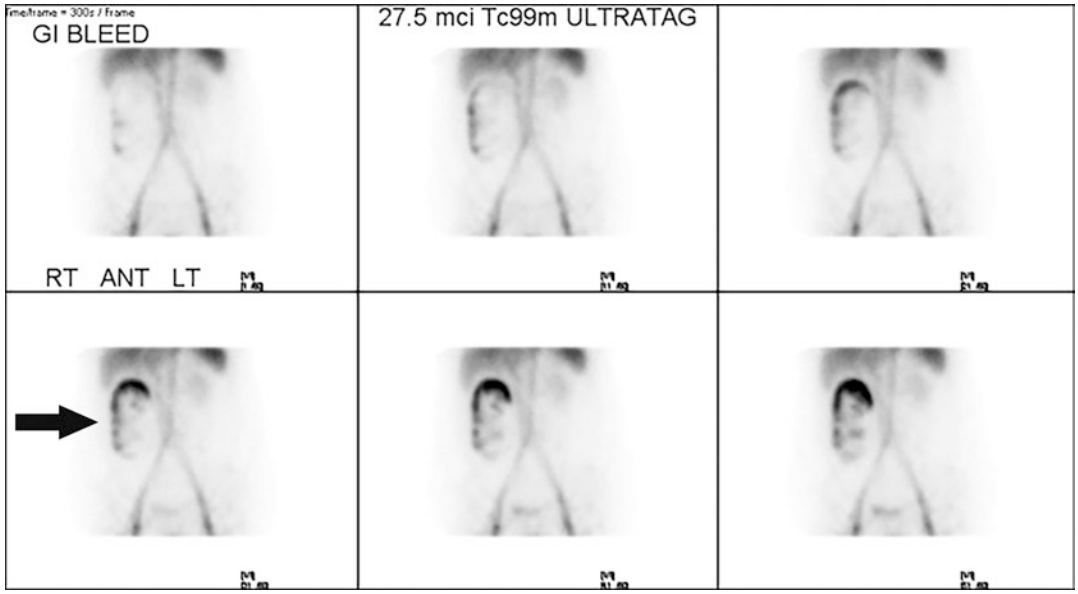

Fig. 8.10 A 51-year-old female with hematochezia. 99mTc tagged RBC scintigraphy shows increasing activity that corresponds to the shape of the right colon (arrow). The source was a bleeding diverticulum

low as 0.05–0.2 mL/min can be detected, with a sensitivity of 93% and specificity of 95% [20]. Detection of bleeding within the first few minutes of the scan predicts a positive angiogram. Advantages of scintigraphy compared to CTA are the capacity to detect lower rates of bleeding over a longer period of observation, lower radiation dose, and avoiding the risk of iodine allergy and nephrotoxicity. Limitations of scintigraphy include relative lack of availability, longer time to perform the study, and lack of anatomic detail compared to CTA [21].

Catheter Angiography

Catheter angiography is usually undertaken as a therapeutic procedure, to treat the source of GI bleeding identified by CTA or scintigraphy. Since iodinated contrast material is used, renal failure and iodine allergy are contraindications. It is performed by an interventional radiologist, in a suite with angiographic equipment. Cone-beam CT, combining cross-sectional imaging with catheter angiography, and automatic vessel detection software are technical advances [22]. Vascular access is most commonly obtained by femoral artery puncture, followed by catheter insertion over a guidewire. The bleeding site is approached by selective catheterization of the feeding artery (Fig. 8.11). Bleeding can be controlled by inject-

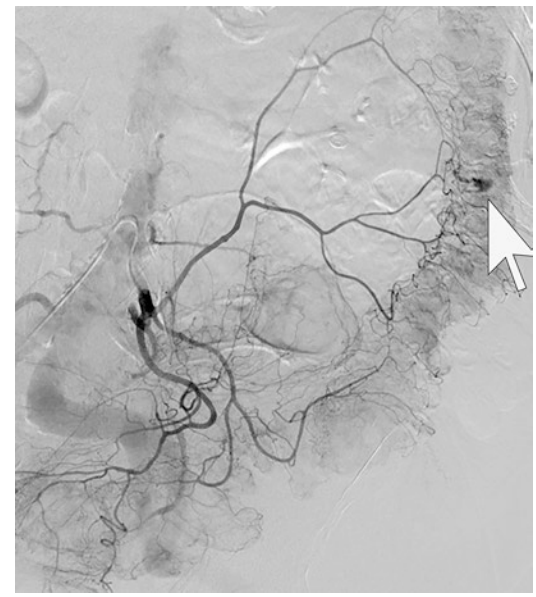

Fig. 8.11 An 85-year-old male with hematochezia. Selective inferior mesenteric artery angiogram shows focal extravasation of contrast in the left colon (arrow), from a bleeding diverticulum

ing embolic material through the catheter. Gelatin sponges, particles, coils, or glue may be used, at the discretion of the operator. Post-embolization angiography is done to determine success. Major hazards are rebleeding and bowel ischemia [23]. A review of outcomes from several small series using super-selective mesenteric embolization has shown rates of immediate hemostasis of 96–100%, with the need for repeat embolization as high as 22% and progression to surgery of 12.5% [24].

Conclusion

Abdominal radiography is a rapid method to detect the presence of intestinal obstruction or perforation. CT with intravenous contrast is a useful and widely available tool to evaluate obstructing anorectal malignancy and its complications. Oral and rectal contrast can also be used with CT. Contrast enema is less often performed, but can directly prove or disprove colon obstruction. MRI is the preferred imaging technique to stage rectal malignancy, but is less useful in the setting of bowel obstruction; it is a valuable alternative to CT for imaging of pregnant patients. CT angiography can simultaneously show the cause of rectal bleeding and associated structural abnormalities and can guide subsequent therapeutic angiography. Scintigraphy is the most sensitive imaging method for GI bleeding and is valuable as an alternative to CTA in patients with renal failure and iodine allergy.

References

1. Matalon S, Mamon H, Fuchs C, et al. Anorectal cancer: critical anatomic and staging distinctions that affect use of radiation therapy. Radiographics. 2015;35:2090–107.
2. Drozdz W, Budzynski P. Change in mechanical bowel obstruction demographic and etiological patterns during the past century: observations from one healthcare institution. Arch Surg. 2012;147(2):175–80.
3. Krawjewski K, Siewert B, Eisenberg R. Colonic dilatation. AJR. 2009;193:W363–72.
4. Yeo H, Lee S. Colorectal emergencies: review and controversies in the management of large bowel obstruction. J Gastrointest Surg. 2013;17:2007–12.
5. Kasznia-Brown J, Cook C. Radiologic signs of pneumoperitoneum: a pictorial review. Br J Hosp Med. 2006;67:634–9.
6. Horton K, Abrams R, Fishman E. Spiral CT of colon cancer: imaging features and role in management. Radiographics. 2000;20:419–30.
7. Jaffe T, Thompson W. Large-bowel obstruction in the adult: classic radiographic and CT findings, etiology, and mimics. Radiology. 2015;275:651–63.
8. Dharmadhikari R, Nice C. Complications of colonic stenting: a pictorial review. Abdom Imaging. 2008;33:278–84.
9. Wysowski D, Nourjah P. Deaths attributed to x-ray contrast media on U.S. death certificates. AJR. 2006;186:613–5.
10. Chapman A, McNamara M, Porter G. The acute contrast enema in suspected large bowel obstruction: value and technique. Clin Radiol. 1992;46:273–8.
11. Jhaveri K, Hosseini-Nik H. MRI of rectal cancer: an overview and update on recent advances. AJR. 2015;205:W42–55.
12. Birchard K, Brown M, Hyslop W. MRI of acute abdominal and pelvic pain in pregnant patients. AJR. 2005;184:452–8.
13. Ghassemi K, Jensen D. Lower GI bleeding: epidemiology and management. Curr Gastroenterol Rep. 2013;15:333.
14. Gralnek I, Neeman Z, Strate L. Acute lower gastrointestinal bleeding. NEJM. 2017;376:1054–63.
15. Artigas J, Marti M, Soto J, et al. Multidetector CT angiography for acute gastrointestinal bleeding: technique and findings. Radiographics. 2013;33:1453–70.
16. Maddu K, Mittal P, Arepali C, et al. Colorectal emergencies and related complications: a comprehensive review—noninfectious and noninflammatory emergencies of the colon. AJR. 2014;203:1217–29.
17. Raman S, Horton K, Fishman E. MDCT and CT angiography evaluation of rectal bleeding: the role of volume visualization. AJR. 2013;201:589–97.
18. Ziessman H, O'Malley J, Thrall J. Nuclear medicine: the requisites. 4th ed. Philadelphia: Elsevier Saundeers; 2013. p. 307–21.
19. Grady E. Gastrointestinal bleeding scintigraphy in the early 21st century. J Nucl Med. 2016;57:252–9.
20. Siddiqui A, Schauwecker D, Wellman H. Comparison of technetium-99m sulfur colloid and in vitro labeled technetium-99m RBCs in the detection of gastrointestinal bleeding. Clin Nucl Med. 1985;10:546–9.
21. ACR appropriateness criteria: radiologic management of lower gastrointestinal tract bleeding. American College of Radiology. Website. https://acsearch.acr.org/docs/69457/Narrative/. Published 2006. Updated 2014. Accessed 10 Apr 2018.
22. Ierardi A, Urbano J, De Marchi G, et al. New advances in lower gastrointestinal bleeding management with embolotherapy. Br J Radiol. 2016;89:20150934.
23. Shiraishi A. Endovascular treatment of gastrointestinal bleeding. Juntendo Med J. 2015;61:242–8.
24. Pham T, Tran B, Ooi K, et al. Super-selective mesenteric embolization provides effective control of lower GI bleeding. Radiol Res Pract. 2017:Article ID 1074804. https://doi.org/10.1155/2017/1074804.

9 Role of Chemoradiation in Obstructing or Bleeding Anal and Rectal Cancers

Daniel Desmond and Tamie L. Kerns

Introduction

Malignancy of the terminal gastrointestinal tract has a unique management approach from more proximal disease. Historically these cancers were managed with surgical resection. Anatomically limited surgical fields within the pelvis and surgical morbidity associated with distal gastrointestinal manipulation and resection (end ileostomy, urinary or sexual dysfunction) have advanced guideline-directed use of chemotherapy and radiation in the treatment of rectal and anal cancer (stages II–IV). These patients who present with bleeding or obstruction due to cancer of the rectum or anus require individualized care and consideration prior to management. Anal cancer has a different set of risk factors, primary histology (squamous cell carcinoma (SCC) versus adenocarcinoma) and management than rectal cancer. This chapter will treat these entities separately and focus on the role of chemotherapy and radiation.

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Rectal Cancer

There is some variability in surgical and pathologic definitions of rectal anatomy. With regard to malignancy, a distance of <12 cm from the anal verge has been suggested [1]. The rectoanal junction is irregular and generally represents a transition from columnar, glandular epithelium of the rectum to squamous cell morphology seen in the anus. Anatomically this occurs at the upper border of the anal sphincter, the puborectalis muscle.

Approximately, 40,000 new cases of rectal cancer present in the United States annually [2, 3]. Rectal cancer is categorized as a subset of colorectal cancer (CRC) owing to its similar predominant histology (adenocarcinoma) and risk factors. This has caused some decreased capture of disease owing to miscategorization in the past. Local recurrence rates are higher in rectal (up to 30%) versus colon cancer due to difficulty in obtaining tumor-free margins because of the anatomic location of the rectum [4]. Twenty percent of cases of rectal cancer present initially with metastatic disease which is associated with a 14%, 5-year survival rate compared with 90% for localized disease [5]. Again, surgery has historically been the primary treatment modality.

Localized disease without high-risk features on histology (lymphovascular invasion, muscularis propria invasion) can be managed exclusively with excision and observation. Review of the SEER CRC database from 1988 to 2000

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https://doi.org/10.1007/978-3-030-12823-4_9

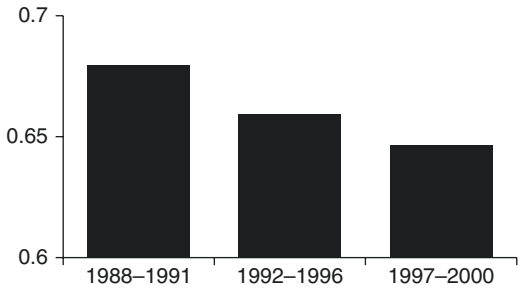

Fig. 9.1 Percentage of patients undergoing resection of primary stage IV colorectal tumors from 1988 to 2000. (Reprinted by permission from Springer Nature, Cook et al. [6])

showed a progressive decrease in the number of patients with stage IV colorectal cancer undergoing resection (Fig. 9.1). Rectal cancer was resected at a much lower rate than colon cancer (45.6% for rectum versus 74% for colon) [6]. The trend of decreased overall CRC resection as well as decreased rectal cancer resection was suggested to be a result of increasing availability of improved chemotherapeutic regimens and surgical technique. If stage II rectal cancer (invasion through the muscularis propria into the pericolorectal tissues (T3, N0)) or stage III (T1-2, N1-2) is present, neoadjuvant chemoradiation (CRT) or chemotherapy alone is necessary prior to surgery [2, 7]. This inclusion of chemotherapy and radiation into treatment guidelines occurred after randomized control trials showed benefit in local control of disease with CRT and significantly improved disease-free survival [8, 9]. A 2013 Cochrane review solidified neoadjuvant CRT or chemotherapy as a standard of care. The duration of neoadjuvant treatment is 5.5 weeks with radiation therapy and capecitabine or 5-fluorouracil (FU), with or without leucovorin. Chemotherapy alone with FOLFOX (FU, leucovorin and oxaliplatin) or CAPEOX (capecitabine, oxaliplatin) is also an option. Recent trials suggest that locally advanced cancer can be treated with total neoadjuvant CRT (adjuvant therapies all delivered preoperatively rather than before and after surgery) [10].

Implementation of neoadjuvant CRT has led to improvement in locoregional failure (30–15%) and survival [11]. A prospective study of 78 patients with synchronous, stage IV rectal cancer who received up-front triple-drug combination chemotherapy resulted in only 6% of patients requiring surgery and an additional 9% receiving nonoperative intervention (stent or radiotherapy) to palliate primary tumor symptoms [12].

Patients who present with obstruction (10–25%) or bleeding (8–26%) represent a complex subset of patients who can have locoregional or metastatic disease requiring significant pretreatment risk stratification prior to surgical intervention [3, 13]. In general, these patients will represent at least stage II disease, and they will be discussed as such going forward. Initial evaluation should focus on stabilization ensuring hemodynamic stability and supportive management including gastric decompression for patients with nausea and vomiting. Transfusion may be necessary if a brisk bleed is identified. Metabolic abnormalities and coagulopathy should be corrected. Diagnostic evaluation of LGIB can be performed with endoscopy, angiography, or tagged red blood cell scan with preference given to the two former modalities because of their therapeutic role in control of acute bleeding. Surgical intervention is a salvage option for patients with uncontrolled bleeding or severe obstruction with risk for perforation. A retrospective study of 85 patients with endoscopically obstructive rectal cancer but without signs of clinical obstruction had favorable outcomes (sphincter preservation, decreased radical pelvic surgery) with the use of neoadjuvant CRT compared to patients treated with immediate diversion which further suggests the favorability of neoadjuvant therapy if possible [14]. Another retrospective review of 452 cases of patients with rectal adenocarcinoma compared those who presented emergently with obstruction, perforation, or massive hemorrhage ($n = 45$) and those who were not emergent ($n = 207$) suggested that those in the non-emergent presentation arm had improved disease-specific survival (stage III: 70–20%, respectively, Fig. 9.2) [15]. The patients in this study received similarly poor pretreatment staging (39% in emergent versus 42% in non-emergent) and interestingly those with emergent presentation had higher incidence of chemotherapy given (63–43%) (pre- or postoperative delivery was not specified) [15]. This

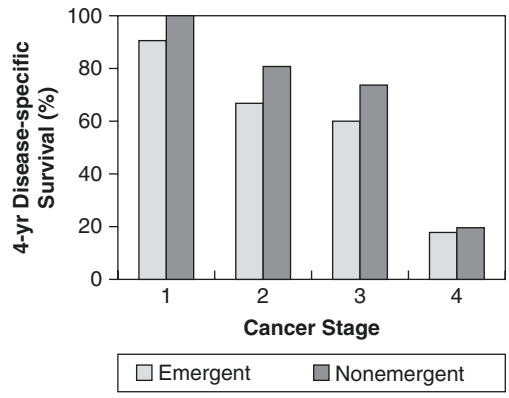

Fig. 9.2 Disease-specific survival for rectal cancer stages I through IV. (Reprinted by permission from Elsevier, Phang et al. [15])

study's design is open to selection bias, and its findings should be viewed cautiously.

Obstruction that is deemed to be unresponsive or unamenable to CRT can be managed with emergent surgery or endoscopic stent placement or cryosurgery based on patient and institutional factors [16]. Stenting should not be performed in patients with recurrent disease already on anti-angiogenic therapy (i.e., anti-VEGF therapy, bevacizumab) due to perforation risk [17]. Short-course radiation therapy, which involves a total of 25 Gy delivered in 5 fractions over 5 days, may represent a reasonable alternative for patients with obstruction, synchronous disease, or poor surgical prognosis due to comorbid conditions [18]. Delivery of this therapy should be completed at the discretion of treating provider taking into account local resources, expertise, and comfort with treatment and complications. These management tactics are performed for palliation in surgically incurable colorectal cancer. Once decompressed, it is reasonable to continue on to neoadjuvant treatment to clinically downstage a patient if possible.

Once clinical stability is achieved, then appropriate clinical and pathologic staging should be performed. Direct visualization of the entire colon to the cecum is recommended although if endoscopic obstruction is present, then virtual colonoscopy could be performed. Patients with metastatic disease should have genetic testing to include RAS (KRAS, NRAS) and BRAF mutations genotyping to help direct immunotherapy. Once the initial clinical and pathologic information is available, management of patients with rectal cancer should be accomplished with a multidisciplinary team Tumor Board including medical oncology, radiologists, surgeons, radiations oncologist, and pathologists [19].

Rectal cancer stages II–IV with obstruction or massive hemorrhage should be treated with up-front chemotherapy or CRT if possible as time to these treatments is suggested to be associated with improved outcomes [14]. However, if patient factors dictate procedural involvement, then several options are available including surgical diversion, stenting, cryotherapy, or radiation. Cryotherapy is a reasonable option for larger tumors, up to 8 cm in size; however, bleeding and both local and systemic response to thermal injury must be accounted for [20]. Treatment selection will vary based on multiple patient and institutional variables.

Anal Cancer

In 1974 Nigro, working at Wayne State University, published a paper on preoperative chemoradiation which caused a paradigm shift in anal cancer management. Neoadjuvant chemotherapy with 5-FU and mitomycin combined with radiation therapy showed complete tumor response with equivalent rates of disease-free and overall survival along with added benefit of sphincter preservation [21]. This regimen has largely remained the standard of care since. Surgical intervention is now limited to local disease and salvage therapy.

An estimated 8200 new cases of anal cancer will occur in the United States in 2017 [5]. The incidence of anal squamous cell carcinoma increased at a rate of 2.9% per year from 1992–2001 [22]. Risk factors for anal cancer include anoreceptive sex, human immunodeficiency virus (HIV), human papillomavirus (HPV), cigarette smoking, immunosuppression, history of local radiation, and inflammatory anal lesions (fissure, fistula, perianal abscess) [23]. Vaccination against high-risk HPV strains (16 and 18) has been suggested as 80% of anal SCC is suspected to be secondary to these [24]. Five-year survival rates for localized anal cancer, regional lymph

node, and metastatic spread were 80%, 60%, and 30.5%, respectively, according to the review of SEER data from 1980 to 1996 [25]. Anal cancer is divided into two different anatomic categories, the anal canal, proximally, and anal margin, distally, which are differentiated by the absence or presence of keratinization, respectively. The histologic and anatomic definitions vary, but functionally the anal canal is defined as the palpable upper border if the anal sphincter and the puborectalis muscles of the anorectal ring extend to the anal verge [26]. Management of these two subtypes varies only in that T1, N0 (localized tumor ≤2 cm) anal margin cancers can be treated with local excision. All other initial treatment involves neoadjuvant or primary use of CRT.

Anal cancer that presents with obstruction or bleeding is likely representative of advanced disease (≥stage II). Evaluation, staging, and decompression should be individualized to the patient as in rectal cancer if needed emergently. However, in anal cancer chemoradiation should be viewed as the primary treatment modality. Multiple nonrandomized trials since the 1970s have supported the findings of Nigro and his coworkers. The ACT II trial showed a complete response rate of 90% at 26 weeks post-chemotherapy in both arms of the trial (mitomycin C versus cisplatin) [27]. Non-metastatic disease is treated with radiation therapy and chemotherapy with mitomycin plus 5-FU, mitomycin and capecitabine, or 5-FU and cisplatin [28]. Patients with HIV require specific consideration if they present with low CD4 counts (<200 cells/mL), requiring dose adjustment of radiation. Metastatic anal squamous cell carcinoma is treated with 5-FU and cisplatin plus RT, chemotherapy, or a clinical trial. Abdominoperineal resection is only rec-

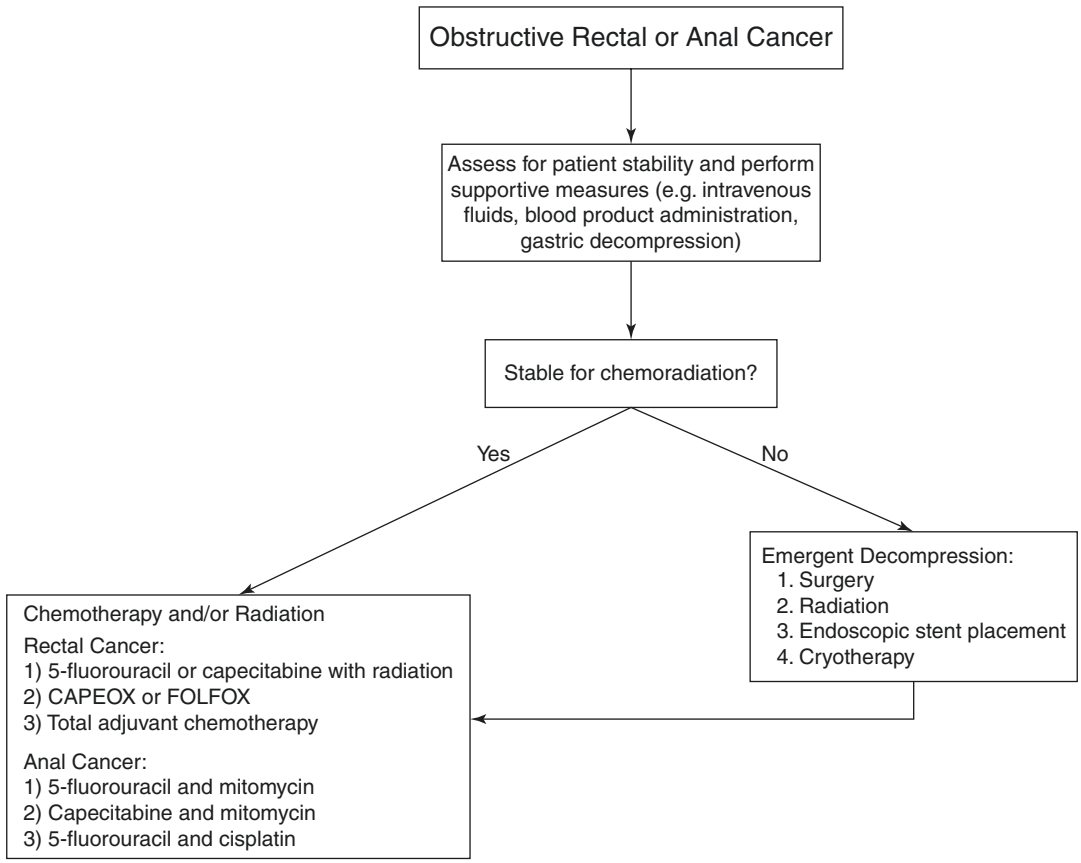

Fig. 9.3 Suggested algorithm for management of obstructive rectal or anal cancer

ommended as salvage therapy for persistent or recurrent disease following CRT in patients who are not candidates for CRT.

Adenocarcinoma of the anus is managed according to rectal cancer recommendations. Melanoma, undifferentiated cancers, and small cell (anaplastic carcinoma) are generally managed with wide local excision with further management determined according to those guidelines (Fig. 9.3).

Conclusion

Definitive management of advanced rectal and anal cancer has historically involved surgical resection. This paradigm continues today; however, incorporation of adjuvant chemotherapy and radiation has proven decreased local recurrence and morbidity, and current guidelines reflect this. Patients with acute presentations of bleeding or obstruction require astute clinical judgment and staging if possible in order to make appropriate treatment decisions. In general, patients with advanced rectal and anal cancer who are able to be treated with neoadjuvant chemotherapy and radiation will have improved outcomes.

References

1. Nelson H, Petrelli N, Carlin A, Couture J, Fleshman J, Guillem J, Miedema B, Ota D, Sargent D. Guidelines 2000 for colon and rectal cancer surgery. JNCI J Natl Cancer Inst. 2004;93(8):583–96.
2. Stintzing S. Management of colorectal cancer. F1000Prime Rep. 2014;6:108.
3. Ronnekleiv-Kelly SM. Management of stage IV rectal cancer: palliative options. World J Gastroenterol. 2011;17(7):835.
4. Sagar PM, Pemberton JH. Surgical management of locally recurrent rectal cancer. Br J Surg. 1996;83:293–304.
5. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin. 2016;66(1):7–30.
6. Cook AD, Single R, McCahill LE. Surgical resection of primary tumors in patients who present with stage IV colorectal cancer: an analysis of surveillance, epidemiology, and end results data, 1988 to 2000. Ann Surg Oncol. 2005;12:637–45.
7. Edge SB. AJCC cancer staging manual. New York: Springer; 2010.
8. Sauer R, Becker H, Hohenberger W, Rödel C, Wittekind C, Fietkau R, Martus P, Tschmelitsch J, Hager E, Hess CF, Karstens JH, Liersch T, Schmidberger H, Raab R. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med. 2010;351(17):1731–40.
9. Roh MS, Colangelo LH, O'connell MJ, Yothers G, Deutsch M, Allegra CJ, Kallenberg MS, Baez-Diaz L, Ursiny CS, Petrelli NJ, Wolmark N. Preoperative multimodality therapy improves disease-free survival in patients with carcinoma of the rectum: NSABP R-03. J Clin Oncol. 2009;27(31):5124–30.
10. Ludmir EB, Palta M, Willett CG, Czito BG. Total neoadjuvant therapy for rectal cancer: an emerging option. Cancer. 2017;123(9):1497–506.
11. Enríquez-Navascués JM, Borda N, Lizerazu A, Placer C, Elosegui JL, Ciria JP, Lacasta A, Bujanda L. Patterns of local recurrence in rectal cancer after a multidisciplinary approach. World J Gastroenterol. 2011;17(13):1674–84.
12. Poultsides GA, Servais EL, Saltz LB, Patil S, Kemeny NE, Guillem JG, Weiser M, Temple LK, Wong WD, Paty PB. Outcome of primary tumor in patients with synchronous stage IV colorectal cancer receiving combination chemotherapy without surgery as initial treatment. J Clin Oncol. 2009;27(20):3379–84.
13. Barnett A, Cefar A, Siddiqui F, Herzig D, Fowlkes E, Thomas CR Jr. Colorectal cancer emergencies. J Gastrointestinal Cancer. 2013;44(2):132–42.
14. Patel JA, Fleshman JW, Hunt SR, Safar B, Birnbaum EH, Lin AY, Mutch MG. Is an elective diverting colostomy warranted in patients with an endoscopically obstructing rectal cancer before neoadjuvant chemotherapy? Dis Colon Rectum. 2012;55(3):249–55.
15. Phang PT, MacFarlane JK, Taylor RH, Cheifetz R, Davis N, Hay J, McGregor G, Speers C, Coldman A. Effect of emergent presentation on outcome from rectal cancer management. Am J Surg. 2003;185(5):450–4.
16. Meijer S, Rahusen FD, Plas LG. Palliative cryosurgery for rectal carcinoma. Int J Color Dis. 1999;14(3):177–80.
17. Hooft JV, Halsema EV, Vanbiervliet G, Beets-Tan R, Dewitt J, Donnellan F, Dumonceau JM, Glynne-Jones RG, Hassan C, Jiménez-Perez J, Meisner S, Muthusamy VR, Parker MC, Regimbeau JM, Sabbagh C, Sagar J, Tanis PJ, Vandervoort J, Webster GJ, Manes G, Barthet MA, Repici A. Self-expandable metal stents for obstructing colonic and extracolonic cancer: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy. 2014;46(11):990–1053.
18. Picardi V, Deodato F, Guido A, Giaccherini L, Macchia G, Frazzoni L, Farioli A, Cuicchi D, Cilla S, Cellini F, Uddin AF, Gambacorta MA, Buwenge M, Ardizzoni A, Poggioli G, Valentini V, Fuccio L, Morganti AG. Palliative short-course radiation therapy in rectal cancer: a phase 2 study. Int J Radiat Oncol Biol Phys. 2016;95(4):1184–90.

19. Beyond TME Collaborative. Consensus statement on the multidisciplinary management of patients with recurrent and primary rectal cancer beyond total mesorectal excision planes. Br J Surg. 2013;100(8):1009–14.
20. Nigro ND, Vaitkevicius VK, Considine B. Combined therapy for cancer of the anal canal. Dis Colon Rectum. 1974;17(3):354–6.
21. Lawes D, Boulos PB. Advances in the management of rectal cancer. J R Soc Med. 2002;95(12):587–90.
22. Shiels MS, Kreimer AR, Coghill AE, Darragh TM, Devesa SS. Anal cancer incidence in the United States, 1977–2011: distinct patterns by histology and behavior. Cancer Epidemiol Biomark Prev. 2015;24(10):1548–56.
23. Gervaz P. Squamous cell carcinoma of the anus-an opportunistic cancer in HIV-positive male homosexuals. World J Gastroenterol. 2011;17(25):2987.
24. Wilkin T, Lee J, Lensing S, Stier E, Goldstone S, Berry J, Jay N, Aboulafia D, Cohn DL, Einstein MH, Saah A, Misuyasu RT, Palefsky J. Safety and immunogenicity of the quadrivalent human papillomavirus vaccine in HIV-1–infected men. J Infect Dis. 2010;202(8):1246–53.
25. Altekruse SF, Kosary CL, Krapcho M, Neyman N, Aminou R, Waldron W, Ruhl J, Howlader N, Tatalovich Z, Cho H, et al. SEER cancer statistics review 1975–2007. Bethesda, MD: National Cancer Institute. Based on November; 2009. p. SEER data submission, posted to the SEER web site, 2010.
26. Ryan DP, Compton CC, Mayer RJ. Carcinoma of the anal canal. N Engl J Med. 2000;342(11):792–800.
27. Ben-Josef E, Moughan J, Ajani JA, Flam M, Gunderson L, Pollock J, Myerson R, Anne R, Rosenthal SA, Willett C. Impact of overall treatment time on survival and local control in patients with anal cancer: a pooled data analysis of Radiation Therapy Oncology Group trials 87-04 and 98-11. J Clin Oncol. 2010;28:5061–6.
28. Goodman K, Rothenstein D, Lajhem C, Wu A, Cercek A, Saltz L. Capecitabine plus mitomycin in patients undergoing definitive chemoradiation for anal squamous cell carcinoma. Int J Radiat Oncol Biol Phys. 2014;90(1):S32–3.

Part III

Acute Presentations of Colon Cancer

Obstructing and Bleeding Colon Cancer: Surgical Management

10

Fia Yi

Anatomy (Fig. 10.1)

The colon is a dynamic organ that differs in size as it starts from the cecum to the rectosigmoid junction. Average length of the colon is approximately 150 cm and varies in diameter from about 7 cm in the cecum to 2.5 cm in the distal colon. The cecum maintains the thinnest wall compared to its distal neighbor which is important to understand when discussing the consequences of obstruction. There is a circular muscular layer and an outer longitudinal muscular layer. The taenia is the result of coalescing of the outer longitudinal muscular layer. The muscular nature of the colon allows for its function to propel material from the small bowel toward the rectum in a systematic and organized fashion. Understanding the general anatomy to include the blood supply is important to understand when ligating vessels for an appropriate oncologic resection as well as understanding the consequences of potentially compromising blood supply to an anastomosis which may then necessitate an extended resection (i.e., extended right hemicolectomy).

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Obstruction

Case scenario: A 65-year-old otherwise healthy male presents with bilious vomiting for the past several days. He has noticed his bowel movements becoming less voluminous over the past 3 months and noticed blood in his stools. On exam, his abdomen is distended with diffuse tenderness throughout. He has had a 30-pound weight loss over the past 6 months that was unintentional.

The use of expandable stents to treat obstruction will have been covered in the next discussion, and so the focus of this chapter will be on the surgical management of obstructions from malignant colon tumors.

A tumor in the colon that goes undetected can increase in size to the point where a physical obstruction can occur. Obstructions can be classified as incomplete or complete. Incomplete obstructions can present like the case above where the patient continues to have some bowel function (passage of stool or gas). Complete obstructions are a diagnosis based on the patient's clinical presentation and diagnostic imaging. These cases will demonstrate an obvious mass on CT scan with dilation of the proximal bowel and sometimes signs of fecalization in the small bowel, especially in the case of more proximal obstructions. When biopsies are unable to be obtained, surgical planning can be difficult. It should be presumed that this

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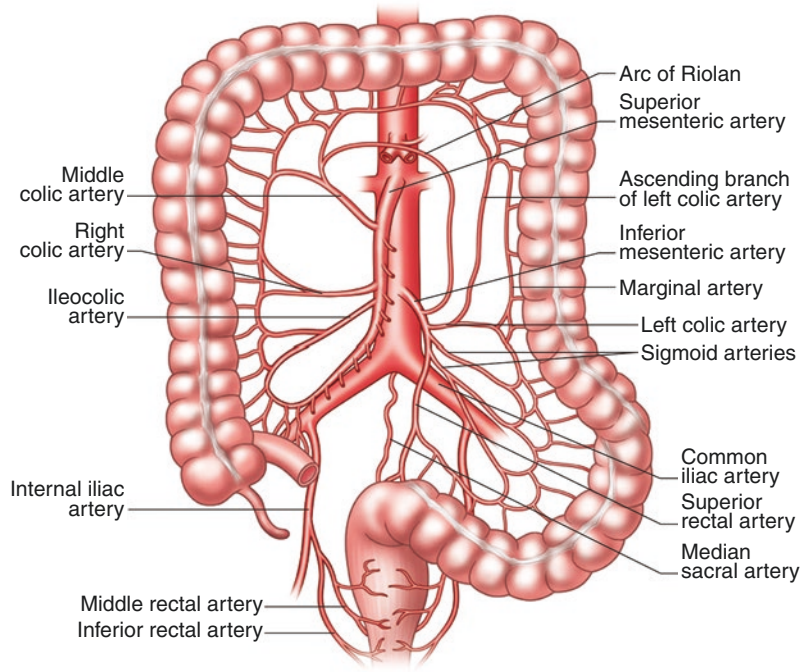

Fig. 10.1 Arterial anatomy of the colon and rectum

is a malignancy, and attempts at an oncologic resection should be done. There should also be thoughts given to a contingency plan in the event that a formal resection is not possible which can often be the case.

As the surgeon, there are a few things to think about prior to the endeavor of operating on these patients: Is this operation for curative or palliative intent? The surgeon's confidence in his or her ability to complete a formal oncologic resection (to include en bloc resection) in the setting of a difficult tumor is one of the issues that needs to be considered. The primary plan should have a contingency plan in the event that the initial intent is unable to be achieved. Obstructing malignant masses, specifically in the left colon, can be approached in a few different ways. A loop colostomy is technically less challenging and easier to perform. A loop colostomy allows decompression and the potential to approach the malignancy in a staged approach. Approaches depend on the ability of the surgeon but can be approached laparoscopically or open. Stoma site marking should be performed by a certified stoma nurse if possible for optimal placement. Loop colostomies have been associated with a higher risk of stomal prolapse when compared to loop ileostomies [1].

Management of obstruction can be thought of as left-sided obstructions from the mid-transverse colon on and right-sided obstructions. Surgical strategies for both cases have slightly different considerations. An algorithm from the 2017 World Society of Emergency Surgery addressing the surgical management of obstructing colon cancer is used for reference (Table 10.1). Left-sided obstructions are fraught with trying to manage stool burden in the proximal part of the colon. This often leads to contamination during the case. In patients who are not completely obstructed, attempts at localization of the tumor via endoscopy and a per oral prep can be attempted. Cases where that is not possible may require an on-table lavage. The appendiceal stump has been described as a location to intubate the colon versus an enterotomy in the terminal ileum. The distal end of the colon is then cannulated with corrugated tubing that is often used in the anesthesia circuit [2]. After lavage, a segmental left colonic resection can then be done. Select cases of on-table lavage with resection have shown no significant

Table 10.1 Surgical options for malignant obstructions

(A) Treatment options for OLCC

Main options	Choices among main options	Ancillary manoeuvres among main option and choices
Loop colostomy (C) bridge to resection or palliation)		
Primary reseution with end colostomy: Hartmann's procedure (HP)		
Resection and primary anastomosis (RPA)	Total/ subtotal colectomy (TC) Segmental colectomy (SC)	Intraoperative colonic irrigation (ICI) Manual decompression (MD) Covering stoma
Tube decompression		
Endoscopie colonic stenting by self expanding metallic stents (SEMS)	Bridge to surgery Palliation	

(B) Treatment option for ORCC

Main options	Choices among main options
Resection and anastomosis	
Resection and anastomosis with proximal stoma creation	
Resection and stoma creation	
Stoma creation	
Intestinal internal bypass	
Endoscopic stent placement	Palliative/ definitive
	Bridge to surgery

Pisano et al. [19]

increase in mortality and morbidity compared to resection for right-sided obstructions [3–5].

Another option in these cases is to perform a subtotal colectomy, which then obviates the need for a lavage intraoperatively. There are also heterogenous studies that have looked at subtotal colectomies as the favored procedure in regard to the increased likelihood of synchronous tumors in patients with obstructing lesions. This does add additional time to the operation and is contingent on the status of the patient [6]. Older studies in the 1990s quoted synchronous cancer rates up to 4.9% in addition to an incidence of benign polyps occurring in up to 29.8% of patients at the time of surgery for an obstructing primary lesion [7]. For this reason, there are some who opt to proceed with the more extensive operation at hand. In the author's opinion, the incidence of these synchronous tumors is fairly low. Current endoscopic guidelines recommend a follow-up colonoscopy within a 3–6-month time period from the time of surgery to clear the remaining portion of the colon that is left, so a segmental colectomy is well within reason to be performed in these cases [8]. Intraoperative colonoscopy is an adjunctive tool that can assist with decision making between performing a subtotal colectomy versus a segmental colectomy. An adequate bowel prep is key to make this an effective tool and is often not possible in cases where there is a complete obstruction. Regardless, options for a primary anastomosis with or without a proximal diverting ostomy in either case are contingent on the stability of the patient (i.e., nutrition, intraoperative stability).

Another option in cases of unresectable or difficult to resect tumors that may benefit from neoadjuvant chemotherapy or that require palliation only is to place a loop colostomy. It is technically less demanding and can allow time to decompress the colon and adequately stage a patient for possibly definitive treatment. In comparison to the Hartmann's procedure, the loop colostomy does not provide any short- or long-term benefit, and it has been shown to increase hospital stay from the multiple operations that are then associated with it [9]. Loop colostomy can also be reserved for patients who are deemed unfit for major surgical procedures or general anesthesia.

The Hartmann's procedure has been well described as an option for resecting an obstructing tumor without performing a primary anastomosis. Avoiding a primary anastomosis is a consideration for several different reasons. Patient factors have been implicated when evaluating anastomotic leak rates especially in emergency surgery. The Association of Coloproctology of Great Britain and Ireland (ACPGBI) identified four important predictors of outcome: age, ASA, grade, and operative urgency and Dukes' stage [10]. Surgeon experience and subspecialty also

appear to have an impact on this outcome [11, 12]. Despite these factors, patients who have undergone a Hartmann's procedure versus resection and primary anastomosis were found to have a slightly lower postoperative mortality rate when done for both curative and palliative intent [13]. On the other hand, it should be mentioned that a majority of patients who have a stoma placed often do not get them reversed secondary to adjuvant treatment and/or disease progression.

If an attempt at a primary resection is feasible, there are a few considerations to think about for preoperative planning. Careful review of imaging prior to surgery is important to consider proximity of the tumor to nearby vital structures. Depending on the size of the tumor, an en bloc resection may have to be done, and both surgeon and patient should be aware of the potential for this beforehand. The use of ureteral stents is also of value in these cases as the usual anatomic course can be deviated from displacement from the tumor. It can also help to localize the ureter if en bloc resection of the ureter is also necessary. Proper oncologic resection of the colon requires at least a 5 cm proximal and distal margin from the tumor. High ligation of the appropriate vessel to the left or right colon will then yield the mesocolic lymph nodes required to appropriately stage the tumor. For right hemicolectomies this would be ligation of the ileocolic artery close to its takeoff from the superior mesenteric artery. Left hemicolectomies would require ligation of the left colic artery from its takeoff of the inferior mesenteric artery. Sigmoid resections would mandate high ligation of the inferior mesenteric artery. The appropriate number of lymph nodes for staging is greater than 12. Anything less than that has been considered a poor prognostic indicator for overall survival and recurrence [14, 15]. As stated previously, a primary anastomosis should only be considered in patients who are hemodynamically stable and who are not malnourished. A single-surgeon series of resection with anastomosis showed no increased risk of anastomotic leakage or mortality when compared to resection and primary anastomosis for right-sided lesions [4]. If at any point it is felt that an attempt at anything less than a sound oncologic resection is not possible (patient not tolerating anesthesia, difficulty in resecting the tumor, etc.) the author recommends calling in for additional help and then considering the option previously discussed of bringing up a loop colostomy.

There will also be cases where the surgeon will take a patient to the operating room for an acute obstruction only to find unresectable metastatic disease (Stage IV). The primary issue of an acute obstruction from the tumor should still be addressed. Biopsies of suspicious lesions should be obtained at the time of surgery as well as a complete intra-abdominal evaluation (palpating and evaluating solid organs and running the small and large bowel). Several studies have looked at the question and role of surgery in Stage IV disease. In two different retrospective studies of patients with well-differentiated tumors, with good performance status, and with only synchronous liver metastases, colonic resection and postoperative chemotherapy provided a survival benefit versus chemotherapy alone [15, 16]. On the other hand, an observational cohort study looking at the National Cancer Database did not reveal an improved survival benefit and therefore did not recommend routine non-curative primary tumor removal [17]. Mention of these studies only serves to reassure the surgeon that the primary issue at hand of an acute obstruction should be dealt with and the effort put into trying to remove a difficult tumor in the face of metastatic disease should not prolong operative time especially if the patient is acutely ill.

Right-sided obstruction secondary to malignancy is amenable to resection and anastomosis almost two-thirds of the time [3, 4]. In cases where resection is not possible, a loop ileostomy, end ileostomy with colonic mucous fistula, and ileocolic bypass are other considerations. A loop ileostomy in the face of a competent ileocecal valve or complete obstruction will not improve the situation of an obstruction. Therefore, the recommendation of an ileocolic bypass has been made [18]. Ileocolic bypasses have been performed in cases of severe obstructing Crohn's disease where an inflammatory phlegmon precludes safe resection of the affected segment of bowel (which is often the terminal ileum in these

cases). Ileocolic bypass consists of mobilizing the ileum up to a healthy segment of colon (transverse colon usually) and performing an end-to-side or side-to-side anastomosis. While this may seem like an attractive option, a few considerations must be examined. Choosing this route would be purely to relieve the obstruction. If the patient is going to be referred to a tertiary center for follow-up on multidisciplinary care, it would behoove the operating surgeon to proceed in a manner that would not obviate another attempt at resecting the primary lesion once the patient completes adjuvant therapy. Examples of this include avoiding maneuvers that could lead to the inadvertent opening of the tumor and potentially increase the risk of spread and avoiding attempts at a primary excision if the tumor is felt to be difficult to excise without compromising the tenets of an appropriate oncologic resection (high ligation, complete mesocolic excision, en bloc resection of surrounding structures involved with the tumor). On the other hand, placing an anastomosis in a patient may also potentially delay life-prolonging adjuvant therapy if any complications were to arise from it. For all intents and purposes, the most likely solution in these cases is to simply bring up an ileostomy.

Surgical cecostomy has been performed for the relief of large bowel obstruction with varying results. A recent study in 2015 looked at the use of percutaneous, image-guided percutaneous cecostomy. Twenty-seven patients underwent the procedure at a single institution with no reported colonic perforation and one major reported complication of subcutaneous emphysema, pneumomediastinum, and sepsis that occurred 8 days post procedure and was successfully treated with cecostomy exchange, soft-tissue drainage, and intravenous antibiotic therapy [19].

In the case of incurable disease, the goals of palliation should be discussed with the patient prior to operative intervention for the acute obstruction. The goals of palliation should be relief of symptoms caused by the tumor and maintenance of quality of life [20]. As mentioned above, these efforts include resection, internal bypass, creation of a diverting stoma, as well as ablative therapy and endoluminal stent therapy. Considerations for a decompressive gastrostomy tube should also be discussed with the patient as another adjunctive palliative procedure.

Bleeding

Case: *A 75 year-old female with atrial fibrillation on Coumadin presents to the emergency room with complaints of dizziness and blood per rectum that has been ongoing for the past several days since she started taking Coumadin 2 weeks ago. An INR of 4 is noted, and she has an episode of frank bloody diarrhea in the bathroom.*

Hemorrhagic complications from tumors are not uncommon especially in the older population that are often on anticoagulation therapy. This is also the situation when malignancies are discovered. Similar to patients who present with lower gastrointestinal bleeding, determining the stability of the patient is of the utmost importance. Patients who are hemodynamically unstable should undergo the appropriate resuscitative measures prior to consideration for surgery. Laboratory studies to include a complete blood count, type and cross, basic chemistry panel, coagulation studies (INR), and a TEG (if available) should be a part of the initial workup and the appropriate resuscitative products administered to correct any coagulopathies. Once the metabolic derangements and coagulopathies are corrected, and if the patient is stable, then a gentle bowel prep should be pursued with the intent to perform a colonoscopy to identify the source of bleeding. The author would recommend the gastroenterologist to place clips proximal and distal to the tumor for more precise identification on plain film X-rays. This will help with surgical planning. If the source can be adequately located, a formal surgical plan can be formulated in a multidisciplinary fashion. On the other hand, if the patient is unable to remain stable despite these efforts, then the patient should be prepared for an urgent operation.

The goal of an operation in this case is to expeditiously remove the segment or the entire colon as these patients are often unable to tolerate prolonged time under general anesthesia. Operative

approach in these urgent cases are often performed open with the intent to identify any additional metastatic lesions along the solid organs as well as palpating the entire colon to identify any additional lesions that may have not been identified (if the patient was unable to undergo endoscopy prior to surgery). Total colectomy can be performed if there are multiple lesions identified. If the lesion was identified prior to surgery, then a segmental resection is appropriate adhering to the principles of a complete oncologic resection making sure distal and proximal margins are appropriate and high ligation to obtain as many lymph nodes for staging. An anastomosis can be done if the patient is not receiving vasopressor support, is hypoalbuminemic or requiring multiple transfusions. An anastomosis does carry the possibility for a complication, which could further delay adjuvant therapy (if needed). For this reason, an end ileostomy is favorable.

In the case of patients who are deemed too unfit for an operation or have inoperable disease, endoscopic laser therapy has been successful in treating symptoms and providing palliation. Published series have used neodymium: yttrium-aluminum-garnet (Nd:YAG) laser. In a study looking at the treatment of 57 patients, 89% had successful palliation of symptoms with only three major complications giving an overall complication rate of 5.3% [21]. Published results using Nd:YAG laser demonstrate palliation of bleeding and discharge to be better controlled than use of the laser for symptoms of obstruction [22–24]. Multiple treatments are often required over a period of weeks. While laser therapy has also been used in cases of obstruction, it has been far less successful than it has been for bleeding (65% vs. 82%, respectively) [25, 26]. Laser therapy may also be used in conjunction with other palliative measures such as stenting or radiation (for rectal tumors).

Conclusions

The various approaches discussed for obstruction and bleeding colon malignancies represent the broad scope of issues the acute care surgeon may encounter. An organized and well-thought-out preoperative plan is key to the success of the procedure chosen as well as preparing the patient for what may be the beginning of a newly diagnosed cancer. Preoperative resuscitation in an ICU setting, correcting coagulopathies, and metabolic derangements all serve to try and set the patient up for as successful of an operation as possible. In patients with confirmed malignancies, a multidisciplinary approach can help guide the surgeon to choose the appropriate operative plan that would help the patient's quality of life and ultimately their outcome, if the patient's condition allows. And finally, employing the assistance of other surgeons/partners is a tool to consider in difficult situations. If this is not possible, then it is of the utmost importance to ensure that alternate surgical plans be thought of so as to optimize the outcome for the patient.

References

1. Rondell F, Reboldi P, Rulli A, et al. Loop ileostomy versus loop colostomy for fecal diversion after colorectal or coloanal anastomosis: a meta-analysis. Int J Color Dis. 2009;24(5):479–88.
2. Lau P, Chung L, Law W. The role of one-stage surgery in acute left-sided colonic obstruction. Am J Surg. 1995;169:406–9.
3. Lee Y, Law W, Chu K, et al. Emergency surgery for obstructing colorectal cancers: a comparison between right-sided ad left-sided lesions. J Am Coll Surg. 2001;192(6):719–25.
4. Hsu T. Comparison of one-stage resection and anastomosis of acute complete obstruction of left and right colon. Am J Surg. 2005;189(4):384–7.
5. Mege D, Manceau G, Beyer-Berjot L, et al. Surgical management of obstructive right-sided colon cancer at a national level results of a multicenter study of the French Surgical Association in 776 patients. Eur J Surg Oncol. 2018. Pii: S0748-7983(18)31171-5. https://doi.org/10.10106/j.ejso.2018.06.027. [Epub ahead of print].
6. Stephenson BM, Shandall AA, Farouk R, et al. Malignant left-sided bowel obstruction managed by subtotal/total colectomy. Br J Surg. 1990;77:1098–102.
7. Arenas RB, Fichera A, Mhoon D, et al. Incidence and therapeutic implications of synchronous colonic pathology in colorectal adenocarcinoma. Surgery. 1997;122(4):706–9.
8. Kahi CJ, Boland CR, Dominitz JA, et al. Colonoscopy surveillance after colorectal cancer resection: recommendations of the US multi-society task

force on colorectal cancer. Am J Gastroenterol. 2016;111:337–46.
9. Ansaloni L, Andersson RE, Bazzoli F, et al. Guidelines in the management of obstructing cancer of the left colon: consensus conference of the world society of emergency surgery (WSES) and peritoneum and surgery (PnS) society. World J Emerg Surg. 2010;5:29.
10. Tekkis PP, Kindsman R, Thompson MR, et al. The Association of Coloproctology of Great Britain and Ireland study of large bowel obstruction caused by colorectal cancer. Ann Surg. 2004;240(1):76–81.
11. Zorcolo L, Covota L, Carlomagno N, et al. Toward lowering morbidity, mortality, and stoma formation in emergency colorectal surgery: the role of specialization. Dis Colon Rectum. 2003;46(11):1461–7.
12. Archampong D, Borowski D, Wille-Jergensen P, et al. Workload and surgeon's specialty for outcome after colorectal cancer surgery. Cochrane Database Syst Rev. 2012;(3):CD005391.
13. Meyer F, Marusch F, Koch A, et al. Emergency operation in carcinomas of the left colon: value of Hartmann's procedure. Tech Coloproctol. 2004;8(suppl 1):s226–9.
14. Chang GJ, Rodriguez-Bigas MA, Skibber JM, et al. Lymph node evaluation and survival after curative resection of colon resection of colon cancer: a systematic review. J Natl Cancer Inst. 2007;99:433–41.
15. George S, Primrose J, Talbot R, et al. Will Rogers revisited: prospective observational study of survival of 3592 patients with colorectal cancer according to number of nodes examined by pathologists. Br J Cancer. 2006;95:841–7.
16. Karoui M, Roudot-Thoraval F, Mesli F, et al. Primary colectomy in patients with stage IV colon cancer and unresectable distant metastases improves overall survival: results of a multicentric study. Dis Colon Rectum. 2011;54(8):930–8.
17. De Mestier L, Neuzillet C, Pozet A, et al. Is primary tumor resection associated with a longer survival in colon cancer and unresectable synchronous metastases? A 4-year multicenter experience. Eur J Surg Oncol. 2014;40(6):685–91.
18. Alawadi Z, Phatak UR, Hu CY, et al. Comparative effectiveness of primary tumor resection in patients with stage IV colon cancer. Cancer. 2017;123(7):1124–33.
19. Pisano M, Zorcolo L, Merli C, et al. 2017 WSES guidelines on colon and rectal cancer emergencies: obstruction and perforation. World J Emerg Surg. 2018;13:36. https://doi.org/10.1186/s13017-018-0192-3. eCollection 2018. Review.
20. Tewari SO, Getrajdman GI, Petre EN, et al. Safety and efficacy of percutaneous cecostomy/colostomy for treatment of large bowel obstruction in adults with cancer. J Vasc Interv Radiol. 2015;26(2):182–8.
21. Chang GJ, Kaiser AM, Mills S, Standards Practice C, Task Force of the American Society of Colon and Rectal Surgeons, et al. Practice parameters for the management of colon cancer. Dis Colon Rectum. 2012;55(8):831–43.
22. Courtney ED, Raja A, Leicester RJ. Eight year experience of high-powered endoscopic diode laser therapy for palliation of colorectal carcinoma. Dis Colon Rectum. 2005;48(4):845–50.
23. Brunetaud JM, Manoury V, Ducrotte P, et al. Palliative treatment of rectosigmoid carcinoma by laser endoscopic photoablation. Gastroenterology. 1987;92:663–8.
24. Loizou LA, Grigg D, Boulos PB, et al. Endoscopic Nd:YAG laser treatment of rectosigmoid cancer. Gut. 1990;31:812–6.
25. Mathus-Vliegen EM, Tytgat CN. Laser ablation and palliation in colorectal malignancy. Results of a multicenter inquiry. Gastrointest Endosc. 1986;32:393–6.
26. Gevers AM, Macken E, Hiele M, et al. Endoscopic laser therapy for palliation of patients with distal colorectal carcinoma: analysis of factors influencing long-term outcome. Gastrointest Endosc. 2000;51:580–5.

11 Endolumenal Therapies for Bleeding and Obstructing Colorectal Malignancy

Kristen T. Crowell and Eric M. Pauli

Introduction

Screening for colorectal cancer in the Unites States increased from 39% in 2000 to 58% in 2013 [1]. While this has resulted in a decrease in the overall incidence of colorectal cancer, the rate of detection of advance stage malignancies has not declined [1]. The overall 5-year survival rate decreases from 90% to 71% to 14% as disease moves from localized to regional involvement to distant metastasis. Nearly 40% of patients with resectable rectal cancer recur, and the majority of these patients are not candidates for repeat surgical treatment with a curative intent [2].

Most colorectal cancer diagnoses are made after a patient becomes symptomatic [3]. Symptoms include rectal bleeding, anemia, weight loss, abdominal pain, and change in bowel habits [4]. Fortunately, life-threatening bleeding and high-grade/complete obstructions are less common initial presentation symptoms. Treatment of symptomatic colon cancers should be based upon disease stage, expected survival, symptoms, and patient preference, but the gold standard therapy for symptomatic colorectal cancer remains surgical resection with a curative intent. In all of these patient populations (advanced stage at time of diagnosis, recurrent disease after intended curative therapy, severe symptoms at the time of diagnosis necessitating emergency intervention), there is a clear role for endoscopic therapy.

Bleeding Colorectal Cancer

Bleeding per rectum is a common symptom that leads to evaluation with a diagnostic colonoscopy [3], and if a bleeding colorectal malignancy is identified, surgical resection should be offered when feasible. In patients who are not surgical candidates due to advanced disease, to an increased risk to undergo surgical resection, or who opt to defer surgical treatment, palliative options are available. Chemotherapy and radiation therapy both can alleviate bleeding symptoms but take weeks to months to achieve peak effect. For bleeding requiring transfusions, necessitating hospitalization, or causing hemodynamic instability, more urgent therapy is indicated. Palliative surgery for bleeding requires a formal surgical resection of the involved segment of the colon and cannot be treated by a simpler diverting ostomy. Endoscopic approaches with laser ablation or argon plasma coagulation (APC) have the advantage in that they are low morbidity, can control bleeding quickly, and can be repeated as needed. They may be used alone or in conjunction with chemo- or radiation therapy [5].

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Nd:YAG Laser

Endoscopic laser therapy using the neodymium-doped yttrium aluminum garnet (Nd:YAG) laser can successfully provide symptom relief [5–10] and improve quality of life for palliation [10] of bleeding tumors in the colon and the rectum, even below the peritoneal reflection [7]. The Nd:YAG laser was initially described for palliation of unresectable esophageal or gastric cancer and expanded to palliate inoperable colorectal cancer in the 1980s. The Nd:YAG laser is composed of a specific fiber with a quartz tip and lumen for cooling gas which is placed through the accessory channel on the colonoscope. At lower power settings, the energy of the laser leads to hemostasis by coagulative necrosis [5].

Palliation of the bleeding usually requires multiple treatments, and laser therapy can be repeated every few days until coagulation is obtained. The initial efficacy ranges from 70% to 100%, and most patients require 2–5 laser sessions to achieve hemorrhage control [5]. Gevers et al. reported 76 patients who underwent laser therapy for palliation of bleeding. The initial success rate was 92%, and most patients (83%) remained symptom free until death [11]. Complications of laser therapy range from 2% to 15% and are usually minor. Major complications are rare but can include perforation (4–6%), fistula (3%), abscess (2%), and bleeding (1–4%) [5, 9, 11].

With a low complication rate and high success rate, laser therapy became the main endoscopic therapy for palliation of bleeding colorectal cancer from the 1980s to the early 2000s [12]. Despite its success, the need for dedicated equipment specific for Nd:YAG laser therapy caused it to fall out of favor in place of the more widely available and more widely applicable argon plasma coagulation.

Argon Plasma Coagulation

Argon plasma coagulation (APC) is a type of monopolar radiofrequency electrosurgery that uses ionized argon gas to fulgurate mucosal vessels and neoplastic tissue resulting in surface coagulation. APC only penetrates 2–3 mm of tissue which limits the ability to treat bulky malignant tissue. APC may be used as a temporizing measure to control bleeding while awaiting another therapy, such as radiation. Similar to Nd:YAG laser therapy, the delivery device for APC is a catheter that passes through the instrument channel of the colonoscope. A variety of tips are available on these accessories that permit easier direction of the therapy (Fig. 11.1).

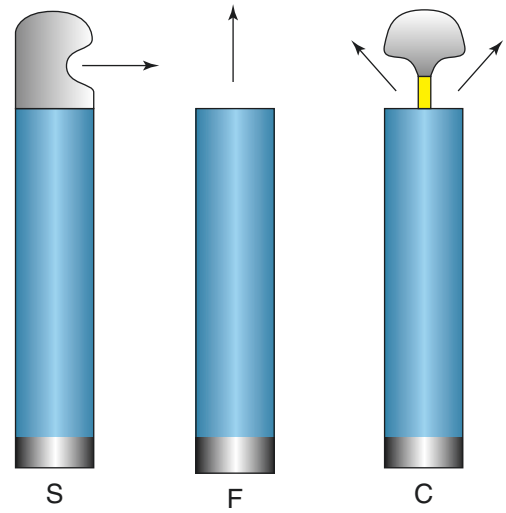

Fig. 11.1 Distal tip options for argon plasma coagulation probes; side fire (S), forward (F), and circumferential (C)

The superficial depth of penetration of APC is sufficient to stop bleeding in a variety of clinical applications, and it is widely available in most endoscopy and operative suites. Perforations related to local tissue necrosis are uncommon, but the higher flow rate of argon gas can result in perforation of the more proximal bowel, which may already be dilated due to tumor-related obstruction. Despite limited data on its efficacy, APC has replaced Nd:YAG laser therapy at many centers as the mainstay of treatment for bleeding colorectal malignancies [5].

Obstructing Colorectal Cancer

Colorectal cancer is the most common cause of a large bowel obstruction, accounting for 80%

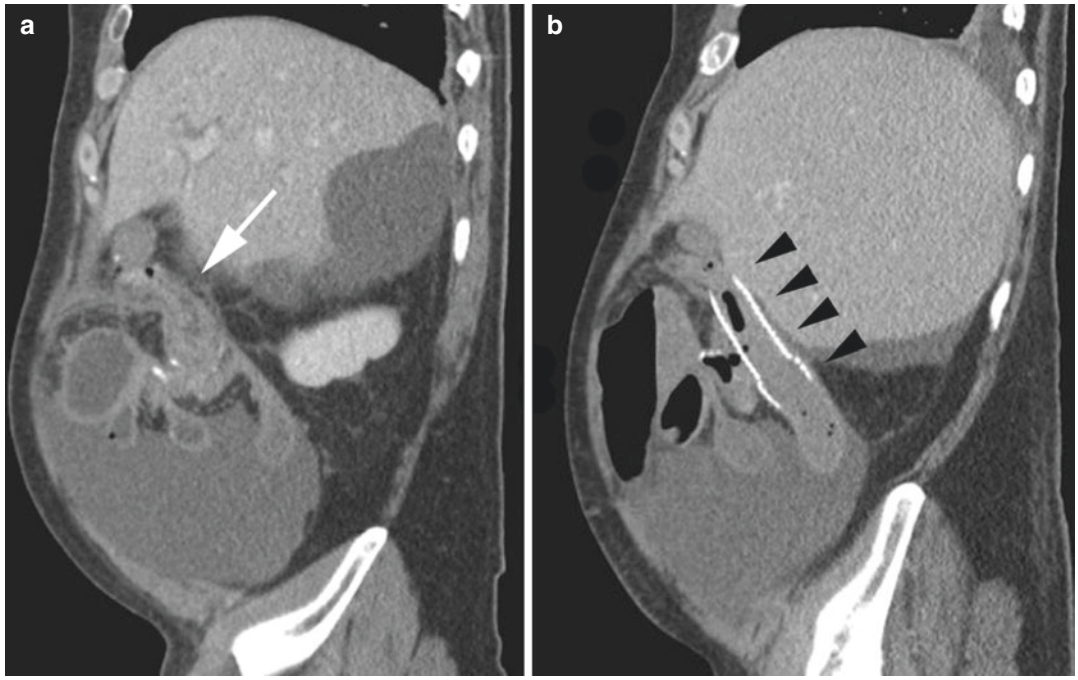

Fig. 11.2 Sagittal CT scan images of an obstructing hepatic flexure cancer (arrow) before (**a**) and after (**b**) endoscopic stent placement (arrowheads)

of obstructions. In patients with colorectal cancer, 10–25% of patients present with obstructive symptoms including periumbilical or hypogastric pain and abdominal distention [12]. The majority of malignant obstructions are localized to the left colon, and the rectosigmoid is the most common location [13]. Patients with severe abdominal pain or peritoneal signs should be evaluated for perforation or ischemic bowel by a surgical consultation. Initial imaging with computed tomography (CT) can assist in locating the obstructing lesion (Fig. 11.2a). If contrast enema is used to determine luminal patency, water-soluble contrast is preferred to avoid barium impaction at the site of obstruction [14].

Emergent or urgent surgical options include a proximal diverting colostomy or surgical resection with or without a stoma; however, emergent surgical intervention in this population is associated with an increased risk of morbidity and mortality and a higher risk of permanent stoma compared to elective surgery [15–20]. Endoscopic alternative approaches to malignant colorectal obstructions include placement of self-expandable metal stent (SEMS), tumor debulking, or placement of a decompressive tube. Endoscopic management should be offered in the absence of peritoneal signs or suspicion of perforation, as surgery is indicated in these circumstances and air insufflation could increase the risk of perforation of the already distended proximal bowel [21]. A collaborative approach between the surgeon and endoscopist results in optimal patient care.

Endoscopic Tumor Debulking

The Nd:YAG laser at higher powers than described above for tissue coagulation can vaporize the malignant tissue to debulk intraluminal tumor. This requires multiple treatments with repeat endoscopic therapy several times a week until the obstruction is relieved. Typically maintenance treatment is continued after luminal patency is achieved.

Gevers et al. described 117 patients who underwent Nd:YAG laser treatment for obstructing rectal

cancer, and the initial success rate was 88.9% (104 of 117 patients) requiring a 2–4 consecutive treatments. Long-term success was achieved in 57% of patients, while 25% of patients eventually required a palliative colostomy [11]. Brunetaud et al. described 272 patients with obstructing rectosigmoid cancer treated with laser therapy and reported an initial success rate of 85% and a complication rate of 2% [22]. Success rate was lower in circumferential tumors or those invading surrounding tissue [7, 11]. Laser therapy should only be used as a palliative measure for patients unwilling or unfit to undergo surgery or stent placement [14].

The efficacy of APC for tumor ablation has only been described in small case series and can be used in palliative management [23, 24]. It is likely less effective than Nd:YAG laser therapy due to the very superficial (2–3 mm) depth of penetration of the APC tissue effect. As noted above, constant attention to evacuation of the argon gas being instilled is mandatory in the setting of proximal dilated colon as perforations related to intraluminal argon instillation have been reported.

Endoscopic Colon Decompression

Endoscopically placed tubes have been described for decompression, but due to the small caliber of the tubing, colonic gas is decompressed better than fecal material. Decompressive tubes can be used in conjunction with or without lavage to decompress and prep the colon as a bridge to surgery. Transanal tubes are not routinely used and are limited by tube dysfunction, patient discomfort, nursing care issues, and tube expulsion [14].

Endolumenal Colonic Wall Stenting

Colonic stenting for obstructing colon cancer was first described in the 1990s and is now commonly used as a bridge to surgery or as a palliative alternative to colostomy [19]. The technique of stenting a malignant colorectal lesion is similar to placing luminal stents in other parts of the GI tract. We prefer to perform colonoscopy under low-flow carbon dioxide insufflation to reduce the amount of gas that will migrate to the more proximal dilated colon.

The colonoscope is advanced to the obstructing lesion (Fig. 11.3a). Due to the high-grade nature of these lesions and the diameter of the colonoscope, it is uncommon to be able to traverse the lesion with the colonoscope, and fluoroscopy is used to guide the remainder of the procedure (Fig. 11.4a). An injection catheter (typically an ERCP sphincterotome or catheter) is advanced into the narrowed lumen at the level of the mass (Fig. 11.3b), and contrast is injected to outline the location of the proximal bowel as well as define the length of the obstructing lesion (Fig. 11.4b). A guidewire is passed endoscopically across the obstructing mass (Fig. 11.3c), and its position is confirmed with fluoroscopy (Fig. 11.4c). The stents are bare metal (i.e., uncovered) self-expanding metallic stents (SEMS) that are thread over this guidewire and deployed through the working channel of a therapeutic endoscope (Figs. 11.3d and 11.4d). Stent should be sized by adding 4–6 cm on to the length of obstructing lesion to ensure that the stent overlaps the lesion both proximally and distally (Figs. 11.3e and 11.4e). After deployed, stent placement and luminal patency can then be evaluated endoscopically (Fig. 11.3f) and fluoroscopically (Fig. 11.4f) [25]. We generally do not try and traverse the stented tumor with the endoscope as this risks perforation and stent dislodgement. Following deployment, the stent may continue to have narrowing and an hourglass shape in the vicinity of the tumor (Fig. 11.5). It can take 48–72 hours for the stent to achieve maximum diameter as the radial forces of the stent work against the tumor (Fig. 11.2b).

Dilation of the tumor prior to or after stent placement should be avoided as dilation increases the risk of perforation [14, 26]. Colonic stents are most advantageous for obstructing left-sided colon cancer. While SEMS can be placed in the rectum, they should not be placed within 3 cm of the anal canal to avoid intractable anal pain, tenesmus, and incontinence [13, 25].

Endoscopic placement of a SEMS for unresectable stage IV obstructing colorectal cancer can alleviate obstructive symptoms. Colonic

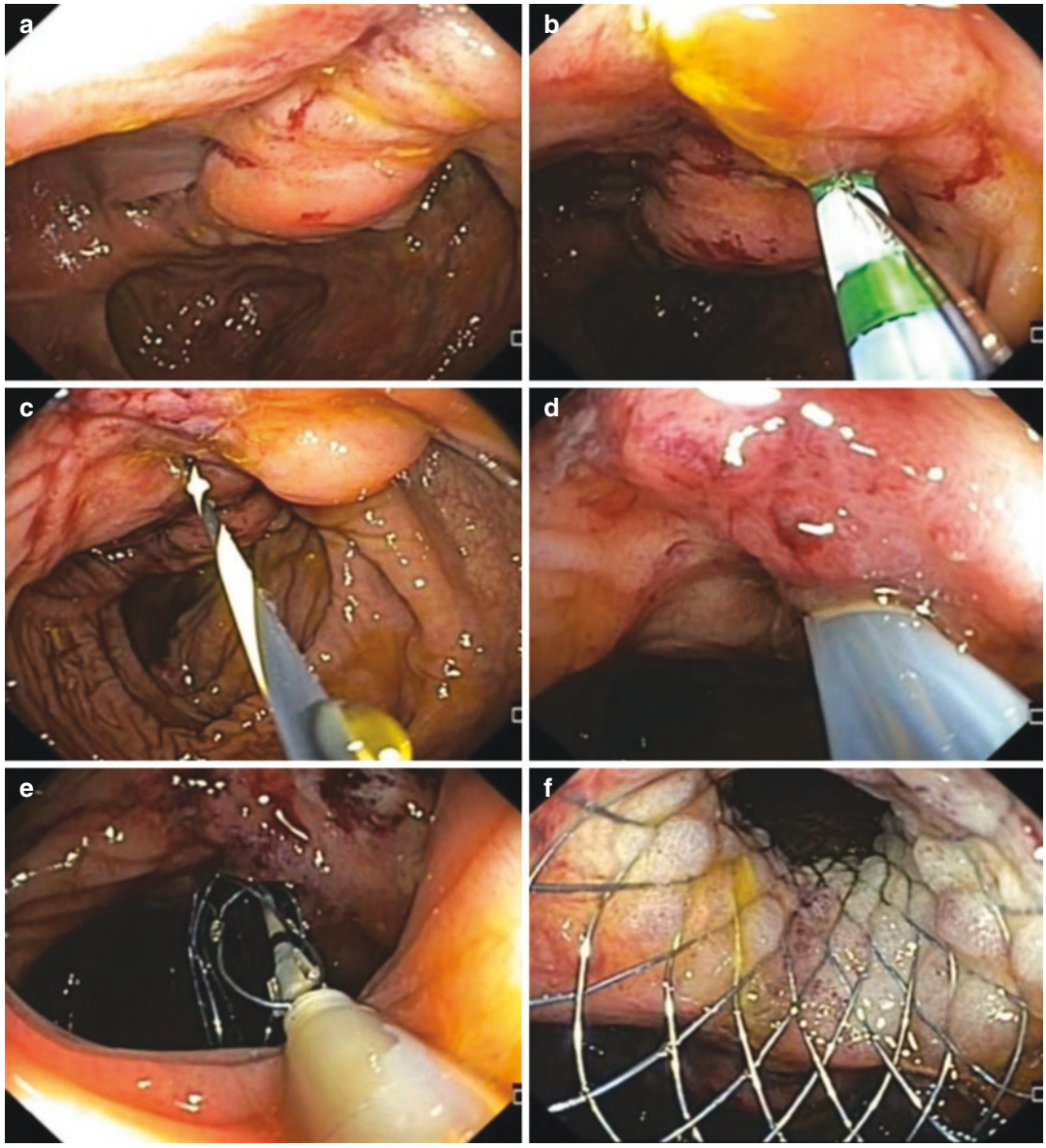

Fig. 11.3 Endoscopic stent placement for a recurrent colon cancer at an ileocolic anastomotic site: (**a**) endoscopic view of the obstructing lesion, (**b**) sphincterotome used to identify the narrowed lumen, (**c**) guidewire access across the lesion, (**d**) stent delivery system passed over the wire, (**e**) distal stent margin ends just distal to the lesion, (**f**) view through the stent of the now partially relieved obstruction

stents avoid creation of a colostomy and prevent a potential delay to chemotherapy by avoiding the postoperative complications associated with surgical intervention [25]. SEMS placement is a safe and less invasive palliative option for unresectable obstructing colorectal cancer, and in the appropriately selected patient, it can decrease length of stay, avoid a colostomy, and possibly allow earlier chemotherapy administration [27].

In a prospective randomized trial, Fiori et al. described 22 patients with chronic subacute obstructing symptoms and compared SEMS to proximal diverting colostomy. The initial success rate was 100% of SEMS, and colonic stenting

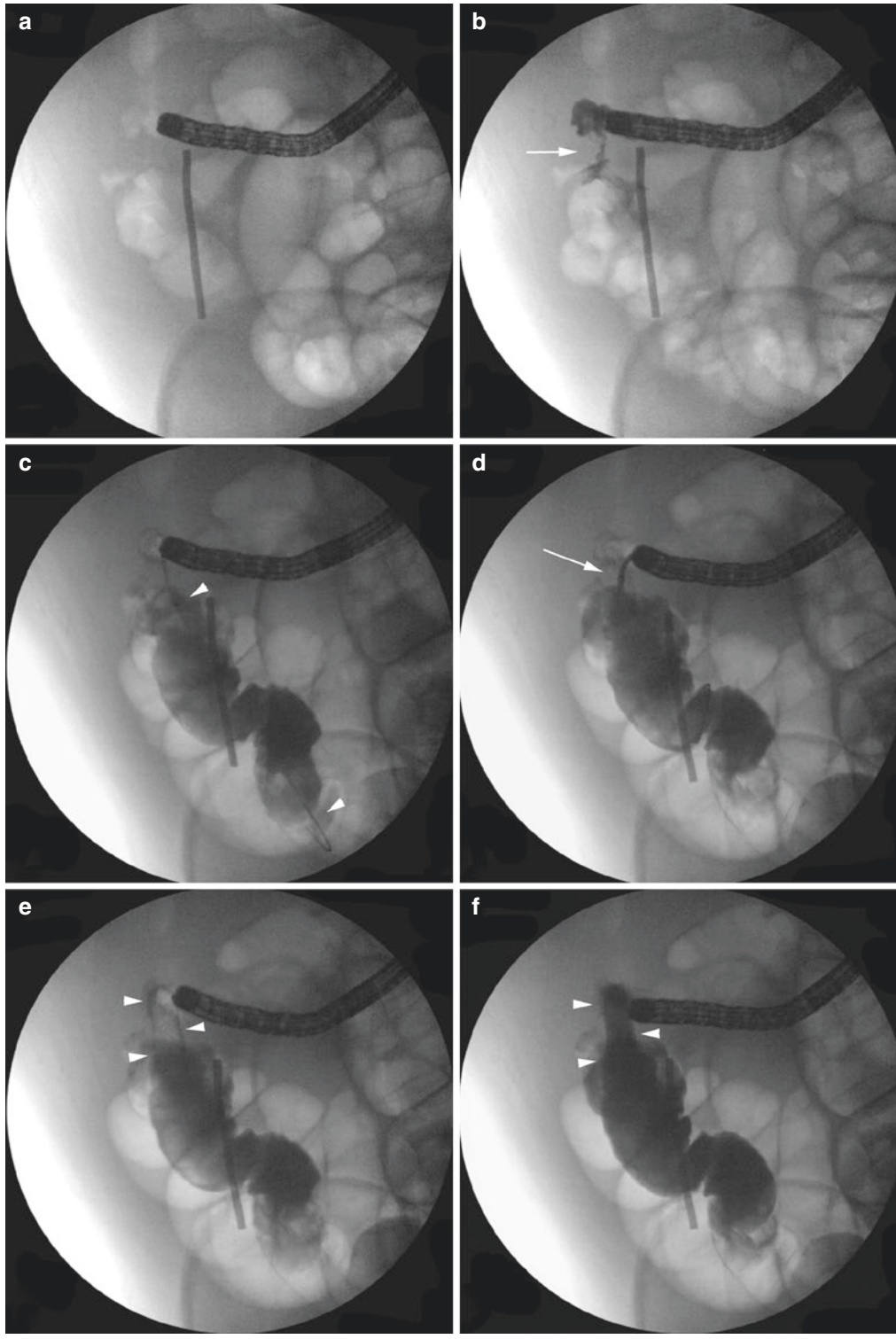

Fig. 11.4 Fluoroscopic images during stent placement for a hepatic flexure colon cancer: (**a**) endoscope approaches the area of obstruction, (**b**) contrast injection demonstrates the string sign of the lesion (arrow), (**c**) guidewire traverses the lesion into the proximal colon (arrowheads), (**d**) stent delivery system passed over the wire, (**e**) deployed stent (arrowheads) permits, (**f**) contrast to pass through the stent (arrowheads) suggesting alleviation of the obstruction

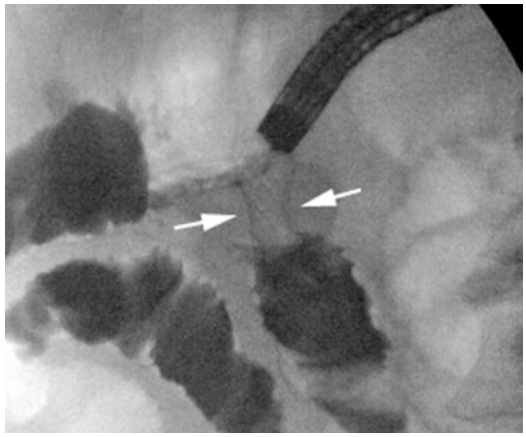

Fig. 11.5 Fluoroscopic image following stent placement for a recurrent colon cancer at an ileocolic anastomotic site demonstrates an hourglass shape to the stent (arrows) where full luminal diameter has not been immediately achieved

leads to a decreased length of stay and earlier oral intake. Median survival was 297 days, and during this time three patients has recurrent obstructions – two due to stool within a stent and one from tumor ingrowth, requiring laser ablation [28]. Lee et al. reported 88 consecutive patients with unresectable colorectal cancer, of which 36 underwent SEMS and 52 had surgical resection either with a primary anastomosis or Hartmann's. The initial success rate of SEMS was 97%, and during the study, 13.9% developed recurrent obstruction with tumor ingrowth and underwent a diverting colostomy. Median overall survival in SEMS patients was 7.6 months compared to 15.9 months for patients who underwent surgery [29]. The decreased survival in this study was suspected to be due to a selection bias as mortality was similar in other studies [13].

Colonic stenting as a bridge to surgery allows for colonic decompression, correction of electrolyte or metabolic disturbances, and colon preparation creating a setting more similar to elective surgery. Numerous studies have been published on this topic; however, results from different series and systemic reviews are conflicting. Initial studies confirm a high success rate of endoscopic and symptomatic relief (78% stent vs 98% surgery). A Cochran review in 2011 confirmed that stent placement is safe, with low rates of perforation (5.9%), stent migration (2.13%), and recurrent obstruction (2.13%). Overall complication rate was no different in SEMS compared to emergency surgery (39% vs 45.7%) [13].

A recent meta-analysis by Arezzo et al. evaluated the eight randomized controlled trials comparing SEMS as a bridge to surgery (SBTS) to emergent surgery in left-sided obstructing colorectal cancer. They reported lower short-term morbidity (34% vs 51%) and rate of permanent stomas (22% vs 35%) with SBTS vs emergent surgery [18]. Mortality was similar in SBTS (9.6%) compared to surgery alone (9.8%).

There have been concerns that SEMS increase the rate of perforation or microscopic perforation and can lead to worsening oncologic results. Verstockt et al. prospectively evaluated long-term outcomes of obstructing but potentially curable malignant large bowel obstruction and found no difference in overall survival at 10 years using SBTS (41%) compared to national cancer registry survival (34%), and similar survival was also seen when compared by stage of cancer [30].

Conclusion

Colorectal cancer that presents as obstruction or with bleeding should undergo intervention. If resection is not indicated for bleeding colorectal cancers, endolumenal laser ablation is a safe and effective method to provide hemostasis. The application of endolumenal treatments for obstructing colorectal cancer is based upon the potential for curative surgical resection. SEMS provide excellent success rate to alleviate obstructions in left-sided colorectal cancer for palliation and can avoid a colostomy. When a curative approach is taken for obstructing colorectal cancer, SEMS can be used as a bridge to alleviate the obstruction and prepare the patient for surgical resection resulting in lower morbidity and permanent stoma rates compared to emergency surgery.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68(1):7–30.
2. Van Cutsem E, Oliveira J, Group EGW. Primary colon cancer: ESMO clinical recommendations for diagnosis, adjuvant treatment and follow-up. Ann Oncol. 2009;20(Suppl 4):49–50.

3. Moreno CC, Mittal PK, Sullivan PS, Rutherford R, Staley CA, Cardona K, et al. Colorectal cancer initial diagnosis: screening colonoscopy, diagnostic colonoscopy, or emergent surgery, and tumor stage and size at initial presentation. Clin Colorectal Cancer. 2016;15(1):67–73.
4. Hamilton W, Round A, Sharp D, Peters TJ. Clinical features of colorectal cancer before diagnosis: a population-based case-control study. Br J Cancer. 2005;93(4):399–405.
5. Kimmey MB. Endoscopic methods (other than stents) for palliation of rectal carcinoma. J Gastrointest Surg. 2004;8(3):270–3.
6. Courtney ED, Raja A, Leicester RJ. Eight years experience of high-powered endoscopic diode laser therapy for palliation of colorectal carcinoma. Dis Colon Rectum. 2005;48(4):845–50.
7. Loizou LA, Grigg D, Boulos PB, Bown SG. Endoscopic Nd:YAG laser treatment of rectosigmoid cancer. Gut. 1990;31(7):812–6.
8. Eckhauser ML. The neodymium-YAG laser and gastrointestinal malignancy. Arch Surg. 1990;125(9):1152–4.
9. Schulze S, Lyng KM. Palliation of rectosigmoid neoplasms with Nd:YAG laser treatment. Dis Colon Rectum. 1994;37(9):882–4.
10. McGowan I, Barr H, Krasner N. Palliative laser therapy for inoperable rectal cancer--does it work? A prospective study of quality of life. Cancer. 1989;63(5):967–9.
11. Gevers AM, Macken E, Hiele M, Rutgeerts P. Endoscopic laser therapy for palliation of patients with distal colorectal carcinoma: analysis of factors influencing long-term outcome. Gastrointest Endosc. 2000;51(5):580–5.
12. Ronnekleiv-Kelly SM, Kennedy GD. Management of stage IV rectal cancer: palliative options. World J Gastroenterol. 2011;17(7):835–47.
13. Sagar J. Colorectal stents for the management of malignant colonic obstructions. Cochrane Database Syst Rev. 2011;(11):CD007378.
14. Committee ASoP, Harrison ME, Anderson MA, Appalaneni V, Banerjee S, Ben-Menachem T, et al. The role of endoscopy in the management of patients with known and suspected colonic obstruction and pseudo-obstruction. Gastrointest Endosc. 2010;71(4):669–79.
15. Frago R, Ramirez E, Millan M, Kreisler E, del Valle E, Biondo S. Current management of acute malignant large bowel obstruction: a systematic review. Am J Surg. 2014;207(1):127–38.
16. van den Berg MW, Sloothaak DA, Dijkgraaf MG, van der Zaag ES, Bemelman WA, Tanis PJ, et al. Bridge-to-surgery stent placement versus emergency surgery for acute malignant colonic obstruction. Br J Surg. 2014;101(7):867–73.
17. Arezzo A, Balague C, Targarona E, Borghi F, Giraudo G, Ghezzo L, et al. Colonic stenting as a bridge to surgery versus emergency surgery for malignant colonic obstruction: results of a multicentre randomised controlled trial (ESCO trial). Surg Endosc. 2017;31(8):3297–305.
18. Arezzo A, Passera R, Lo Secco G, Verra M, Bonino MA, Targarona E, et al. Stent as bridge to surgery for left-sided malignant colonic obstruction reduces adverse events and stoma rate compared with emergency surgery: results of a systematic review and meta-analysis of randomized controlled trials. Gastrointest Endosc. 2017;86(3):416–26.
19. Phang PT, MacFarlane JK, Taylor RH, Cheifetz R, Davis N, Hay J, et al. Effect of emergent presentation on outcome from rectal cancer management. Am J Surg. 2003;185(5):450–4.
20. Zorcolo L, Covotta L, Carlomagno N, Bartolo DC. Safety of primary anastomosis in emergency colo-rectal surgery. Color Dis. 2003;5(3):262–9.
21. Davila RE, Rajan E, Adler D, Hirota WK, Jacobson BC, Leighton JA, et al. ASGE guideline: the role of endoscopy in the diagnosis, staging, and management of colorectal cancer. Gastrointest Endosc. 2005;61(1):1–7.
22. Brunetaud JM, Maunoury V, Cochelard D. Lasers in rectosigmoid tumors. Semin Surg Oncol. 1995;11(4):319–27.
23. Solecki R, Zajac A, Richter P, Szura M. Bifocal esophageal and rectal cancer palliatively treated with argon plasma coagulation. Surg Endosc. 2004;18(2):346.
24. Baumhoer D, Armbrust T, Ramadori G. Nonsurgical treatment of the primary tumor in four consecutive cases of metastasized colorectal carcinoma. Endoscopy. 2005;37(12):1232–6.
25. Hunerbein M, Krause M, Moesta KT, Rau B, Schlag PM. Palliation of malignant rectal obstruction with self-expanding metal stents. Surgery. 2005;137(1):42–7.
26. Bonin EA, Baron TH. Update on the indications and use of colonic stents. Curr Gastroenterol Rep. 2010;12(5):374–82.
27. Zhao XD, Cai BB, Cao RS, Shi RH. Palliative treatment for incurable malignant colorectal obstructions: a meta-analysis. World J Gastroenterol. 2013;19(33):5565–74.
28. Fiori E, Lamazza A, De Cesare A, Bononi M, Volpino P, Schillaci A, et al. Palliative management of malignant rectosigmoidal obstruction. Colostomy vs. endoscopic stenting. A randomized prospective trial. Anticancer Res. 2004;24(1):265–8.
29. Lee WS, Baek JH, Kang JM, Choi S, Kwon KA. The outcome after stent placement or surgery as the initial treatment for obstructive primary tumor in patients with stage IV colon cancer. Am J Surg. 2012;203(6):715–9.
30. Verstockt B, Van Driessche A, De Man M, van der Spek P, Hendrickx K, Casneuf V, et al. Ten-year survival after endoscopic stent placement as a bridge to surgery in obstructing colon cancer. Gastrointest Endosc. 2018;87(3):705–13 e2.

Part IV

Complications of Inflammatory Bowel Disease

12 Complications of Inflammatory Bowel Disease: Initial Medical Management and Role of Endoscopy

Nicholas R. Crews and Matthew E. Bohm

Introduction

Ulcerative colitis (UC) and Crohn's disease (CD) are the two major forms of inflammatory bowel disease (IBD). While UC is limited to inflammation of the colonic mucosal layers, CD can involve the entire gastrointestinal tract from mouth to anus with transmural involvement. In CD, the most common sites of involvement include the ileum alone (50%), ileum and colon (30%), or isolated colonic disease (20%). Perianal disease occurs in approximately 25% of patients with CD, with 45% of those patients having perianal involvement at initial presentation. The typical presentation of UC is diarrhea, bloody stools, urgency, and tenesmus. The most common CD symptoms include abdominal pain, diarrhea which is usually non-bloody, and unintentional weight loss. A severe colitis flare requiring hospitalization occurs in 18–25% of patients with UC typically after failing outpatient therapy [1, 2]. Patients with CD are typically hospitalized as a result of penetrating complications of the disease (intra-abdominal abscess, fistula, or perianal abscess), intestinal obstruction, or severe diarrhea with concomitant malnutrition. This chapter will focus on the inpatient evaluation and management of IBD complications.

Severe/Fulminant Ulcerative Colitis

Severe UC is defined by the presence of ≥6 stools daily with bleeding and abdominal pain with systemic toxicity evident by tachycardia (pulse ≥90 beats/min), fever (temperature ≥37.5 °C), anemia (hemoglobin <10.5 g/dL), and elevated inflammatory markers [3]. Severe CD colitis has similar clinical manifestations. Fulminant colitis is characterized as ≥10 bowel habits daily, continuous bleeding with or without a transfusion requirement, and severe toxicity with an increased risk (1–2%) of developing toxic megacolon [4]. Initial evaluation should include comprehensive laboratory testing including C-reactive protein (CRP), stool testing with culture and *C. difficile* PCR for toxin, and abdominal imaging. Abdominal imaging can consist of an abdominal X-ray or CT scan if indicated based on examination. Colonic dilation >6 cm or cecum dilation >9 cm is high risk for toxic megacolon and perforation. Severe IBD activity is associated with hypercoagulability which increases the risk for venous thromboembolic events (VTE) approximately threefold

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compared to hospitalized patients without IBD [5, 6]. Thus, administration of thrombo-prophylaxis to patients hospitalized with severe IBD flares without severe gastrointestinal bleeding is recommended [7].

Endoscopic evaluation is the standard diagnostic modality which allows assessment of severity and biopsies for histopathologic examination and cytomegalovirus testing. CMV inclusions are commonly identified in colonic tissue in 16–36% of patients with IBD [8–10]. While the pathogenicity of CMV remains poorly understood, the presence of CMV with ≥5 inclusion bodies/high-power field like signifies clinically significant infection and should be treated with ganciclovir in patients with severe colitis, particularly if the patients are steroid-refractory or chronically immunosuppressed [11]. *C. difficile* infection has been associated with 7–10% of IBD flares in two retrospective studies [12, 13]. Presence of both IBD and *C. difficile* increases colectomy risk 6.6-fold compared to patients with only *C. difficile* colitis [14]. *C. difficile* colitis should be treated with oral vancomycin 125 mg four times per day whether the presentation is non-severe or severe (white blood cell count of ≥15,000 cells/mL or a serum creatinine level >1.5 mg/dL) [15]. Patients with fulminant *C. difficile* with colonic dilation or an ileus should be treated with high-dose oral vancomycin 500 mg four times per day, intravenous metronidazole 500 mg IV every 8 hours, and vancomycin enemas 500 mg in 100 ml of saline every 6 hours particularly if ileus is present [15]. Patients who fail to respond to this therapy should undergo fecal microbiota transplant.

Corticosteroids have remained the backbone of medical therapy to induce remission of active IBD since initial studies demonstrated efficacy in the 1950s–1960s [16, 17]. Intravenous methylprednisolone 40–60 mg total daily dose (or equivalent) is recommended as first-line therapy for severe colitis requiring hospitalization. Steroid refractoriness is defined by minimal improvement in active disease by clinical and/or laboratory parameters after 3–5 days. A 2007 systematic review of 23 studies noted steroid therapy failure requiring colectomy in 27% of 1991 patients with severe UC colitis [18]. Prior to colectomy, rescue medical therapy is recommended with cyclosporine or infliximab for severe UC colitis [3]. A 1994 study demonstrated cyclosporine was efficacious for severe steroid-refractory UC; further studies showed 2 mg/kg/day to be an ideal dose [19–21]. Cyclosporine induces remission in 64–90% of cases, becoming a short-term bridge therapy, while co-administered slow-acting immunomodulators (azathioprine/6-MP) become effective [22–24]. Infliximab, an antitumor necrosis factor-α (TNF-α) agent, has been shown to be efficacious for UC and CD in multiple placebo-controlled trials, including ACT 1 and 2, and specifically effective in studies enrolling patients with moderate/severe steroid-refractory UC [25–28]. Recent trials including CONSTRUCT found no significant difference in clinical efficacy of cyclosporine compared to infliximab [29–31]. While initial response rates to rescue medical therapy are favorable, durable remission rates at 1 year are 30% with subsequent colectomy rates of 30–42% at 1 year [31, 32]. Response of rescue medical therapy should be decided after 5–7 days of therapy, and surgical intervention should be pursued if medical therapy has failed [20, 21, 33].

Intestinal Obstruction in CD

Fibro-stenotic CD phenotype is reported to be present in 10% of patients at initial CD diagnosis, while fibro-stenotic disease complications occur in 20–30% of CD patients overall [34]. Obstruction is the main indication for major abdominal surgery for CD in 24–40% of patients [35]. CD strictures result from intestinal fibrosis, which can occur at any time during the disease course and involve any intestinal segment, including the upper gastrointestinal tract. Fibrostenotic disease can cause intestinal obstructive symptoms of nausea and vomiting, abdominal distension, bloating, early satiety, and small-caliber stools or even paucity of stooling.

Two types of strictures in CD are identified: de novo and anastomotic. The most common sites of de novo strictures are the terminal ileum and the ileo-colonic region. Postoperative CD recurrence at the anastomosis occurs commonly after

intestinal resection, particularly in patients with an ileo-colonic anastomosis. Strictures may be further subdivided into inflammatory, fibrotic, and mixed types. Differentiating the composition of the strictures, specifically the relative proportions of inflammation and fibrosis, aids treatment decisions. This is accomplished using clinical history, imaging, and inflammatory markers such as fecal calprotectin and C-reactive protein (CRP). Endoscopy with biopsies are unable to measure the amount of fibrosis existing in the intestinal wall, as inflammation and fibrosis in CD are transmural. Cross-sectional imaging is the best diagnostic study for evaluating patients presenting with obstructive symptoms. Three imaging techniques have high accuracy for evaluation of strictures affecting the small bowel or the colon: for CT enterography (CTE), sensitivity is 89% and specificity 99%; for magnetic resonance enterography (MRE), sensitivity is 89% and specificity 94%; and for US, sensitivity is 79% and specificity 92% [36]. CTE and MRE are most commonly employed based on the center's expertise, but kidney dysfunction can restrict the use of these contrasted studies.

A multidisciplinary approach is necessary for management which should include acute care surgeons, colorectal surgeons, gastroenterologists, radiologists, pathologists, and dietitians. Initial management includes bowel rest, intravenous fluids with electrolyte replacement, and nasogastric decompression tube if the patient is vomiting or has significant abdominal distension. Corticosteroids are used for patients with strictures that have predominantly active inflammation, whereas predominantly fibrotic strictures are best managed by endoscopic or surgical approaches. Endoscopic balloon dilation (EBD) therapy can be pursued for short (<5 cm), non-complex, non-angulated strictures that are within endoscopic reach. Numerous case series have shown the short-term efficacy of EBD to be 70–87% [37]. A 2017 systematic review including 1463 patients demonstrated a clinical efficacy of 81% with a 2.8% complication rate, although 43% of patients required surgical resection during the 24-month follow-up period [38]. The efficacy rates stratified by location (small bowel vs. colon) are comparable, though EBD may be more effective for secondary compared to primary strictures [39]. The target dilation caliber is 16–20 mm. Dilation to at least 16–18 mm has been reported to be associated with less frequent maintenance dilations [40]. Endoscopic stricturotomy with needle knife has been shown to be effective at centers with technical expertise [41]. Strictures that are long, angulated, or associated with concurrent fistula and/or abscess should be considered for strictureplasty or surgical resection. Additionally, the presence of multiple strictures has been found to be a predictor for EBD failure and requirement of surgical intervention [42]. Ultimately, surgical intervention is required in up to 66% of patients with stricturing disease [43]. Indications and contraindication for strictureplasty are presented in Table 12.1 [44]. Early complications occur in up to 13% of patients, while late complications can occur in 26% of patients. A suggested algorithm is presented in Fig. 12.1 describing which patients should

Table 12.1 Indications and contraindications for strictureplasty

Indications
1. Fibrotic strictures within diffuse involvement of the small bowel
2. Previous extensive (>100 cm) small bowel resections
3. Short bowel syndrome
4. Recurrent strictures within 12 months of previous surgery
5. Strictures at previous anastomotic sites, particularly ileorectal or ileo-colonic
6. Strictures without phlegmon or septic fistula
7. Duodenal strictures, particularly in the retroperitoneal segment
Contraindications
1. Perforation of the small bowel, with or without peritonitis
2. Preoperative malnutrition (serum albumin <2.0 g/dL)
3. Fistula or phlegmonous inflammation at intended strictureplasty site
4. Bleeding from planned strictureplasty site
5. Suspicion for carcinoma
6. Likelihood of tension on closure of strictureplasty
7. Intended strictureplasty site next to segment requiring resection

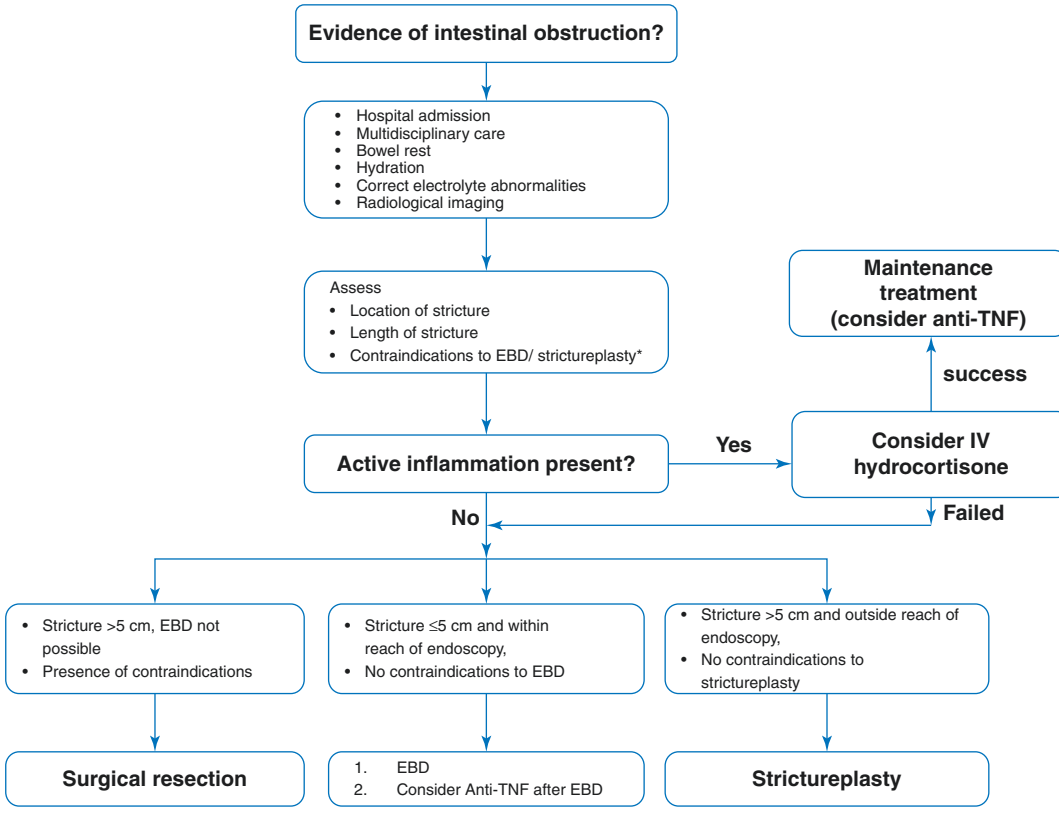

Fig. 12.1 Algorithm for management of intestinal strictures

undergo medical therapy, endoscopic therapy, or surgical therapy for CD-related strictures [44].

Penetrating Disease

Penetrating CD with fistula and/or abscess formation is common occurring at a rate of 3.8–7.5% per year [45]. Population-based studies report fistula formation in 50% of patients after 20 years of disease and intra-abdominal abscess in 25–30% of patients [46, 47]. Penetrating disease can be associated with intestinal stenosis which frequently causes increased proximal luminal pressure leading to upstream intestinal dilation followed by perforation with development of a fistula and/or abscess. Perianal disease occurs in 35–45% of patients with CD and may precede intestinal disease by years in 5–19% of cases [48–51]. Clinical manifestations of intra-abdominal abscess include fevers and/or chills, localized abdominal pain with peritoneal signs, and infrequently, a palpable mass.

CT abdomen and pelvis optimized with IV and oral contrast remains the standard diagnostic method [52, 53]. Initial management should include antibiotic therapy with adequate coverage of the typical polymicrobial bowel flora. Percutaneous drainage is now standard of care for abscess management as similar efficacy rates to surgical intervention have been demonstrated though with a less-invasive approach [54]. Abscess drainage may be guided by CT or ultrasound depending on location, depth of abscess within the abdominal cavity, and center expertise. The majority (80–90%) of abscesses are amenable to percutaneous drainage [55]. Contraindications include intestinal perforation, generalized peritonitis, or unsafe window to pass needle into the abscess [55]. Abscesses <3 cm in size can be aspirated completely without need of drain placement [47]. Figure 12.2 shows a proposed algorithm for

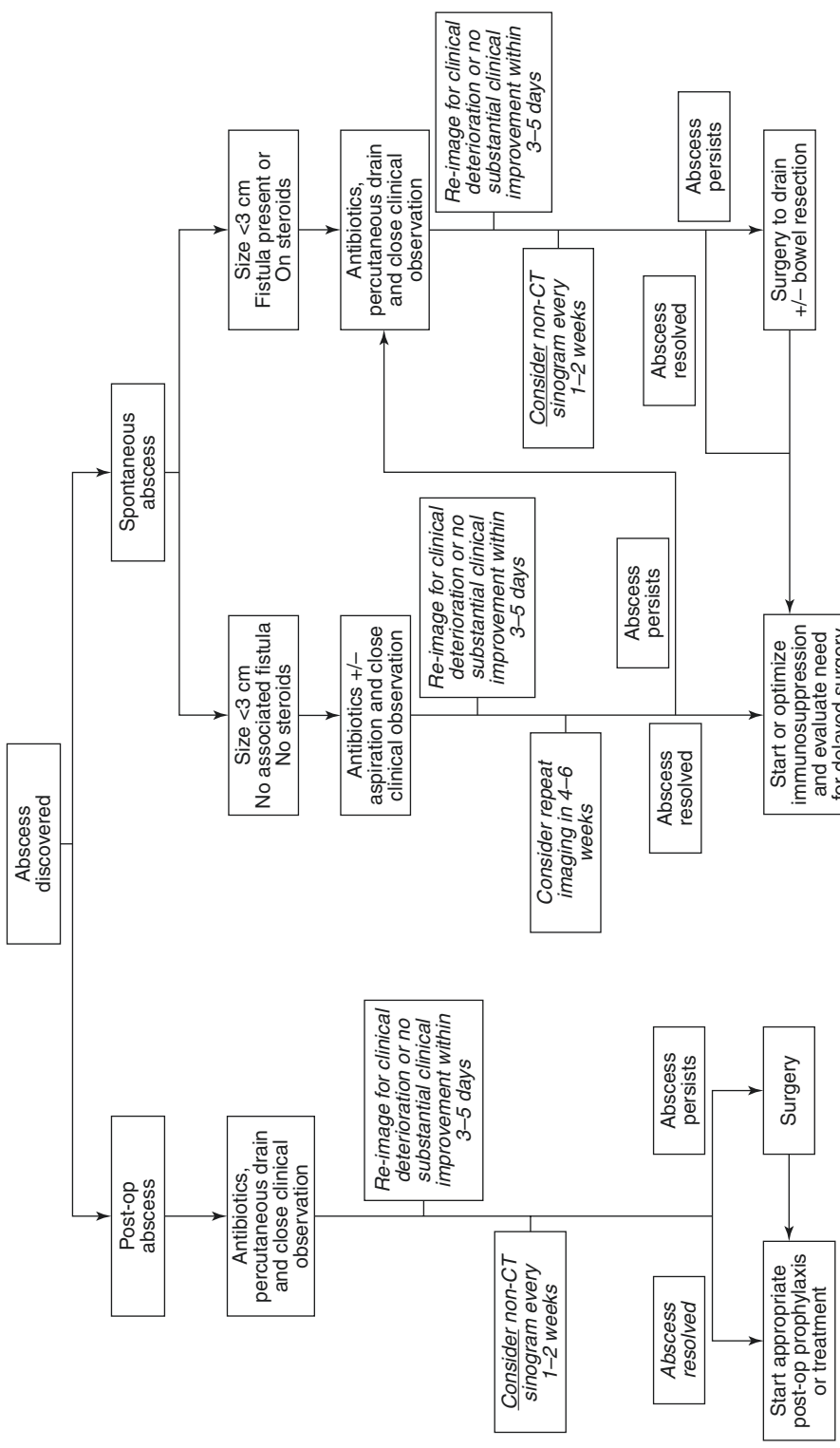

Fig. 12.2 Algorithm for management of intestinal abscess

management [47]. Drain removal can be considered when drain output decreases to 20 ml/day or less, while persistently high drainage should prompt consideration for intestinal perforation/fistula. If an abscess recurs (recurrence rates are reported to be 1–9%), repeat percutaneous drainage should be considered as it has shown to be successful in 91% of cases of recurrent abscess [54, 56]. Surgical management is indicated in cases with contraindications to percutaneous drainage, previous failed drainage attempt, and multiloculated collections or if a concurrent downstream stricture or fistula is present.

Perianal disease categorically includes fissure, fistula, abscess, and/or stenosis formation in the anorectal or perianal area. Clinical manifestations may include anal pain, painful defecation, and/or purulent discharge. Perianal fistulas are classified by their anatomic extension and location to the anal sphincter complex. Entero-cutaneous fistulas (ECFs) led to leakage of stool from a skin perforation and are classified by their output as high output (>500 mL/24 hours) and low output (<200 mL/24 hours).

MRI of the pelvis is favored for perianal disease assessment as it is superior in delineating involvement of key anal structures. MRI is as an adjunct to examination under anesthesia (EUA), which remains the standard for perianal disease evaluation and treatment. Endoscopic ultrasound (EUS) can be used as well with high sensitivity to locate perianal fistulas [57]. Antibiotics may be helpful in induction therapy and prevention of fistulous disease-associated abscess formation [58]. The most common antibiotic regimen is ciprofloxacin and metronidazole. Infliximab was demonstrated in a 1999 randomized, placebo-controlled study to be efficacious for initial fistula closure with success in 55% of patients receiving infliximab compared to 13% of patients in the placebo arm [59]. ACCENT II trial showed sustained fistula closure with maintenance infliximab therapy in 46% of patients compared to 23% in placebo group at 54 weeks follow-up [60]. Seton placement during EUA combined with infliximab has been shown to be superior to either as monotherapy in perianal disease [61]. Two randomized placebo-controlled studies showed antibiotics in combination with infliximab or adalimumab were more effective than biologic therapy alone initially (71% vs. 47% in adalimumab trial); however, the superior clinical response did not remain after antibiotics were stopped [62, 63].

High-output ECFs require initial volume resuscitation, electrolyte repletion, sepsis control if present, and then matching daily output with intake. Nutritional support is a necessity with enteral nutrition if able or TPN as fistula closure rates double in patients receiving supplemental nutrition compared to those who are not [64]. While 27–38% of IBD-related ECFs spontaneously close, 50% require definitive surgical closure and 50% recur.

Conclusion

In summary, the natural history of UC is frequently complicated by severe colitis and at times fulminant colitis or toxic megacolon. Complications of CD include severe colitis, fibro-stenotic or inflammatory intestinal obstruction, and penetrating diseases of intra-abdominal abscess, fistula, and perianal disease. Medical therapy including corticosteroids and biologic therapies has limited effectiveness, and surgical intervention is frequently indicated. Successful management of these complex IBD complications requires a carefully planned multidisciplinary approach including surgeons, gastroenterologists, radiologists, pathologists, and dieticians.

References

1. Dinesen LC, Walsh AJ, Protic MN, et al. The pattern and outcome of acute severe colitis. J Crohns Colitis. 2010;4(4):431–7.
2. Edwards FC, Truelove SC. The course and prognosis of ulcerative colitis. Gut. 1963;4:299–315.
3. Bitton A, Buie D, Enns R, et al. Treatment of hospitalized adult patients with severe ulcerative colitis: Toronto consensus statements. Am J Gastroenterol. 2012;107(2):179–94. author reply 95
4. Grieco MB, Bordan DL, Geiss AC, Beil AR Jr. Toxic megacolon complicating Crohn's colitis. Ann Surg. 1980;191(1):75–80.
5. Kappelman MD, Horvath-Puho E, Sandler RS, et al. Thromboembolic risk among Danish children and adults with inflammatory bowel diseases: a population-based nationwide study. Gut. 2011;60(7):937–43.

6. Nguyen GC, Sam J. Rising prevalence of venous thromboembolism and its impact on mortality among hospitalized inflammatory bowel disease patients. Am J Gastroenterol. 2008;103(9):2272–80.
7. Nguyen GC, Bernstein CN, Bitton A, et al. Consensus statements on the risk, prevention, and treatment of venous thromboembolism in inflammatory bowel disease: Canadian Association of Gastroenterology. Gastroenterology. 2014;146(3):835–48 e6.
8. Domenech E, Vega R, Ojanguren I, et al. Cytomegalovirus infection in ulcerative colitis: a prospective, comparative study on prevalence and diagnostic strategy. Inflamm Bowel Dis. 2008;14(10):1373–9.
9. Criscuoli V, Casa A, Orlando A, et al. Severe acute colitis associated with CMV: a prevalence study. Dig Liver Dis. 2004;36(12):818–20.
10. Cottone M, Pietrosi G, Martorana G, et al. Prevalence of cytomegalovirus infection in severe refractory ulcerative and Crohn's colitis. Am J Gastroenterol. 2001;96(3):773–5.
11. Kandiel A, Lashner B. Cytomegalovirus colitis complicating inflammatory bowel disease. Am J Gastroenterol. 2006;101(12):2857–65.
12. Maharshak N, Barzilay I, Zinger H, Hod K, Dotan I. *Clostridium difficile* infection in hospitalized patients with inflammatory bowel disease: prevalence, risk factors, and prognosis. Medicine (Baltimore). 2018;97(5):e9772.
13. Mylonaki M, Langmead L, Pantes A, Johnson F, Rampton DS. Enteric infection in relapse of inflammatory bowel disease: importance of microbiological examination of stool. Eur J Gastroenterol Hepatol. 2004;16(8):775–8.
14. Ananthakrishnan AN, McGinley EL, Binion DG. Excess hospitalisation burden associated with *Clostridium difficile* in patients with inflammatory bowel disease. Gut. 2008;57(2):205–10.
15. McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis. 2018;66(7):e1–e48.
16. Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955;2(4947):1041–8.
17. Jones JH, Lennard-Jones JE. Corticosteroids and corticotrophin in the treatment of Crohn's disease. Gut. 1966;7(2):181–7.
18. Turner D, Walsh CM, Steinhart AH, Griffiths AM. Response to corticosteroids in severe ulcerative colitis: a systematic review of the literature and a meta-regression. Clin Gastroenterol Hepatol. 2007;5(1):103–10.
19. Van Assche G, D'Haens G, Noman M, et al. Randomized, double-blind comparison of 4 mg/kg versus 2 mg/kg intravenous cyclosporine in severe ulcerative colitis. Gastroenterology. 2003;125(4):1025–31.
20. Lichtiger S, Present DH, Kornbluth A, et al. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. N Engl J Med. 1994;330(26):1841–5.
21. D'Haens G, Lemmens L, Geboes K, et al. Intravenous cyclosporine versus intravenous corticosteroids as single therapy for severe attacks of ulcerative colitis. Gastroenterology. 2001;120(6):1323–9.
22. Cohen RD, Stein R, Hanauer SB. Intravenous cyclosporin in ulcerative colitis: a five-year experience. Am J Gastroenterol. 1999;94(6):1587–92.
23. Arts J, D'Haens G, Zeegers M, et al. Long-term outcome of treatment with intravenous cyclosporin in patients with severe ulcerative colitis. Inflamm Bowel Dis. 2004;10(2):73–8.
24. Moskovitz DN, Van Assche G, Maenhout B, et al. Incidence of colectomy during long-term follow-up after cyclosporine-induced remission of severe ulcerative colitis. Clin Gastroenterol Hepatol. 2006;4(6):760–5.
25. Ford AC, Sandborn WJ, Khan KJ, Hanauer SB, Talley NJ, Moayyedi P. Efficacy of biological therapies in inflammatory bowel disease: systematic review and meta-analysis. Am J Gastroenterol. 2011;106(4):644–59. quiz 60
26. Lawson MM, Thomas AG, Akobeng AK. Tumour necrosis factor alpha blocking agents for induction of remission in ulcerative colitis. Cochrane Database Syst Rev. 2006;(3):CD005112.
27. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005;353(23):2462–76.
28. Probert CS, Hearing SD, Schreiber S, et al. Infliximab in moderately severe glucocorticoid resistant ulcerative colitis: a randomised controlled trial. Gut. 2003;52(7):998–1002.
29. Laharie D, Bourreille A, Branche J, et al. Ciclosporin versus infliximab in patients with severe ulcerative colitis refractory to intravenous steroids: a parallel, open-label randomised controlled trial. Lancet. 2012;380(9857):1909–15.
30. Williams JG, Alam MF, Alrubaiy L, et al. Infliximab versus ciclosporin for steroid-resistant acute severe ulcerative colitis (CONSTRUCT): a mixed methods, open-label, pragmatic randomised trial. Lancet Gastroenterol Hepatol. 2016;1(1):15–24.
31. Laharie D, Bourreille A, Branche J, et al. Long-term outcome of patients with steroid-refractory acute severe UC treated with ciclosporin or infliximab. Gut. 2018;67(2):237–43.
32. Narula N, Fine M, Colombel JF, Marshall JK, Reinisch W. Systematic review: sequential rescue therapy in severe ulcerative colitis: do the benefits outweigh the risks? Inflamm Bowel Dis. 2015;21(7):1683–94.
33. Jarnerot G, Hertervig E, Friis-Liby I, et al. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: a randomized, placebo-controlled study. Gastroenterology. 2005;128(7):1805–11.
34. Rieder F, Fiocchi C, Rogler G. Mechanisms, management, and treatment of fibrosis in patients with inflammatory bowel diseases. Gastroenterology. 2017;152(2):340–50 e6.
35. Peyrin-Biroulet L, Harmsen WS, Tremaine WJ, Zinsmeister AR, Sandborn WJ, Loftus EV Jr. Surgery in a population-based cohort of Crohn's disease from Olmsted County, Minnesota (1970-2004). Am J Gastroenterol. 2012;107(11):1693–701.

36. Panes J, Bouzas R, Chaparro M, et al. Systematic review: the use of ultrasonography, computed tomography and magnetic resonance imaging for the diagnosis, assessment of activity and abdominal complications of Crohn's disease. Aliment Pharmacol Ther. 2011;34(2):125–45.
37. Hirai F, Andoh A, Ueno F, et al. Efficacy of endoscopic balloon dilation for small bowel strictures in patients with Crohn's disease: a nationwide, multicentre, open-label, prospective cohort study. J Crohns Colitis. 2018;12(4):394–401.
38. Bettenworth D, Gustavsson A, Atreja A, et al. A Pooled analysis of efficacy, safety, and long-term outcome of endoscopic balloon dilation therapy for patients with stricturing Crohn's disease. Inflamm Bowel Dis. 2017;23(1):133–42.
39. Ding NS, Yip WM, Choi CH, et al. Endoscopic dilatation of Crohn's anastomotic strictures is effective in the long term, and escalation of medical therapy improves outcomes in the biologic era. J Crohns Colitis. 2016;10(10):1172–8.
40. Reutemann BA, Turkeltaub JA, Al-Hawary M, Waljee AK, Higgins PDR, Stidham RW. Endoscopic balloon dilation size and avoidance of surgery in stricturing Crohn's disease. Inflamm Bowel Dis. 2017;23(10):1803–9.
41. Lan N, Shen B. Endoscopic stricturotomy with needle knife in the treatment of strictures from inflammatory bowel disease. Inflamm Bowel Dis. 2017;23(4):502–13.
42. Nishida Y, Hosomi S, Yamagami H, et al. Analysis of the risk factors of surgery after endoscopic balloon dilation for small intestinal strictures in Crohn's disease using double-balloon endoscopy. Intern Med. 2017;56(17):2245–52.
43. Campos C, Perrey A, Lambert C, et al. Medical therapies for stricturing Crohn's disease: efficacy and cross-sectional imaging predictors of therapeutic failure. Dig Dis Sci. 2017;62(6):1628–36.
44. Chan WPW, Mourad F, Leong RW. Crohn's disease associated strictures. J Gastroenterol Hepatol. 2018;33(5):998–1008.
45. Church PC, Turner D, Feldman BM, et al. Systematic review with meta-analysis: magnetic resonance enterography signs for the detection of inflammation and intestinal damage in Crohn's disease. Aliment Pharmacol Ther. 2015;41(2):153–66.
46. Schwartz DA, Loftus EV Jr, Tremaine WJ, et al. The natural history of fistulizing Crohn's disease in Olmsted County, Minnesota. Gastroenterology. 2002;122(4):875–80.
47. Feagins LA, Holubar SD, Kane SV, Spechler SJ. Current strategies in the management of intra-abdominal abscesses in Crohn's disease. Clin Gastroenterol Hepatol. 2011;9(10):842–50.
48. Pescatori M, Interisano A, Basso L, et al. Management of perianal Crohn's disease. Results of a multicenter study in Italy. Dis Colon Rectum. 1995;38(2):121–4.
49. McKee RF, Keenan RA. Perianal Crohn's disease--is it all bad news? Dis Colon Rectum. 1996;39(2):136–42.
50. Platell C, Mackay J, Collopy B, Fink R, Ryan P, Woods R. Anal pathology in patients with Crohn's disease. Aust N Z J Surg. 1996;66(1):5–9.
51. Rankin GB, Watts HD, Melnyk CS, Kelley ML Jr. National Cooperative Crohn's disease study: extraintestinal manifestations and perianal complications. Gastroenterology. 1979;77(4 Pt 2):914–20.
52. Callen PW. Computed tomographic evaluation of abdominal and pelvic abscesses. Radiology. 1979;131(1):171–5.
53. Allen BC, Barnhart H, Bashir M, Nieman C, Breault S, Jaffe TA. Diagnostic accuracy of intra-abdominal fluid collection characterization in the era of multidetector computed tomography. Am Surg. 2012;78(2):185–9.
54. Golfieri R, Cappelli A. Computed tomography-guided percutaneous abscess drainage in coloproctology: review of the literature. Tech Coloproctol. 2007;11(3):197–208.
55. Ananthakrishnan AN, McGinley EL. Treatment of intra-abdominal abscesses in Crohn's disease: a nationwide analysis of patterns and outcomes of care. Dig Dis Sci. 2013;58(7):2013–8.
56. Gervais DA, Ho CH, O'Neill MJ, Arellano RS, Hahn PF, Mueller PR. Recurrent abdominal and pelvic abscesses: incidence, results of repeated percutaneous drainage, and underlying causes in 956 drainages. AJR Am J Roentgenol. 2004;182(2):463–6.
57. Siddiqui MR, Ashrafian H, Tozer P, et al. A diagnostic accuracy meta-analysis of endoanal ultrasound and MRI for perianal fistula assessment. Dis Colon Rectum. 2012;55(5):576–85.
58. Kotze PG, Shen B, Lightner A, et al. Modern management of perianal fistulas in Crohn's disease: future directions. Gut. 2018;67:1181.
59. Present DH, Rutgeerts P, Targan S, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med. 1999;340(18):1398–405.
60. Sands BE, Anderson FH, Bernstein CN, et al. Infliximab maintenance therapy for fistulizing Crohn's disease. N Engl J Med. 2004;350(9):876–85.
61. de Groof EJ, Sahami S, Lucas C, Ponsioen CY, Bemelman WA, Buskens CJ. Treatment of perianal fistula in Crohn's disease: a systematic review and meta-analysis comparing seton drainage and anti-tumour necrosis factor treatment. Color Dis. 2016;18(7):667–75.
62. West RL, van der Woude CJ, Hansen BE, et al. Clinical and endosonographic effect of ciprofloxacin on the treatment of perianal fistulae in Crohn's disease with infliximab: a double-blind placebo-controlled study. Aliment Pharmacol Ther. 2004;20(11–12):1329–36.
63. Dewint P, Hansen BE, Verhey E, et al. Adalimumab combined with ciprofloxacin is superior to adalimumab monotherapy in perianal fistula closure in Crohn's disease: a randomised, double-blind, placebo controlled trial (ADAFI). Gut. 2014;63(2):292–9.
64. Davis KG, Johnson EK. Controversies in the care of the enterocutaneous fistula. Surg Clin North Am. 2013;93(1):231–50.

Inflammatory Bowel Disease

13

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A patient with inflammatory bowel disease (IBD) can be a very intimidating consult for the general surgeon. Although there have been significant advances in medical management, ulcerative colitis (UC) and Crohn's disease (CD) often still present with acute and emergent surgical issues. Surgical intervention is generally reserved for failed medical therapy or complications of the disease. IBD patients should ideally be admitted and managed on a Medicine Service with care directed by a multidisciplinary team of specialists to include a gastroenterologist.

Medical Management of Inflammatory Bowel Disease (IBD)

With a multitude of medications available, there are many nuances involved in the care of IBD patients, and therefore the medical management of these patients should be directed by a gastroenterologist. However, it is important for the surgeon to understand a few basic principles of medical management. The medical treatment for acute flares of IBD is aimed at reducing inflammation and inducing remission of the disease. For CD, the inflamed tissue can be anywhere along the gastrointestinal tract but most commonly is found in the terminal ileum and cecum [1]. The inflammation in UC begins in the rectum and advances proximally [2].

In the acute setting, systemic steroids are the first treatment. Systemic steroids have been shown to induce remission in up to 92% of patients, but are not as effective at maintenance of remission and are rife with side effects when used long term [1, 3]. Corticosteroids will usually result in improvement of symptoms within 48–72 hours [4]. If this does not occur, or sometimes concurrently, patients will also get treated with a biologic agent. The anti-TNF agents are the most common biologics used in the acute setting and include infliximab (Remicade®, Inflectra®, Renflexis™), adalimumab (Humira®), and certolizumab pegol (Cimzia®). Newer biologic agents are the integrin-receptor antagonists, to include natalizumab (Tysabri®) and vedolizumab (Entyvio®), with their role in an acutely ill patient still being studied. The addition of the biologic medications should lead to improvement in symptoms within 5–7 days. If clinical improvement is not seen at this point, surgery is often indicated.

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The following topics discussed in this chapter are the possible presentations of IBD that may lead to urgent or emergent surgery.

Acute Colitis

Either UC or CD can cause colitis, and the treatment strategies are similar for both. The management of colitis depends on its severity. Mild and moderate colitis is usually defined as less than ten bowel movements per day with no systemic symptoms. The term severe colitis is used to describe ≥6 bloody bowel movements (BMs) combined with at least one sign of systemic toxicity, such as anemia, elevated erythrocyte sedimentation rate (ESR), fever, or tachycardia. The term fulminant colitis is used when there are >10 bloody BMs daily along with signs of systemic toxicity, a transfusion requirement, abdominal tenderness and distention, and imaging that shows colonic dilation [5]. Finally, toxic megacolon is defined as focal or diffuse colonic dilation, greater than 6 cm, with severe systemic toxicity, and usually represents impending perforation [6]. Surgery in the context of colitis is warranted with toxic megacolon, imminent or existing perforation, or if there is ongoing or worsening of colonic dilation, peritonitis, and/or systemic toxicity [7, 8].

For severe and fulminant colitis, a short trial of medical management is recommended, but clinical improvement should begin within 2–3 days of starting glucocorticoids or 5–7 days within initiating biologics [1, 2]. It is also necessary to rule out other infectious etiologies for colitis, such as *Clostridium difficile* or *Cytomegalovirus*. In addition, the use of medications that slow intestinal transit, such as narcotics and antidiarrheal agents, may lead to progression of colitis to toxic megacolon and should be abandoned [7, 8].

When emergent surgery is indicated, the procedure of choice is a total abdominal colectomy with end ileostomy and Hartmann closure or mucus fistula, regardless of the segments of bowel that are involved [7, 8]. The goal of surgery is to rescue the patient from life-threatening toxicity by removing as much of the diseased colon in the safest, most efficient way. The rectum should be left in place and pelvic dissection avoided in this setting [9]. The distal point of transection should be on the distal sigmoid colon at or near the level of the inferior mesenteric artery. Not only does this reduce the operative time and potential complications of the surgery but also allows for a technically easier restorative operation. There is a risk of staple line leak from the Hartmann pouch due to inflammation. The surgeon should consider placing the end of the rectosigmoid stump in the extrafascial superficial tissue or place pelvic and transanal drains to mitigate this risk [7–9].

Restorative procedures are usually completed 4–6 months after colectomy, once inflammation has subsided, nutrition is optimized, and immunologic medications are reduced or stopped [9]. For UC, a second stage operation is required and may include a completion proctectomy with an ileal pouch anal anastomosis (IPAA) and diverting loop ileostomy or a completion proctectomy with an end ileostomy. If an IPAA is performed, the loop ileostomy is later reversed as the third stage operation. IPAA should not be used in patients with CD as the pouch can become involved with the disease and lead to additional complications. As long as there is no inflammation of the rectum, an ileal-rectal anastomosis may be performed for CD patients, but if proctitis is present, the patient will likely need to keep the end ileostomy [7, 9].

Acute Hemorrhage

Acute lower gastrointestinal hemorrhage is a very rare complication of both UC and CD. The bleeding from IBD is most often caused by inflammation and can often be successfully treated with medical management [10]. IBD patients with significant hemorrhage should immediately undergo resuscitation and diagnostic imaging with CT angiography. Stable patients may be treated by endoscopic or interventional radiologic techniques [7, 8]. Operative intervention should be limited to those patients that are clinically unstable. In the case of both Crohn's colitis and UC, it is recommended that a total abdominal colectomy be performed with end ileostomy [7, 8].

Obstruction

IBD can cause bowel obstruction primarily from strictures but also secondarily from adhesive disease, malignancy, fistulae, and abscesses. Intestinal strictures in IBD can arise from inflammation, fibrosis, or a previous anastomosis. Evaluation begins with a CT scan with oral and intravenous contrast, which is useful to also identify abscess, fistula, perforation, or other complications of IBD. CT or MR enterography are also often used, as they both have a high sensitivity and specificity for identifying an obstruction from active inflammation or fibrostenosis [7]. Barium small bowel follow-through and capsule endoscopy are other modalities used for evaluating small bowel strictures and obstruction, but these provide more limited information and are not often used in the acute setting [11].

Medical management again is the first line of treatment and well preferred over surgical intervention. The patient should undergo nasogastric tube placement for decompression, fluid resuscitation, and a trial of IV corticosteroids. In the setting of inflammation, the obstruction will usually resolve with steroid treatment, and surgery can be avoided [12]. Endoscopic management with balloon dilation may be considered for fibrotic strictures when they are located in an accessible segment of bowel. The best results for endoscopic treatment are strictures in an isolated short segment (<5 cm) with no signs of active inflammation or associated abscess, fistula, or perforation [7]. Endoscopic dilation is the preferred treatment for anastomotic strictures, with over 80% success rate [13].

If medical and/or endoscopic treatments fail to relieve symptoms, surgical resection of the stricture is recommended. The primary goal of surgery in this setting is to minimize the amount of bowel removed because recurrence rates are high and as many as 45% of patients require additional resections within 10 years [14]. Strictureplasty is a surgical option but should be reserved for patients who have fibrotic strictures with no evidence of inflammation and associated abscess or fistula, diffuse involvement of the small bowel, short bowel syndrome, impending short bowel syndrome, or disease that recurs very rapidly [7]. Strictureplasty allows for maximal preservation of bowel length while achieving the primary goal of relieving the obstruction; however, it can lead to bacterial overgrowth and potential for malignant degeneration [15, 16]. The most commonly performed strictureplasty is the Heineke-Mikulicz. This is performed by making a longitudinal incision on the antimesenteric side of the bowel followed by closure of the enterotomy transversely and is best utilized for strictures less than 10 cm in length. Other types of strictureplasty include the Finney and Michelassi, or longitudinal isoperistaltic strictureplasty, which are utilized for longer strictures [17]. Proximal CD-related strictures of the stomach and duodenum that are not responsive to medical therapy or endoscopic dilation may require proximal bypass procedures rather than resection or stricturoplasty.

In the case of colonic strictures for either UC or CD, the site should be thoroughly biopsied endoscopically given the increased risk for colon cancer. A colonic stricture in the setting of UC harbors a malignancy approximately 25% of the time, regardless of negative biopsy results, and therefore an oncologic resection with total abdominal colectomy is indicated in these patients [8].

Perforation

Although infrequent, patients with Crohn's disease may present with perforation of the small or large bowel. The most common etiologies are an obstruction or toxic colitis. The presenting symptoms may be masked in the setting of immunomodulatory therapy, particularly high-dose steroids. A high clinical suspicion should be maintained in any patient with an active Crohn's flare who clinically deteriorates. Resuscitation and emergent surgery are indicated when perforation is identified. The procedure of choice for small bowel perforation is resection of the diseased segment with primary anastomosis to bowel that does not clinically appear inflamed [18]. Primary closure of the perforation is not recommended as studies show this technique results in high failure rate and increased mortality, with rates of up to 41% in one case series [7, 18].

In the instance of CD- or UC-related colonic perforation, resuscitation and immediate surgery are again recommended. If a colonic perforation occurs at the cecum due to distal stricture or at the site of necrosis in the setting of toxic colitis, it is recommended to perform a total abdominal colectomy and end ileostomy [8]. In both small and large bowel perforation cases, if the patient is unstable and unfit to undergo an anastomosis at the time of the index operation, the surgeon should obtain source control, and the patient may be left in discontinuity until conditions are more optimal to restore continuity.

Abdominal Abscess

Intra-abdominal abscess formation is common in CD patients and usually occurs secondary to a perforation or a penetrating ulcer. The management of this issue is complex and requires a multidisciplinary approach involving gastroenterology, surgery, and interventional radiology. Initial management in the setting of a hemodynamically stable patient consists of fluid resuscitation, drainage, broad-spectrum antibiotics with bowel rest, and the consideration of parenteral nutrition [19]. For larger abscesses (>3 cm) that are amenable, the treatment strategy of choice is parenteral antibiotics in addition to percutaneous drainage of the abscess performed by interventional radiology [20, 21]. Percutaneous drainage is successful in achieving resolution of the abscess up to 78% of the time and allows for avoidance of urgent surgery [22]. Although nearly 30% of patients who undergo percutaneous drainage require surgery within a year, it serves as a bridge to definitive surgery resulting in decreased operative complications [21, 23]. If emergent surgery is required, a resection is preferred over operative drainage alone [7].

Enteric Fistula

Patients with CD often develop fistulas. The most common CD-related fistula is enterocolonic (29%), followed by enterosigmoid (17–26%) and enteroenteric (18–24%). Enterocutaneous fistulas occur in about 6–16% of patients [24]. Fistulas to other organs, such as the bladder, vagina, or stomach, may also develop.

Most fistulas do not require urgent or emergent surgical intervention. The first step in management is to determine if sepsis is present. If the patient is septic, he or she should be appropriately resuscitated and parenteral antibiotics initiated. A CT scan should be performed to look for uncontrolled source of sepsis, such as an associated abscess, in which case a percutaneous drain should be considered as described above. If the patient continues to be septic, operative intervention is required with resection of the diseased bowel [7].

More commonly, in the non-septic patient, initial medical management of fistulas focuses on optimizing nutrition, hydration, and correction of electrolyte imbalances. Patients can become malnourished from a fistula if the output remains high, or large segments of bowel are bypassed. If the patient is asymptomatic, surgery is not indicated. Once the symptomatic patient is medically optimized, surgery is recommended with resection of the diseased portion of bowel. The non-diseased portion of bowel or other involved organs such as the vagina or bladder may be closed primarily [7].

Intraoperative Considerations

There are many challenges a surgeon faces when operating on an IBD patient. One of the biggest questions pondered intraoperatively is whether a proximal diversion is needed. Ultimately, there is no single all-encompassing answer as each patient should be considered individually. However, there are several factors that should contribute to this decision. The patient's nutritional status, and specifically serum albumin of less than 3.5 g/dL, has been shown to be a preoperative risk factor for anastomotic leak in elective colon surgery, and this data has been replicated for IBD patients [25, 26]. The dosage and chronicity of immunosuppressive medications is also critical to consider. The impact of high-dose glu-

cocorticoids and other immunomodulators such as the anti-TNF agents on septic complications and anastomotic leaks has yet to be universally agreed upon in the literature [27]. Nonetheless, it is generally accepted that they likely play some role in increasing the risk of postoperative complications and therefore must be considered when operating on these patients. The intraoperative considerations that must be factored into the decision to perform a diversion include the patient's hemodynamic stability, the amount of intra-abdominal contamination present at the time of surgery, the extent of disease burden, and the extent of bowel wall edema [7].

The extent of small bowel resection has been well studied. It has been shown that patients should undergo a limited resection with gross negative margins of disease of approximately 2 cm. Fortunately, recurrence rates do not increase with presence of microscopic CD at the margins [28]. One technique to determine healthy bowel intraoperatively is to use the thumb and index finger to palpate the mesenteric border of the bowel. A healthy target for resection will be where the thumb and index finger can be felt with minimal thickening and the bowel edges are soft [29]. Another important intraoperative consideration is to note if the mesentery associated with the diseased bowel is very thick or if it tears or bleeds easily. This is not be the portion of bowel to create an anastomosis.

There has also been debate about how to create the small bowel anastomosis with IBD. Multiple studies have demonstrated that a stapled anastomosis has lower morbidity, recurrence rates, and anastomotic leak rates than a hand-sewn one [30–32]. However, some still advocate for hand-sewn anastomosis when thickened, edematous bowel must be used [33]. Recent data demonstrate a lower rate of anastomotic stricture with a hand-sewn Kono-S-type column-supported anastomosis [34].

The role of laparoscopy in treatment of IBD has also been well argued. Initially, surgeons may have been discouraged from utilizing laparoscopic approaches in patients with CD due to the potential for less than ideal surgical conditions and concerns regarding poor tissue quality. However, recent studies have shown that there may be benefits to the laparoscopic approach, such as earlier return of bowel function and shorter length of hospital stay, with similar rates of disease recurrence and significantly lower overall morbidity [35–37]. Even in the emergent setting of acute severe colitis and toxic megacolon, studies support that laparoscopic colectomy is safe and effective in experienced hands with appropriate patient selection [8, 35, 36]. In addition, the current data suggest that laparoscopy may allow for shorter time interval between each surgery of the three-stage surgical approach to UC [38].

Conclusion

IBD is a complicated disease process that is best managed initially by medial therapy directed by a multidisciplinary team of gastroenterologist and medical doctors. However, there are times when complications occur and need the urgent attention of the general surgeon. Though medical management resolves the complications of IBD the majority of the time, acute decompensation during the period of medical management and observation can still occur. If the decompensation is due to a perforation or abscess formation, then surgery- or radiology-guided drainage is necessary. In cases involving the small bowel, every effort should be made to preserve as much small bowel as possible and individual consideration given to the creation of a diverting ileostomy. For patients with colonic emergencies, an abdominal colectomy with end ileostomy is the treatment of choice. Laparoscopy can be safe and beneficial in IBD patients and should be considered, even in the emergent setting.

In general, acute flares of IBD that result in an obstruction or colitis should be treated by steroids, and consideration given to adding a biologic agents. The surgical team should exercise strict vigilance because if symptoms worsen or the patient decompensates, a perforation may be occurring. Initial symptoms of worsening may be masked by the steroids or biologic agents. As such, urgent surgical intervention is indicated for a suspected perforation or if the patient clinically worsens.

References

1. Scott FI, Osterman MT. Medical management of crohn disease. Clin Colon Rectal Surg. 2013;26(2):67–74.
2. Mahadevan U. Medical treatment of ulcerative colitis. Clin Colon Rectal Surg. 2004;17(1):7–19.
3. Chan WPW, Mourad F, Leong RW. Crohn's disease associated strictures. J Gastroenterol Hepatol. 2018;33(5):998–1008.
4. Munkholm P, Langholz E, Davidsen M, Binder V. Frequency of glucocorticoid resistance and dependency in Crohn's disease. Gut. 1994;35(3):360–2.
5. Hanauer SB. Inflammatory bowel disease. N Engl J Med. 1996;334(13):841–8.
6. Jones JH, Chapman M. Definition of megacolon in colitis. Gut. 1969;10(7):562–4.
7. Strong S, Steele SR, Boutrous M, et al. Clinical practice guideline for the surgical management of Crohn's disease. Dis Colon Rectum. 2015;58(11):1021–36.
8. Ross H, Steele SR, Varma M, et al. Practice parameters for the surgical treatment of ulcerative colitis. Dis Colon Rectum. 2014;57(1):5–22.
9. Martin S, Vogel J. Restorative procedures in colonic Crohn disease. Clin Colon Rectal Surg. 2013;26(02):100–5.
10. Kim K-J, Han BJ, Yang S-K, et al. Risk factors and outcome of acute severe lower gastrointestinal bleeding in Crohn's disease. Dig Liver Dis. 2012;44(9):723–8.
11. Fakhoury M, Negrulj R, Mooranian A, Al-Salami H. Inflammatory bowel disease: clinical aspects and treatments. J Inflamm Res. 2014;7:113–20.
12. Lichtenstein GR, Hanauer SB, Sandborn WJ, Practice Parameters Committee of American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2009;104(2):465–483; quiz 464, 484.
13. Ajlouni Y, Iser JH, Gibson PR. Endoscopic balloon dilatation of intestinal strictures in Crohn's disease: safe alternative to surgery. J Gastroenterol Hepatol. 2007;22(4):486–90.
14. Fornaro R, Caratto E, Caratto M, et al. Postoperative recurrence in Crohn's disease. Critical analysis of potential risk factors. An update. Surgeon. 2015;13(6):330–47.
15. Drenick EJ, Ament ME, Finegold SM, Corrodi P, Passaro E. Bypass enteropathy. Intestinal and systemic manifestations following small-bowel bypass. JAMA. 1976;236(3):269–72.
16. Hawker PC, Gyde SN, Thompson H, Allan RN. Adenocarcinoma of the small intestine complicating Crohn's disease. Gut. 1982;23(3):188–93.
17. Yamamoto T, Fazio VW, Tekkis PP. Safety and efficacy of strictureplasty for Crohn's disease: a systematic review and meta-analysis. Dis Colon Rectum. 2007;50(11):1968–86.
18. Greenstein AJ, Mann D, Sachar DB, Aufses AH Jr. Free perforation in Crohn's disease: I. A survey of 99 cases. Am J Gastroenterol. 1985;80(9):682–9.
19. Graham E, Rao K, Cinti S. Medical versus interventional treatment of intra-abdominal abscess in patients with Crohn disease. Infect Dis (Auckl). 2017;10:117991611770173.
20. Feagins LA, Holubar SD, Kane SV, Spechler SJ. Current strategies in the management of intra-abdominal abscesses in Crohn's disease. Clin Gastroenterol Hepatol. 2011;9(10):842–50.
21. Clancy C, Boland T, Deasy J, McNamara D, Burke JP. A meta-analysis of percutaneous drainage versus surgery as the initial treatment of Crohn's disease-related intra-abdominal abscess. J Crohns Colitis. 2016;10(2):202–8.
22. Golfieri R, Cappelli A, Giampalma E, et al. CT-guided percutaneous pelvic abscess drainage in Crohn's disease. Tech Coloproctol. 2006;10(2):99–105.
23. Gutierrez A, Lee H, Sands BE. Outcome of surgical versus percutaneous drainage of abdominal and pelvic abscesses in Crohn's disease. Am J Gastroenterol. 2006;101(10):2283–9.
24. Hirten RP, Shah S, Sachar DB, Colombel J-F. The management of intestinal penetrating Crohn's disease. Inflamm Bowel Dis. 2018;24(4):752–65.
25. Suding P. Definitive risk factors for anastomotic leaks in elective open colorectal resection. Arch Surg. 2008;143(9):907.
26. Telem DA. Risk factors for anastomotic leak following colorectal surgery. Arch Surg. 2010;145(4):371.
27. Sharma A, Chinn BT. Preoperative optimization of crohn disease. Clin Colon Rectal Surg. 2013;26(2):75–9.
28. Fazio VW, Marchetti F, Church M, et al. Effect of resection margins on the recurrence of Crohn's disease in the small bowel. A randomized controlled trial. Ann Surg. 1996;224(4):563–571; discussion 571-573.
29. Chandra R, Moore JWE. The surgical options and management of intestinal Crohn's disease. Indian J Surg. 2011;73(6):432–8.
30. Muñoz-Juárez M, Yamamoto T, Wolff BG, Keighley MRB. Wide-lumen stapled anastomosis vs. conventional end-to-end anastomosis in the treatment of Crohn's disease. Dis Colon Rectum. 2001;44(1):20–5.
31. Tersigni R, Alessandroni L, Barreca M, Piovanello P, Prantera C. Does stapled functional end-to-end anastomosis affect recurrence of Crohn's disease after ileocolonic resection? Hepato-Gastroenterology. 2003;50(53):1422–5.
32. Resegotti A, Astegiano M, Farina EC, et al. Side-to-side stapled anastomosis strongly reduces anastomotic leak rates in Crohn's disease surgery. Dis Colon Rectum. 2005;48(3):464–8.
33. Gardiner KR, Dasari BVM. Operative management of small bowel Crohn's disease. Surg Clin North Am. 2007;87(3):587–610.
34. Kono T, Fichera A, Maeda K, et al. Kono-S Anastomosis for surgical prophylaxis of anastomotic recurrence in Crohn's disease: an inter-

national multicenter study. J Gastrointest Surg. 2016;20(4):783–90.
35. Aarons CB. Laparoscopic surgery for crohn disease: a brief review of the literature. Clin Colon Rectal Surg. 2013;26(2):122–7.
36. Kessler H, Mudter J, Hohenberger W. Recent results of laparoscopic surgery in inflammatory bowel disease. World J Gastroenterol. 2011;17(9):1116–25.
37. Tan JJY, Tjandra JJ. Laparoscopic surgery for Crohn's disease: a meta-analysis. Dis Colon Rectum. 2007;50(5):576–85.
38. Chung TP, Fleshman JW, Birnbaum EH, et al. Laparoscopic vs. open total abdominal colectomy for severe colitis: impact on recovery and subsequent completion restorative proctectomy. Dis Colon Rectum. 2009;52(1):4–10.

Part V

Incarcerated Paraesophageal Hernia

14 Incarcerated Paraesophageal Hernia: Incidence, Presentation, and Initial Management

Will Cole

Pathophysiology and Classification

Paraesophageal hernia (PEH), a term often used interchangeably with hiatal hernia (HH), is a spectrum of disorders. PEH occurs as a result of increased intra-abdominal pressure, leading to an increased transdiaphragmatic pressure gradient, with resultant widening of the esophageal hiatus and weakening of the phrenoesophageal ligament. Predisposing conditions may include advanced age, obesity, pregnancy, chronic constipation, chronic obstructive pulmonary disorder, spinal and chest wall deformities, and blunt abdominal trauma. A shortened esophagus, either congenital or acquired due to fibrosis and scarring from chronic reflux, may also be a factor, and disorders of collagen metabolism may also play a role. The end result of these changes is herniation of abdominal viscera into the mediastinum through the esophageal hiatus [1, 2].

PEHs are typically divided into four subtypes, which are defined by the degree of herniation and contents of the hernia sac. Type 1 PEH, often referred to as a sliding hiatal hernia, involves herniation of the gastroesophageal junction (GEJ) into the mediastinum. Type 2 PEH, or "true" PEH, also called a "rolling hernia," involves migration of the gastric cardia or fundus through the esophageal hiatus while the GEJ is not displaced. In this condition, the phrenoesophageal ligament remains intact. Type 3 PEH involves herniation of the stomach with the GEJ into the mediastinum. Type 4 PEH, which may also be called "giant PEH," includes not only the stomach and GEJ but also other abdominal viscera in the hernia sac. This is often the transverse colon, but the small bowel, liver, spleen, or pancreas may also be found in the mediastinum [1].

Prevalence

The true prevalence of PEH is difficult to determine, as many are asymptomatic. With the increased use of imaging studies in clinical medicine, it seems they are more common than previously thought and estimates vary from 10% to 80% of the adult population in the United States [2]. Approximately 95% of PEH are type 1, while types 2, 3, and 4 make up about 5% of all PEH. Of these, types 3 and 4 make up a 78%, with a type 2 "true" PEH accounting for only 14% of PEH [3]. As these more advanced hernias, types 2–4, are more likely to become symptomatic or complicated by obstruction, volvulus, or bleeding, they will be the focus of this chapter.

The annual incidence of acute symptoms among those with PEH is estimated between

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0.7% and 7% with about 1% per year needing emergent surgical repair [3]. The clinical presentation of complicated PEH is often nonspecific. Patients may present with a spectrum of complaints, including heartburn, regurgitation, retching, frank oral intolerance, chest or upper abdominal pain, or dyspnea [2]. PEH may also result in acute or chronic gastrointestinal bleeding from Cameron's ulcers, which may occur in up to 13% of large PEH [9]. In unusual cases, type 4 PEH may present initially as biliary obstruction, pancreatitis, or splenic rupture, depending upon the contents of the hernia sac [4–6]. While interesting, these unusual complications are quite rare, and so this chapter will focus on the initial diagnosis and management of PEH incarceration, volvulus, and bleeding.

Complications and Initial Management

PEH may be complicated by incarceration or volvulus of the herniated stomach, leading to obstruction and ischemic necrosis of the stomach if not promptly recognized and treated. Volvulus may be organoaxial, along a line connecting the pylorus and GEJ, or mesenteroaxial, about a line connecting the middle of the greater and lesser curves. Of these, organoaxial volvulus is most common. Patients often present with chest pain, nausea, retching, and possibly hematemesis. They may demonstrate Borchardt's triad: severe epigastric pain and distention, vomiting followed by retching, and difficulty passing an NG tube [7].

The initial diagnosis is sometimes suggested on initial upright abdominal films or chest X-ray with findings of a retrocardiac bubble or an air-fluid level in the chest. A barium upper GI study may be helpful to confirm the diagnosis in the stable patient. Findings include the greater curve and pylorus superior to the lesser curve with the pylorus pointing inferiorly (Fig. 14.1) or, in the lateral view, the antrum and pylorus anterior or posterior to the GEJ with a downward pointing pylorus (Fig. 14.2). CT scan may be more useful in defining not only the gastric anatomy but also the size of the hiatal defect and the presence or absence of additional herniated organs, which can facilitate operative planning (Fig. 14.3) [7].

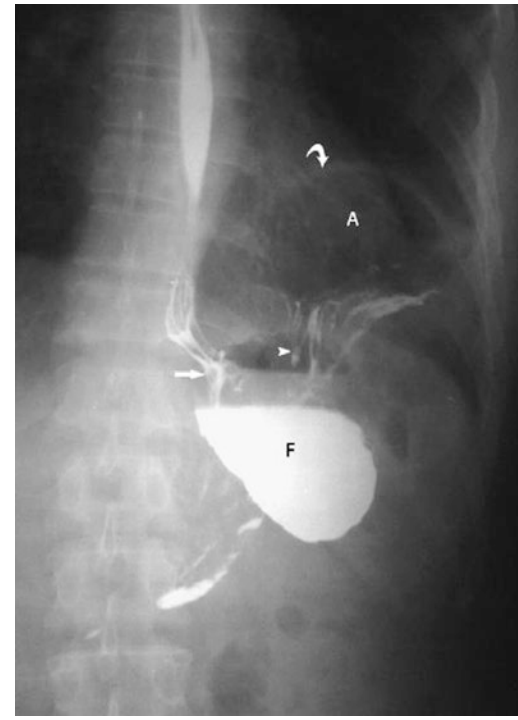

Fig. 14.1 AP view of the stomach during upper gastrointestinal Barium study showing an upside down herniated distal stomach including antrum (A) into the left hemithorax. The gastric fundus and proximal body (F) is normally located. The greater curvature of the stomach (curved arrow) is facing upward and is located above the level of lesser curvature. Notice the downward pointing pylorus (arrowhead). Straight arrow is pointing to the gastroesophageal junction. (Al-Balas et al. [7])

Perhaps the best initial management option for an incarcerated paraesophageal hernia is prevention. Most authors recommend that symptomatic patients who are appropriate operative candidates undergo elective repair. Conservative management of symptomatic PEH is associated with a high mortality rate, up to 16–30% in those who required hospitalization, while mortality after operative intervention may be lower than 10% if operation is undertaken prior to gastric necrosis, perforation, or development of tension physiology [3]. In the urgent situation, definitive management includes surgical reduction of

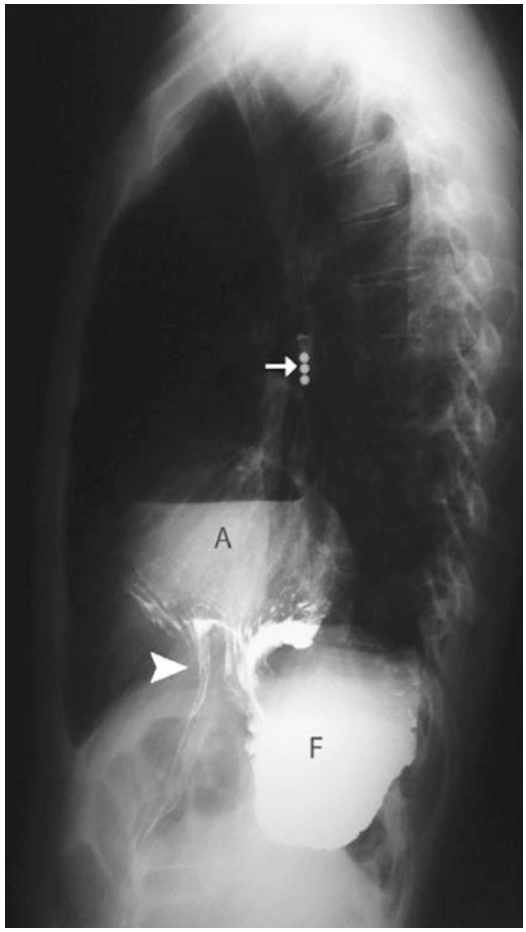

Fig. 14.2 Upright lateral chest radiograph after administration of oral Barium. The gastric fundus (F) is normally located. The antrum (A) herniated through diaphragmatic defect. Arrow indicates the distal marker of a nasogastric tube failed to pass into the stomach. Downward pointing pylorus is indicated by arrowhead. (Al-Balas et al. [7])

the hernia, resection of any necrotic tissues, and, optimally, repair of the hiatal hernia or at least gastropexy. Further details of the surgical management will be discussed in a separate chapter.

Initial management of incarcerated or volvulized PEH focuses on rapid passage of an NG tube into the herniated stomach. Patients may present in extremis due to compression of the IVC and right atrium by the dilated stomach. NG decompression can relieve the tension physiology. Patient often requires aggressive repletion of intravascular volume lost to vomiting and fluid shifts. This may improve the patient's clinical status and to allow for additional preoperative optimization of an often frail, elderly patient. It may also facilitate diagnostic maneuvers including CT scan or barium upper GI study. In the setting of obstruction or gastric volvulus, however, passage of the NG tube may be difficult [8].

Patients may also present with signs of systemic sepsis with or without respiratory failure and pleural effusion, which suggests severe gastric ischemia or perforation. In these cases, NG decompression should be attempted, the patient aggressively resuscitated, broad-spectrum antibiotics administered, and preparations made expeditiously for operation. In these situations, the gastric volvulus can lead to gastric venous engorgement, which may also result in significant GI hemorrhage. Consequently, blood products may be required during the patient's resuscitation.

PEH can also be complicated by Cameron lesions, gastric erosions which occur at the constriction point as the herniated stomach passes through the diaphragmatic hiatus. They are thought to occur as a result of mechanical trauma at the hiatus, in combination with mucosal damage from acid exposure. These occur in about 3–5% of all patients with HH, though incidence increases with the size of the hernia from about 1% in hernias smaller than 3 cm to more than 12% in those larger than 5 cm. They are also associated with NSAID use. Most often, these lesions present with gastrointestinal bleeding, rather than pain. About 40% will present with overt bleeding and about 35% with clinically occult bleeding. In total, bleeding complicates over half of all Cameron lesions. Initial therapy for GI hemorrhage from Cameron's ulcers is similar to that for upper GI hemorrhage from other sources and includes appropriate resuscitation with crystalloid and blood products, administration of high-dose PPI, correction of any coagulopathy, and prompt endoscopy. In cases of GI hemorrhage resulting from Cameron's ulcers, surgical correction of the hiatal hernia is also recommended in medically fit patients, especially those with a large HH or paraesophageal component [9].

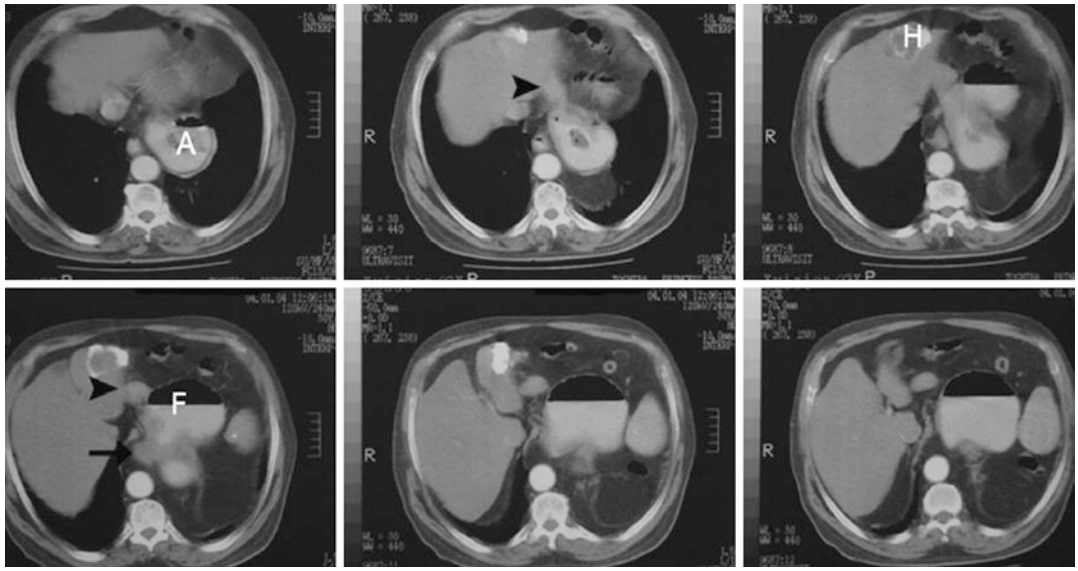

Fig. 14.3 Helical axial CT images of the lower chest and upper abdomen show the gastric fundus (F) is normally located in the upper abdomen and the gastric antrum (A) is located superiorly in left hemithorax. Arrow indicates the gastroesophageal junction, and the arrowhead indicates the gastric pylorus. Incidentally noted is a calcified Hydatid cyst (H) in left liver lobe. (Al-Balas et al. [7])

Conclusion

Hiatal hernias are common and often asymptomatic. Their etiology is multifactorial but largely related to chronically elevated intra-abdominal pressure. Advanced paraesophageal hernias are rare and may be complicated by incarceration or gastric volvulus with subsequent ischemic necrosis and perforation if not recognized and treated promptly. This may be difficult as initial presenting symptoms are often vague and may rapidly progress to cardiovascular collapse or sepsis and respiratory failure. They may also be complicated by gastrointestinal hemorrhage from Cameron lesions, which often presents as overt bleeding. Initial management of incarceration or volvulus is resuscitation and rapid gastric decompression. If necrosis or perforation is suspected, antibiotics are administered. Bleeding is temporized initially with acid suppression, resuscitation, and endoscopic therapies. Definitive management of complicated paraesophageal hernia is surgical, and perhaps the best strategy of all is repair of symptomatic hernias in fit patients prior to the development of serious complications.

References

1. Oleynikov D, Jolley J. Paraesophageal hernia. Surg Clin N Am. 2015;95:555–65.
2. Roman S, Kahrilas P. The diagnosis and management of hiatus hernia. BMJ. 2014;349:g6154.
3. Sihvo EI, et al. Fatal complications of adult paraesophageal hernia: a population-based study. J Thorac Cardiovasc Surg. 2009;137:419–24.
4. Mandaliya R, Amberker D, Breckenridge J. Biliary obstruction from paraesophageal hernia. Clin Gastroenterol Hepatol. 2014;12:e99.
5. Kafka NJ, Leitman IM, Tromba J. Acute pancreatitis secondary to incarcerated paraesophageal hernia. Surgery. 1994;115:653–5.
6. Serralheiro P, Kumar B, Cheong E. Splenic rupture caused by giant paraesophageal hernia. Ann Thorac Surg. 2015;100:2343.
7. Al-Balas H, Hani MB, Omari H. Radiological features of acute gastric volvulus in adult patients. Clin Imaging. 2010;34:344–7.
8. Dunn DB, Quick G. Incarcerated paraesophageal hernia. Am J Emerg Med. 1990;8:36–9.
9. Gray DM II, et al. Cameron lesions in patients with hiatal hernias: prevalence, presentation, and outcome. Dis Esophagus. 2015;28:448–52.

15 Surgical Management of Complicated Paraesophageal Hernias

Angela M. Kao and Paul D. Colavita

Introduction

The acute surgical management of complicated paraesophageal hernias (PEH) remains technically challenging for many surgeons. Nonelective repairs are associated with increased perioperative risk, particularly in elderly, frail patients due to the presence of other medical comorbidities [1–3]. Acute presentation with complications of strangulation, perforation, and severe ulceration causing gastrointestinal (GI) hemorrhage has been shown to significantly increase patient morbidity, with a recently reported mortality rate of 5.5% after all emergent paraesophageal hernia repairs (PEHR) [4]. Few studies have specifically evaluated the options for surgical management of complicated PEH, including the utility of minimally invasive approaches in the emergent setting. Furthermore, damage control options in the contaminated setting of necrosis or perforation remain poorly described, yet may be life-saving temporizing measures in medically frail patients or cases where surgeons lack adequate expertise to perform a definitive repair.

Indications for Repair

Although the pendulum has recently shifted toward conservative management for asymptomatic and mildly symptomatic patients [5], surgical consultation is warranted for symptomatic patients, often with consideration for surgical repair in the semi-elective or elective setting. Acute presentation with intractable or obstructive symptoms should raise concern for potential complications associated with PEH that warrant inpatient admission and surgical evaluation for urgent operative treatment. Progression from incarceration or volvulus to acute strangulation is characterized by vascular compromise of the stomach or other organs that can result in mucosal ischemia, gangrene, and impending perforation. Emergent complications associated with PEH, such as perforation and necrosis, can be life-threatening and require immediate intervention [6, 7].

In addition to symptomatic patients, PEHR is often recommended for surgically fit patients with type IV PEH or massive PEH, as these are rarely asymptomatic and symptoms of dysphagia and early satiety tend to increase over time [8]. Furthermore, patients with large PEH often have accompanying respiratory complaints due

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to the reduction in thoracic volume. Although the degree of PEH-related dyspnea is often underappreciated and attributed to other patient comorbidities, the benefits of PEHR for respiratory symptoms have been studied [9]. Carrott et al. evaluated 120 patients with large PEH and demonstrated improved pulmonary function tests (PFT) after PEHR with a correlation between degree of PFT improvement and amount of intrathoracic stomach [10]. Additionally, among patients with large PEH and preoperative dyspnea, 75% reported complete relief of respiratory symptoms after PEHR [10].

Although Cameron ulcers are more likely to manifest as occult gastrointestinal bleeding (GIB) and chronic anemia, acutely bleeding ulcers can occasionally cause massive hemorrhage and are unlikely to be controlled with endoscopic therapies alone [11]. In one case series of 25 patients with severe upper gastrointestinal hemorrhage secondary to Cameron ulcers, surgery was performed in 10 patients who failed initial medical therapy, including 3 patients who required rehospitalization for rebleeding [12]. Clinically significant GIB originating from Cameron ulcers occurs with greater frequency when patients have multiple ulcerations in a large hiatal hernia; however, their location at the hernia neck often leads to missed endoscopic detection [12].

In patients with linear gastric erosions or ulcers associated with a paraesophageal hernia, surgical indications include massive GI hemorrhage, failure of ulcer to heal, or recurrent ulceration [13]. Typically medical treatment for Cameron ulcers is initiated first, beginning with high-dose PPIs and iron supplementation, with surgery reserved for patients who fail medical therapy [12, 14]. Early elective surgical intervention is also recommended in high-risk patients on steroids or NSAIDs with medically refractory ulcers. Paraesophageal hernia repair has also been associated with improved outcomes in patients with chronic anemia [9, 15–17]. In one study of 77 patients with giant paraesophageal hernia, mean hemoglobin level improved from preoperative levels of 9.6–13.6 mg/dL at 1-year follow-up [15]. Similarly, Hayden et al. demonstrated occult bleeding with chronic anemia resolved in 90% of patients after PEHR [17].

Timing of Repair

With no clear existing guidelines or consensus on optimal timing of repair, complicated PEH are often treated on an individual case-by-case basis with management guided by presence of irreversible tissue damage and patient hemodynamic stability [18]. Initial management in patients with acutely symptomatic PEH should always include an immediate attempt at nasogastric tube placement in addition to fluid resuscitation and correction of electrolytes. In cases where the nasogastric tube is unable to be placed, use of endoscopy may facilitate placement of the nasogastric tube and gastric detorsion, as well as enable evaluation for mucosal ischemia [19, 20].

Emergent repair is indicated in patients with hemodynamic instability and need for vasopressor support. Patients with clinical suspicion of gastric necrosis or perforation often present with systemic signs of sepsis and require an immediate operation to obtain source control, while patients presenting with hemorrhagic shock secondary to acutely bleeding ulcers also require emergent surgical intervention, as endoscopic hemostasis is unlikely. Early intervention within 24 hours in patients presenting with acute symptoms has been associated with reduced patient morbidity, including lower rates of postoperative sepsis, pulmonary edema, and shorter hospital length of stay (LOS) [21]. In patients with perforated ulcer associated with PEH, delayed time to surgical treatment has been shown to significantly increase patient mortality with rates reported as high as 60% [22, 23].

Urgent surgery is warranted in patients where nasogastric tube insertion or decompression is unsuccessful due to significant increased morbidity associated with delayed repair [19]. One management algorithm (Fig. 15.1), proposed by Bawahab et al., utilized an upper GI contrast study to determine timing of treatment for clinically stable patients with acute presentation. Failure of contrast passage into the duodenum

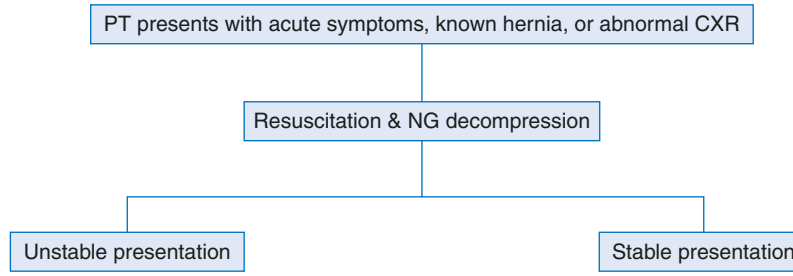

Fig. 15.1 Algorithm from Bawahab et al.

after nasogastric decompression was an indication for urgent repair, while patients who had passage of contrast had their repair delayed to the semi-elective setting within the same hospitalization [18].

In stable patients without evidence of ischemia or perforation, successful nasogastric decompression may relieve partial strangulation and decrease pulmonary aspiration risk, allowing for surgery to be temporarily postponed until the patient is medically optimized [18, 22, 24]. In one study by Kohler et al., patients who underwent semi-elective repair within the same hospitalization had improved outcomes compared to those requiring emergency repair [19]. Similarly, in cases where a surgeon with advanced expertise is not readily available, decompression may allow for transfer to a surgery center with appropriate surgeon expertise in complex foregut surgery.

Surgical Approach

Laparoscopy is increasingly considered the preferred approach for urgent or emergent cases, and in one recent analysis of surgeon practices, 70% of urgent/emergent PEHR were performed laparoscopically [25]. The majority of strangulated PEH in stable patients can be repaired laparoscopically, with established safety and efficacy [26, 27]. For surgeons with experience in complex laparoscopic foregut surgery including antireflux procedures, Schiergens et al. also support its use as the initial surgical approach for stable patients with ischemia or perforation [28]. Additionally, in experienced hands, laparoscopy has been established as an efficacious approach for patients with acutely bleeding ulcers [27, 29].

Compared to the traditional open surgical approach with mortality rates previously reported as high as 56%, laparoscopic repair is associated with reduced patient morbidity, including respiratory complications, decreased pain, and shorter LOS [30, 31]. Comparing transthoracic and transabdominal open approaches, available data does not demonstrate a mortality difference between transabdominal and transthoracic approaches, but morbidity is felt to be higher with a transthoracic approach [32].

Other advantages of laparoscopic approach include better visualization of the hiatus and mediastinum that largely facilitates esophageal mobilization and ease of performing a fundoplication [33]. As such, concomitant antireflux procedure in the urgent/emergent setting is more commonly performed with laparoscopic approach compared to open, likely reflecting improved patient stability and ease of access with laparoscopy [25].

However, a low threshold for conversion to laparotomy should be maintained, particularly in damage control settings [34, 35]. An open surgical approach remains the recommended approach for unstable patients and is recommended for surgeons lacking adequate laparoscopic expertise [6, 18, 28, 36]. Other contraindications to laparoscopic approach include patient inability to tolerate pneumoperitoneum, and gross peritoneal or mediastinal contamination. In patients with persistent hemodynamic instability, consideration should be given to a damage control operation, with definitive repair postponed until the patient is clinically stable.

Comparisons of open transthoracic and transabdominal approaches have demonstrated similar recurrence rates after PEHR, and thus, preferred

approach is largely based on surgeon preference [11]. Advantages of the open transthoracic approach include superior access for mobilization of the esophagus and ability to create a tension-free repair [37]. In rare situations where maximum exposure is required, a left thoracoabdominal incision can be performed, although it is associated with significant pain and morbidity [38]. Although a left thoracotomy incision may be preferred in patients with a hostile abdomen, a transabdominal approach via laparotomy incision may enable detorsion of gastric volvulus or reduction of an obstructed, distended stomach. Additionally, in cases with a high index of suspicion for perforation, pleural or mediastinal contamination significantly increases risk of respiratory complications including pneumonia, empyema, and mediastinitis. Thus, laparotomy often is the preferred approach over thoracotomy for patients with suspected ischemia or perforation. Disadvantages of laparotomy include difficult access to the mediastinum and diaphragmatic hiatus, especially in obese patients.

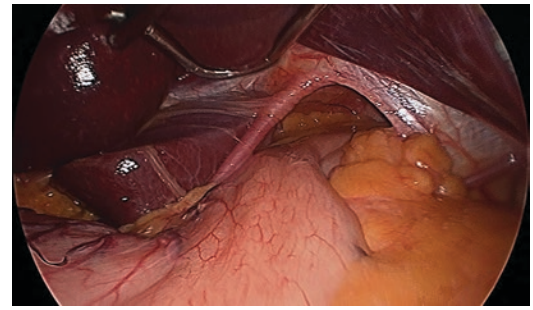

Fig. 15.2 Paraesophageal hernia

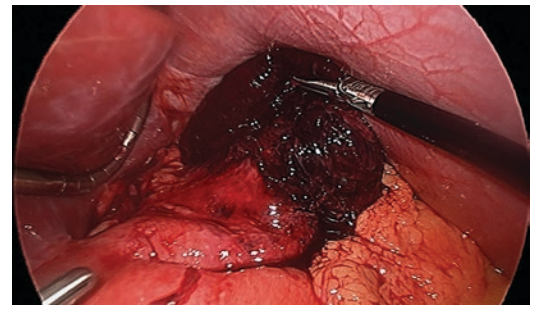

Fig. 15.3 Ischemic fundus in traumatic diaphragmatic hernia

Operative Management

Unlike optimal repair techniques described in the elective setting, the primary operative goals of complicated PEHR center on hernia reduction, relief of acute obstructive symptoms, and resection of ischemic tissue [11, 37]. Surgical treatment begins with attempted reduction of the migrated stomach to its intra-abdominal position and assessment for tissue viability (Fig. 15.2). Prolonged venous compression can result in thrombosis of the mesenteric vessels, resulting in irreversible tissue damage after restoration of circulation [36]. In cases where gastric necrosis or gangrene is present, limited gastric resection of ischemic areas is warranted [6] (Fig. 15.3). Wide drainage is critical for source control particularly in patients with gross contamination, perforation, or devitalized tissue. These cases can be approached from a laparoscopic, transabdominal, or transthoracic approach. The benefits of laparoscopy are similar to those in uncomplicated cases; however, familiarity with foregut anatomy and minimally invasive techniques is paramount, as the anatomy and visualization may be distorted from any contamination.

Techniques for Repair

Regardless of surgical approach, techniques for successful definitive PEHR are aimed at reducing hernia recurrence and include reduction of the hernia sac and herniated organs, esophageal mobilization (Fig. 15.4), hiatal cruroplasty (Fig. 15.5), and intra-abdominal fixation of the migrated stomach using tailored fundoplication or gastropexy. Additional surgical maneuvers including Collis gastroplasty and prosthetic mesh reinforcement (Fig. 15.6) are also performed as necessary to reduce axial and radial tension forces on the hiatal repair. Closure of the hiatus is performed using permanent suture and may include a combination of anterior (Fig. 15.7) and posterior crural sutures (Fig. 15.5). In patients with large hiatal defects where reapproximation of the

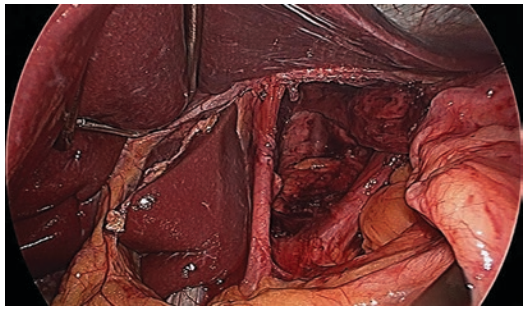

Fig. 15.4 Standard paraesophageal hernia after mediastinal dissection and reduction of hernia sac

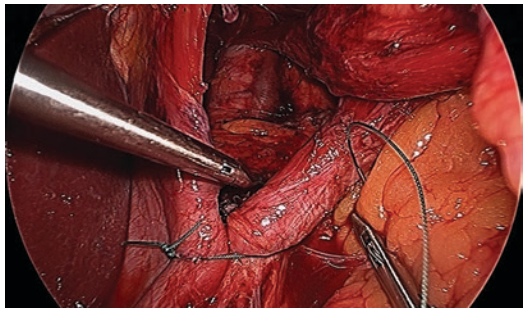

Fig. 15.5 Sutured closure of hiatus

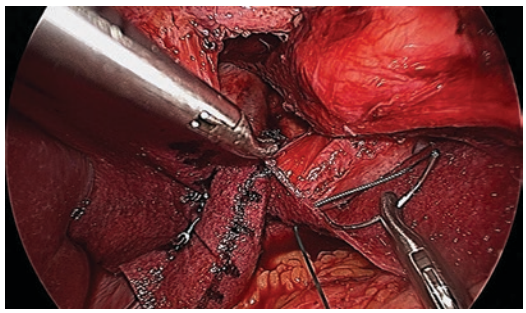

Fig. 15.6 Mesh reinforcement of hiatus, mesh secured simultaneously with hiatal closure using horizontal mattress sutures

crura is difficult, a diaphragmatic relaxing incision can also be performed to reduce excessive radial tension [39]. Most surgeons typically start with relaxing incisions in the right diaphragmatic crus; however, a left diaphragmatic relaxing incision can also be performed if crural mobilization is insufficient [40].

Following relocation of the stomach to its correct intra-abdominal position, a tailored fundoplication is often performed during PEHR, particularly in patients with preoperative symptoms of reflux [8]. Some believe that a fundoplication helps anchor the newly reduced stomach below the diaphragm, and other benefits of fundoplication include restoring LES competency and reducing postoperative reflux symptoms, with one study reporting abnormal esophageal acid exposure in 39% of patients without fundoplication [41]. In patients with foreshortened esophagus, addition of a Collis gastroplasty can increase the length of the intra-abdominal esophagus, reducing axial tension on the repair and risk of hernia recurrence [39]. However, the benefits of fundoplication should be weighed against the potential risks of gastroplasty staple line leak and ischemic stricture, particularly in unstable patients with reduced mucosal perfusion. Additionally, performance of a fundoplication prolongs the duration of surgery and general anesthesia, which can pose significantly detrimental consequences in elderly or frail patients with reduced cardiovascular reserve. In one study evaluating laparoscopic PEHR in elective and emergent settings, Parker et al. observed significantly fewer fundoplications and shorter operative times in acutely symptomatic patients [26]. In frail or debilitated patients with insufficient length of intra-abdominal esophagus after mobilization, gastrostomy tube placement is often performed to allow for postoperative decompression and enteral feeding access.

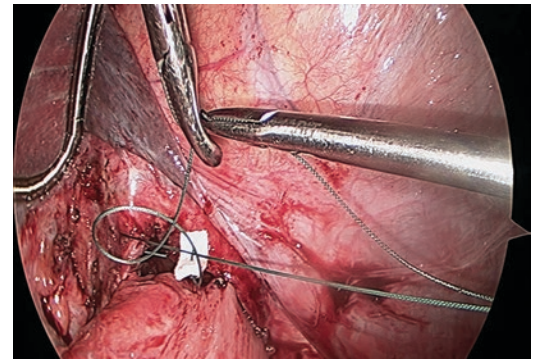

Fig. 15.7 Anterior hiatal closure can be performed when necessary. Pictured: hiatal hernia repair after prior esophagectomy. Anterior hiatal closure can avoid unnecessary risk to gastric conduit blood supply, as long as hiatus is amenable to anterior closure

Hernia sac dissection and excision remains a controversial topic in PEHR. Dissection of the hernia sac off the crura and mediastinum helps in restoring intra-abdominal configuration of the stomach, while hernia sac excision allows for improved esophageal mobilization and better performance of concomitant antireflux procedure [8, 11]. One study of elective PEHR demonstrated an association between failure of hernia sac excision with increased early PEH recurrence in 20% of patients within the first 2 months [42]. However, mediastinal dissection of the hernia sac is technically challenging in large, chronic PEH due to fusion of the sac to surrounding structures and associated with increased risk of iatrogenic injuries including damage to the vagal nerves [11]. Unlike patients who undergo elective PEHR, excision of the peritoneal hernia sac is not recommended in the context of ulcer perforation or necrotic tissue given the risk of pleural and mediastinal contamination [43]. Partial sac excision may reduce the potential morbidity of an intraoperative injury and be a feasible alternative in high-risk or frail patients with limited physiologic reserve [44].

Prosthetic mesh for hiatal reinforcement has also been described as an adjunct for PEHR in the elective setting, particularly in patients with large hiatal defects [39, 45, 46]. However, the use of synthetic mesh for complicated PEHR is generally not recommended, particularly in the contaminated settings of necrosis and perforation given the increased risk of infectious complications and subsequent abscess formation [47, 48]. Biologic meshes have been used in contaminated settings and have been associated with reduced short-term recurrence; however they may not significantly affect long-term recurrence rates [49].

In patients with ulceration, therapeutic endoscopy is rarely successful in achieving hemostasis, although one study by Lin et al. described the successful use of endoscopic band ligation in a patient with life-threatening hemorrhage [50]. The need for definitive ulcer treatment in addition to PEHR is also controversial. While some surgeons advocate for definitive ulcer treatment including gastric resection or vagotomy and drainage [13], others have suggested that ulceration results from erosion of the hernia sac and consequently is resolved by PEHR alone [43]. In the largest study of hiatal hernia related ulcers, Boyd et al. observed a poor response to medical treatment with improved ulcer resolution after surgical treatment [51].

Perforations associated with hiatal hernia can manifest as a contained perforation within the lesser sac or result in free peritoneal contamination causing diffuse peritonitis. Surgical management differs slightly from strangulated PEH or non-perforated ulceration. The primary operative goal is to obtain source control with resection of nonviable tissue and wide drainage. After irrigation and excision of devitalized tissue, repair or formal resection of the perforated area is performed. Various surgical techniques for management of perforation have been described, including partial gastrectomy using a linear stapler for larger perforations [52] and double-layered omental patch repair for smaller perforated ulcers [47]. In addition to omental buttresses, the use of fundoplication using the mobilized stomach to reinforce the gastrotomy repair has also been reported [43].

The role of definitive PEHR in the emergent setting is largely based on surgeon expertise as well as patient's clinical presentation and operative findings. Pol et al. reported a patient with perforated prepyloric ulcer associated with a paraesophageal hernia who underwent an omental patch repair and intrathoracic drainage given their septic presentation [47]. Although the hiatal hernia was identified, the surgeons elected not to perform a herniorrhaphy or mesh repair of the hiatus given the anticipated risk of infection and subsequent abscess formation.

Damage Control Versus Definitive Care

Given the high acuity of complicated PEH patients and technical complexity of surgical repair, the role for definitive management in this setting remains controversial. As such, options for damage control surgery for patients with complicated PEH can be temporizing and life-saving in

settings where patient comorbidities or surgeon expertise may prohibit definitive repair.

Damage control strategies for complicated PEH largely focus on reduction of herniated organs, debridement of necrotic tissue, and closure of perforated viscus. Others have also described excision of devitalized tissue at the perforation site with placement of a Stamm gastrostomy tube to provide anterior abdominal wall fixation and means for decompression or enteral access [43]. In patients requiring resection of nonviable esophageal or gastric tissue, partial esophagogastrectomy with proximal diversion and placement of distal feeding access can be performed urgently, followed by planned delayed reconstruction. Similarly, patients can undergo immediate hernia reduction with definitive PEHR delayed to a semi-elective or elective setting.

Anterior gastropexy is another technique used in the damage control setting to help anchor the stomach in its intra-abdominal location and is often described in high-risk patients as an alternative means to fundoplication [53–56]. Higashi et al. described the safety and efficacy of hiatal repair with laparoscopic anterior gastropexy in elderly patients with PEH and reported minimal perioperative complications [53]. Gastropexy alone without diaphragmatic hiatus closure has also been described as a salvage technique, although high recurrence rates should be expected in this setting, with one study reporting 23% recurrence within 3 months [57]. Gastropexy can be performed using suture fixation, T-fasteners, or with gastrostomy tube placement in patients also requiring enteral feeding access [44, 53, 54]. When anterior gastropexy is performed, the authors routinely place three transfascial sutures along the greater curve of the stomach (Figs. 15.8, 15.9, 15.10, 15.11, and 15.12). The stomach is drawn up to the abdominal wall with decreased laparoscopic insufflation to identify the appropriate location for gastropexy sutures (Fig. 15.8). Permanent sutures are then placed with seromuscular bites, careful to avoid mucosal entry (Fig. 15.9). Both ends of each suture are then drawn through the abdominal wall individually using a suture passer (Fig. 15.10). The sutures are not tied until the end of the procedure. After all three sutures are placed (Fig. 15.11), endoscopy is used to confirm no mucosal penetration of the sutures, in hopes of avoiding gastric fistula. The sutures are then drawn taught (Fig. 15.12), confirming appropriate location and orientation of the sutures. When the procedure is complete, the abdomen is desufflated, and the sutures are tied. Excessive tension with knot tying is avoiding in

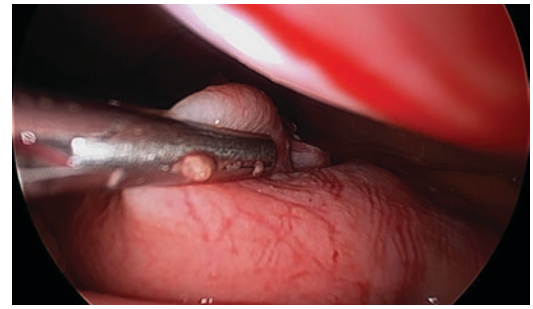

Fig. 15.8 Assessing appropriate position of gastropexy sutures along greater curve

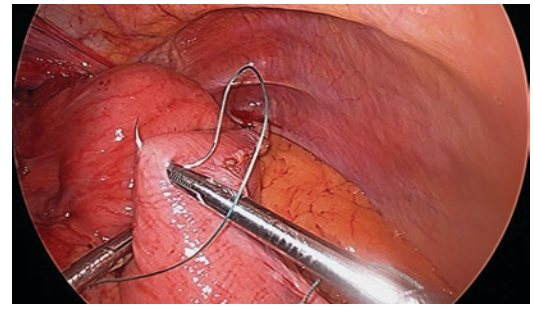

Fig. 15.9 Interrupted gastropexy suture (endoscopy performed to ensure suture is not full thickness)

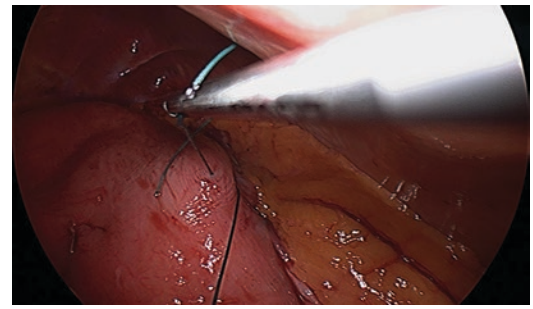

Fig. 15.10 Suture passer used to draw each end of suture through transfascial stab incision

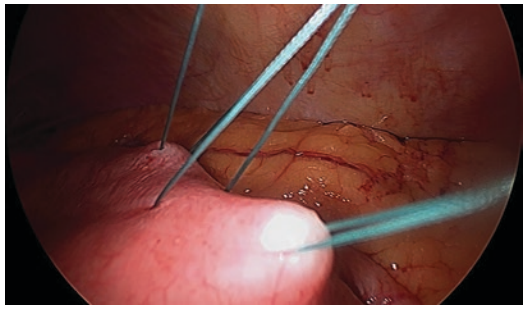

Fig. 15.11 Three permanent gastropexy sutures placed

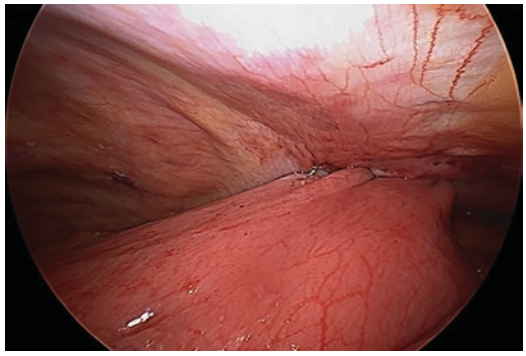

Fig. 15.12 View from right upper quadrant demonstrating suture position prior to tying transfascial sutures

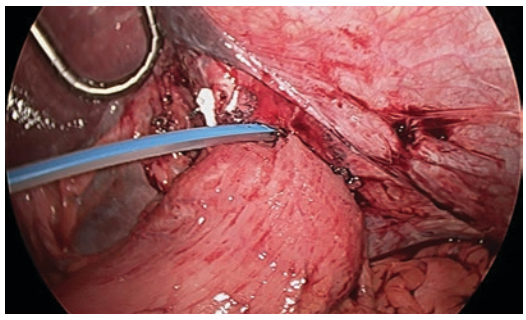

Fig. 15.13 The authors routinely leave a mediastinal drain in elective and emergent paraesophageal hernia repairs. This can drain seromas and also be used to monitor drain fluid for amylase to detect leak. Pictured: hiatal hernia repair after prior esophagectomy

hopes of preventing local ischemia from the gastric compression by the knot.

Placement of a surgical or percutaneous endoscopic gastrostomy (PEG) should also be considered in elderly or debilitated patients with foreshortened esophagus as an alternative to Collis gastroplasty. In such patients where risk of delayed gastric emptying is high, gastrostomy tube provides means for gastric decompression and enteral access. In the damage control, emergent, or elective setting, the authors routinely place drains. In the elective setting, a mediastinal drain can prevent or reduce seroma formation. In the emergent or damage control setting, drain fluid can be tested for amylase to detect a leak (Fig. 15.13).

Summary

In patients with paraesophageal hernias, acute presentation with intractable obstructive symptoms, systemic sepsis, or hemodynamic instability raises clinical suspicion for dreaded complications of hemorrhage, strangulation, necrosis, or perforation. Emergent surgery is required, and early intervention has been shown to improve postoperative outcomes. In clinically stable patients with successful nasogastric decompression, repair can be temporarily delayed to a semi-elective setting allowing for medical optimization or transfer to centers with advanced laparoscopic expertise. Initial operative management should include reduction of herniated organs and resection of ischemic or devitalized tissue. Perforations should be repaired or formally resected, with appropriate drainage. In unstable patients, options for damage control include delaying enteral reconstruction or definitive PEHR until patients can be stabilized. Use of anterior gastropexy and gastrostomy tube placement can be life-saving alternatives to fundoplication and Collis gastroplasty in poor surgical candidates, including medically frail patients.

References

1. Ballian N, Luketich JD, Levy RM, Awais O, Winger D, Weksler B, Landreneau RJ, Nason KS. A clinical prediction rule for perioperative mortality and major morbidity after laparoscopic giant paraesophageal hernia repair. J Thorac Cardiovasc Surg. 2013;145:721–9. https://doi.org/10.1016/j.jtcvs.2012.12.026.

2. Tam V, Luketich JD, Winger DG, Sarkaria IS, Levy RM, Christie NA, Awais O, Shende MR, Nason KS. Non-elective paraesophageal hernia repair portends worse outcomes in comparable patients: a propensity-adjusted analysis. J Gastrointest Surg. 2017;21:137–45. https://doi.org/10.1007/s11605-016-3231-y.
3. Poulose BK, Gosen C, Marks JM, Khaitan L, Rosen MJ, Onders RP, Trunzo JA, Ponsky JL. Inpatient mortality analysis of paraesophageal hernia repair in octogenarians. J Gastrointest Surg. 2008;12:1888–92. https://doi.org/10.1007/s11605-008-0625-5.
4. Jassim H, Seligman JT, Frelich M, Goldblatt M, Kastenmeier A, Wallace J, Zhao HS, Szabo A, Gould JC. A population-based analysis of emergent versus elective paraesophageal hernia repair using the Nationwide Inpatient Sample. Surg Endosc. 2014;28:3473–8. https://doi.org/10.1007/s00464-014-3626-3.
5. Stylopoulos N, Gazelle GS, Rattner DW. Paraesophageal hernias: operation or observation. Ann Surg. 2002;236:492–500.; discussion 500–1. https://doi.org/10.1097/01.SLA.0000029000.06861.17.
6. Kohn GP, Price RR, DeMeester SR, Zehetner J, Muensterer OJ, Awad Z, Mittal SK, Richardson WS, Stefanidis D, Fanelli RD. Guidelines for the management of hiatal hernia. Surg Endosc. 2013;27:4409–28. https://doi.org/10.1007/s00464-013-3173-3.
7. Sihvo EI, Salo JA, Räsänen JV, Rantanen TK. Fatal complications of adult paraesophageal hernia: a population-based study. J Thorac Cardiovasc Surg. 2009;137:419–24. https://doi.org/10.1016/j.jtcvs.2008.05.042.
8. Lebenthal A, Waterford SD, Fisichella PM. Treatment and controversies in paraesophageal hernia repair. Front Surg. 2015;2:1–6. https://doi.org/10.3389/fsurg.2015.00013.
9. Mekhael M, El-Hussuna A. Acute abdomen in a patient with paraesophageal hernia, resulting in acute compromised respiratory function: a case report. Int J Surg Case Rep. 2017;31:180–3. https://doi.org/10.1016/j.ijscr.2017.01.051.
10. Carrott PW, Hong J, Kuppusamy M, Kirtland S, Koehler RP, Low DE. Repair of giant paraesophageal hernias routinely produces improvement in respiratory function. J Thorac Cardiovasc Surg. 2012;143:398–404. https://doi.org/10.1016/j.jtcvs.2011.10.025.
11. Sihag S, Rattner DW. Management of complicated and strangulated hiatal hernias. In: Di Saverio S, Catena F, Ansaloni L, Coccolini F, Velmahos G, editors. Acute care surgery handbook, vol. 2. Cham: Springer; 2016. p. 65–90.
12. Camus M, Jensen DM, Ohning GV, Kovacs TO, Ghassemi KA, Jutabha R, Machicado GA, Dulai GS, Hines OJ. Severe upper gastrointestinal hemorrhage from linear gastric ulcers in large hiatal hernias: a large prospective case series of Cameron ulcers. Endoscopy. 2013;45:397–400. https://doi.org/10.1055/s-0032-1326294.
13. Otsuka Y, Nara S, Ito K, Nakajima K, Mieno H, Konishi T. Perforated duodenal ulcer associated with an incarcerated hiatal hernia: report of a case. Surg Today. 2002;32:1085–7. https://doi.org/10.1007/s005950200219.
14. Hirshberg A, Schein M. Gastric ulcer in diaphragmatic hernia. Surg Gynecol Obstet. 1992;174:165–71.
15. Carrott PW, Markar SR, Hong J, Kuppusamy MK, Koehler RP, Low DE. Iron-deficiency anemia is a common presenting issue with giant paraesophageal hernia and resolves following repair. J Gastrointest Surg. 2013;17:858–62. https://doi.org/10.1007/s11605-013-2184-7.
16. Haurani C, Carlin AM, Hammoud ZT, Velanovich V. Prevalence and resolution of anemia with paraesophageal hernia repair. J Gastrointest Surg. 2012;16:1817–20. https://doi.org/10.1007/s11605-012-1967-6.
17. Hayden JD, Jamieson GG. Effect on iron deficiency anemia of laparoscopic repair of large paraesophageal hernias. Dis Esophagus. 2005;18:329–31. https://doi.org/10.1111/j.1442-2050.2005.00508.x.
18. Bawahab M, Mitchell P, Church N, Debru E. Management of acute paraesophageal hernia. Surg Endosc Other Interv Tech. 2009;23:255–9. https://doi.org/10.1007/s00464-008-0190-8.
19. Köhler G, Koch OO, Antoniou SA, Emmanuel K, Pointner R. "Acute intrathoracic stomach!" How should we deal with complicated type IV paraesophageal hernias? Hernia. 2015;19:627–33. https://doi.org/10.1007/s10029-014-1285-x.
20. Light D, Links D, Griffin M. The threatened stomach: management of the acute gastric volvulus. Surg Endosc. 2016;30:1847–52. https://doi.org/10.1007/s00464-015-4425-1.
21. Bhayani NH, Kurian AA, Sharata AM, Reavis KM, Dunst CM, Swanstrom LL. Wait only to resuscitate: early surgery for acutely presenting paraesophageal hernias yields better outcomes. Surg Endosc Other Interv Tech. 2013;27:267–71. https://doi.org/10.1007/s00464-012-2436-8.
22. Ekelund M, Ribbe E, Willner J, Zilling T. Perforated peptic duodenal ulcer in a paraesophageal hernia--a case report of a rare surgical emergency. BMC Surg. 2006;6:1. https://doi.org/10.1186/1471-2482-6-1.
23. Trainor D, Duffy M, Kennedy A, Glover P, Mullan B. Gastric perforation secondary to incarcerated hiatus hernia: an important differential in the diagnosis of central crushing chest pain. Emerg Med J. 2007;24:603–4. https://doi.org/10.1136/emj.2007.048777.
24. Hill LD. Incarcerated paraesophageal hernia: a surgical emergency. Am J Surg. 1973;126:286–91. https://doi.org/10.1016/S0002-9610(73)80165-5.
25. Klinginsmith M, Jolley J, Lomelin D, Krause C, Heiden J, Oleynikov D. Paraesophageal hernia repair in the emergency setting: is laparoscopy with the addition of a fundoplication the new gold standard? Surg Endosc Other Interv Tech. 2016;30:1790–5. https://doi.org/10.1007/s00464-015-4447-8.

26. Parker DM, Rambhajan A, Johanson K, Ibele A, Gabrielsen JD, Petrick AT. Urgent laparoscopic repair of acutely symptomatic PEH is safe and effective. Surg Endosc Other Interv Tech. 2013;27:4081–6. https://doi.org/10.1007/s00464-013-3064-7.
27. Pierre AF, Luketich JD, Fernando HC, Christie NA, Buenaventura PO, Litle VR, Schauer PR, Pearson FG, Demeester SR. Results of laparoscopic repair of giant paraesophageal hernias: 200 consecutive patients. Ann Thorac Surg. 2002;74:1909–16. https://doi.org/10.1016/S0003-4975(02)04088-2.
28. Schiergens TS, Thomas MN, Hüttl TP, Thasler WE. Management of acute upside-down stomach. BMC Surg. 2013;13 https://doi.org/10.1186/1471-2482-13-55.
29. Andujar JJ, Papasavas PK, Birdas T, Robke J, Raftopoulos Y, Gagné DJ, Caushaj PF, Landreneau RJ, Keenan RJ. Laparoscopic repair of large paraesophageal hernia is associated with a low incidence of recurrence and reoperation. Surg Endosc Other Interv Tech. 2004;18:444–7. https://doi.org/10.1007/s00464-003-8823-4.
30. Dallemagne B, Quero G, Lapergola A, Guerriero L, Fiorillo C, Perretta S. Treatment of giant paraesophageal hernia: pro laparoscopic approach. Hernia. 2017:1–11. https://doi.org/10.1007/s10029-017-1706-8.
31. Latzko M, Borao F, Squillaro A, Mansson J, Barker W, Baker T. Laparoscopic repair of paraesophageal hernias. JSLS. 2014;18:e2014.00009. https://doi.org/10.4293/JSLS.2014.00009.
32. Davis SS. Current controversies in paraesophageal hernia repair. Surg Clin N Am. 2008;88(5):959–78. https://doi.org/10.1016/j.suc.2008.05.005.
33. Oelschlager BK, Petersen RP, Brunt LM, Soper NJ, Sheppard BC, Mitsumori L, Rohrmann C, Swanstrom LL, Pellegrini CA. Laparoscopic paraesophageal hernia repair: defining long-term clinical and anatomic outcomes. J Gastrointest Surg. 2012;16:453–9. https://doi.org/10.1007/s11605-011-1743-z.
34. Katkhouda N, Mavor E, Achanta K, Friedlander MH, Grant SW, Essani R, Mason RJ, Foster M, Mouiel J. Laparoscopic repair of chronic intrathoracic gastric volvulus. Surgery. 2000;128:784–90. https://doi.org/10.1067/msy.2000.108658.
35. Koger K, Stone J. Laparoscopic reduction of acute gastric volvulus. Am Surg. 1993;59:325–8.
36. Keshishian JM, Cox PA. Diagnosis and management of strangulated diaphragmatic hernias. Surg Gynecol Obstet. 1962;115:626–32.
37. Andolfi C, Jalilvand A, Plana A, Fisichella PM. Surgical treatment of paraesophageal hernias: a review. J Laparoendosc Adv Surg Tech A. 2016;26:778–83. https://doi.org/10.1089/lap.2016.0332.
38. Iqbal A, Naik R, Mohanan PK. Gastric gangrene due to a strangulated paraesophageal hernia—a case report. Indian J Surg. 2015;77:66–8. https://doi.org/10.1007/s12262-014-1135-1.
39. Cohn TD, Soper NJ. Paraesophageal hernia repair: techniques for success. J Laparoendosc Adv Surg Tech A. 2016;27:19–23. https://doi.org/10.1089/lap.2016.0496.
40. Greene CL, Demeester SR, Zehetner J, Worrell SG, Oh DS, Hagen JA. Diaphragmatic relaxing incisions during laparoscopic paraesophageal hernia repair. Surg Endosc Other Interv Tech. 2013;27:4532–8. https://doi.org/10.1007/s00464-013-3107-0.
41. Furnée EJB, Draaisma WA, Gooszen HG, Hazebroek EJ, Smout AJPM, Broeders IAMJ. Tailored or routine addition of an antireflux fundoplication in laparoscopic large hiatal hernia repair: a comparative Cohort study. World J Surg. 2011;35:78–84. https://doi.org/10.1007/s00268-010-0814-8.
42. Edye M, Salky B, Posner A, Fierer A. Sac excision is essential to adequate laparoscopic repair of paraesophageal hernia. Surg Endosc. 1998;12:1259–63.
43. Rakic S, Hissink RJ, Schiff BW. Perforation of gastric ulcer associated with paraesophageal hernia causing diffuse peritonitis. Dig Surg. 2000;17:83–4. https://doi.org/10.1159/000018806.
44. Arevalo G, Wilkerson J, Saxe J. Acute paraesophageal hernia: laparoscopic repair with adjunct T-fastener gastropexy for the high operative risk patient. Surg Laparosc Endosc Percutan Tech. 2018;28:123–7. https://doi.org/10.1097/SLE.0000000000000509.
45. Oelschlager BK, Pellegrini CA, Hunter JG, Brunt ML, Soper NJ, Sheppard BC, Polissar NL, Neradilek MB, Mitsumori LM, Rohrmann CA, Swanstrom LL. Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. J Am Coll Surg. 2011;213:461–8. https://doi.org/10.1016/j.jamcollsurg.2011.05.017.
46. Frantzides CT. A prospective, randomized trial of laparoscopic Polytetrafluoroethylene (PTFE) patch repair vs simple cruroplasty for large hiatal hernia. Arch Surg. 2002;137:649. https://doi.org/10.1001/archsurg.137.6.649.
47. Pol RA, Wiersma HW, Zonneveld BJGL, Schattenkerk ME. Intrathoracic drainage of a perforated prepyloric gastric ulcer with a type II paraoesophageal hernia. World J Emerg Surg. 2008;3:1–5. https://doi.org/10.1186/1749-7922-3-34.
48. Shiwani MH, Thornton MP. Supradiaphragmatic perforated duodenal ulcer in a giant hiatus hernia. Can J Surg. 2008;51(4):E89.
49. Antoniou SA, Pointner R, Granderath F-A, Kockerling F. The use of biological Meshes in Diaphragmatic defects - an evidence-based review of the literature. Front Surg. 2015;2:56. https://doi.org/10.3389/fsurg.2015.00056.
50. Lin C, Chen T, Ho W, CHen T. Endoscopic treatment of a Cameron lesion presenting as life-threatening gastrointestinal hemorrhage. J Clin Gastroenterol. 2001;33:423–4.
51. Boyd EJS, Periston JG, Russell RI, Wormsley KG. Hiatal hernial ulcers: clinical features and fol-

low-up. Postgrad Med J. 1991;67:900–3. https://doi.org/10.1136/pgmj.67.792.900.
52. Maruyama T, Fukue M, Imamura F, Nozue M. Incarcerated Paraesophageal Hernia associated with perforation of the fundus of the stomach: report of a case. Surg Today. 2001;31(5):454.
53. Higashi S, Nakajima K, Tanaka K, Miyazaki Y, Makino T, Takahashi T, Kurokawa Y, Yamasaki M, Takiguchi S, Mori M, Doki Y. Laparoscopic anterior gastropexy for type III/IV hiatal hernia in elderly patients. Surg Case Rep. 2017;3:45. https://doi.org/10.1186/s40792-017-0323-1.
54. Kercher KW, Matthews BD, Ponsky JL, Goldstein SL, Yavorski RT, Sing RF, Heniford BT. Minimally invasive management of paraesophageal herniation in the high-risk surgical patient. Am J Surg. 2001;182:510–4.
55. Ponsky J, Rosen M, Fanning A, Malm J. Anterior gastropexy may reduce the recurrence rate after laparoscopic paraesophageal hernia repair. Surg Endosc Other Interv Tech. 2003;17:1036–41. https://doi.org/10.1007/s00464-002-8765-2.
56. Naim HJ, Smith R, Gorecki PJ. Emergent laparoscopic reduction of acute gastric volvulus with anterior gastropexy. Surg Laparosc Endosc Percutan Tech. 2003;13:389–91.
57. Agwunobi AO, Bancewicz J, Attwood SEA. Simple laparoscopic gastropexy as the initial treatment of paraoesophageal hiatal hernia. Br J Surg. 1998;85:604–6. https://doi.org/10.1046/j.1365-2168.1998.00639.x.

Part VI

Choledocolithiasis

16 Gallstone Disease and the Timing of Cholecystectomy for Acute Cholecystitis and Gallstone Pancreatitis

Dylan Russell

Background

Prevalence and Incidence

The prevalence of gallstone disease varies dramatically. In the United States, the third National Health and Nutrition Examination Survey published in 1999 reported that more than 20 million persons have gallbladder disease with approximately one million new cases diagnosed per year. The prevalence was demonstrated to differ according to sex and ethnicity with non-Hispanic black men having the lowest prevalence (5.3%) and Mexican American women having the highest (26.7%). From 1890 to 1980, various autopsy and oral cholecystography studies determined the prevalence of cholelithiasis to range from extremely low rates in Africa (1%) and Asia (<7%) to much higher rates in Europe (up to 18.5%). This was similar in the Americas with reported rates by autopsy of 9.1%, 14.3%, 19.4%, and 26.6% in Chicago, USA; Mexico; São Paulo, Brazil; and Chile, respectively. The highest recorded prevalence in a single population was 48.6% in a sample of 596 Pima Indians in Phoenix, Arizona. The advent of ultrasound in the early 1980s allowed larger population-based studies to be conducted due to its less-invasive nature. These studies reported similar rates ranging between 5 and 30% depending on the study population. Factors that affect the prevalence and incidence of gallstone disease include *age*, *sex*, *obesity and rapid weight loss*, ethnicity, diet, physical inactivity, genetics, and medical comorbidities.

Cholecystectomy rates in the United States are three times higher in patients 65 years and older compared to the 15–44 age range and twice as high in females versus males (except in the age range 60–74). Obesity; high-calorie, low-fiber, high-fat diets; dyslipidemia; insulin resistance; rapid weight loss; and physical inactivity have all been demonstrated to cause hepatic secretion of supersaturated bile, hypersecretion of biliary mucin, gallbladder stasis, intestinal hypomotility, and faster cholesterol crystallization and solid crystal precipitation. Genetic factors are thought to be responsible for at least 30% of symptomatic gallstone disease. The incidence of gallstones in patients with affected first-degree relatives appears to be two or three times higher compared to patients without family history. Twin studies support the role of genetics in gallstone pathogenesis. The cited studies included only patients with symptomatic disease, and thus the actual role of genetics is likely even higher if asymptomatic gallstone disease is included.

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Natural History

Despite being common in the general population relatively few patients will progress to symptomatic cholelithiasis. Approximately two-thirds of gallstones are asymptomatic. Only about 2–3% per year, 10% in 5 years, or 15–25% of patients over 10–20 years with asymptomatic gallstones will progress to symptomatic gallstone disease. This occurs when a gallstone obstructs the cystic or common bile duct and is inaccurately referred to as biliary colic. Even fewer (1–3%) will progress to complications of gallstone disease, of which acute cholecystitis is the most common. Symptomatic patients are more likely than asymptomatic patients to develop complications. Other complications include chronic cholecystitis, choledocholithiasis with or without cholangitis, gallstone pancreatitis, fistulas of the biliary tract and digestive system, and gallbladder carcinoma. Almost all patients will experience symptoms before developing complications.

Behind endoscopy of the small and large intestine, cholecystectomy is the most performed digestive system operation with a rate of 13.4 per 10,000 population per year. However, not all patients with gallstones will require cholecystectomy. There is wide agreement that surgical treatment is indicated for symptomatic patients and primarily only for those who remain symptomatic despite medical management over a sustained period of time unless acute complication develops. Even the onset of biliary colic does not portend inevitable surgery as the symptoms are known to self-abate without surgical intervention frequently. In a population-based cohort study involving 580 asymptomatic patients with gallstones, 453 remained asymptomatic; 127 patients went on to develop mild or severe symptoms. Approximately half of those that became symptomatic experienced resolution without operative intervention. Therefore, expectant management is the best approach for asymptomatic patients, and medical management is advisable for symptomatic patients prior to undergoing surgery, excepting complications or special circumstances (e.g., porcelain gallbladder, hemolytic anemia, large gallstones, bariatric surgery, patients who have received a transplant).

Presentation

In order to discuss the appropriate timing of operative intervention for acute cholecystitis and gallstone pancreatitis, it is required to understand their presentation.

Acute Cholecystitis

Cholelithiasis with cholecystitis is the second most common gastrointestinal admission diagnosis in the United States and is associated with an aggregate cost of 4.4 billion dollars per year. Acute cholecystitis is secondary to gallstones >90% of the time and is the most common complication occurring in patients with cholelithiasis (see section "Natural History"). Acalculous cholecystitis accounts for the remaining 5–10%. Certain patients, such as critically ill patients in intensive care units or those with extensive burns, receiving parenteral nutrition, sepsis, trauma, or multi-organ disease are at higher risk for acalculous cholecystitis. Cystic duct obstruction by a tumor is a very rare cause of acute cholecystitis.

The majority of patients with acute cholecystitis will present with a history of chronic cholecystitis. This history consists of recurrent attacks of pain, referred to as biliary colic, and is caused most commonly by a gallstone attempting to pass the cystic duct. The pain is constant and steadily increasing in severity for the first 30–45 minutes. It will last anywhere from 1 to 6 hours and is typically located in the right hypochondrium or midline epigastrium. Referred pain to the inferior angle of the right scapula, acromion, or clavicle may also be felt. These attacks are traditionally taught to be worse at night or after eating fatty foods; however, studies have demonstrated biliary colic and referred pain to be the only symptoms consistently related to gallstones.

Biliary colic is a misnomer because the pain is not typically paroxysmal but is constant and steadily increasing. It can last up to 4–6 hours. It is not colicky in nature because the muscle wall of the gallbladder and bile ducts is scant (a

distinct muscle layer is not present in the human common bile duct). Any episode of biliary colic can progress to acute cholecystitis, but it is impossible to predict which. This occurs when obstruction of the cystic duct persists and leads to gallbladder distension, inflammation, edema, and eventually necrosis and supervening bacterial infection. After experiencing the symptoms described above, a pain-free interval with subsequent return of pain in the right hypochondrium is often described. This pain is usually felt to be worse or of a different character and often exacerbated by movement, deep breathing, or coughing due to irritation of the parietal peritoneum. Fever, anorexia, nausea, and vomiting may accompany the pain. An arrest of inspiration with palpation of the right subcostal area may be elicited, famously known as Murphy's sign. The reported positive likelihood ratio of Murphy's sign varies dramatically between studies from 0.8 to 8.6. Trowbridge et al. report a summary positive likelihood ratio of 2.8, the highest for any single physical exam or laboratory finding.

A mild or moderate leukocytosis (>10,000 cells/mm^3) is often present but not necessary. A severe leukocytosis suggests a worsening complication, such as gallbladder necrosis or rupture. Jaundice and hyperbilirubinemia are typically absent unless the gallstone has impacted in the common bile duct or impaction of the stone in Hartmann's pouch compresses the common hepatic duct (Mirrizzi syndrome). Serum liver enzymes are typically normal or mildly elevated.

Gallstone Pancreatitis

Acute pancreatitis is the third most common gastrointestinal admission diagnosis in the United States and is associated with an aggregate cost of 2.6 billion dollars per year. Gallstones and alcohol account as the cause for the vast majority of cases. The ratio of gallstone-induced pancreatitis to alcohol-induced pancreatitis varies regionally, but gallstones appear to be the casual factor in women and the elderly more than other demographic groups.

Impaction of the common bile duct, pancreatic duct, or the ampulla of Vater is associated with acute pancreatitis. The exact pathophysiology is not clearly defined. Multiple hypotheses have been proposed to include reflux of bile into the pancreatic duct; duodenal fluid reflux into the pancreatic duct due to stenting open of the ampulla by a gallstone; or ductal hypertension leading to ductal disruption and extravasation of pancreatic juices and enzymes caused by pancreatic duct obstruction. These hypotheses have not been reproduced in experimental models.

The clinical presentation is similar to acute pancreatitis of other etiologies. This includes persistent, gnawing epigastric pain that often radiates to the back. Nausea and vomiting, hypotension, tachycardia, and abdominal distension may be present. Though rare, blue discoloration of the flank or umbilicus (Grey Turner's sign and Cullen's sign, respectively) can be appreciated in cases of hemorrhagic pancreatitis. When gallstones are causative, signs and symptoms of biliary obstruction such as right upper quadrant pain, jaundice, and fever will likely be present. Gallstone pancreatitis will typically be associated with elevated serum liver tests. Elevation of alanine aminotransferase (ALT) to a value three times greater than normal has been found to have a positive predictive value of 95% for gallstone pancreatitis. Definitively differentiating gallstone pancreatitis from other causes of acute pancreatitis requires imaging. Ultrasound is the modality of choice and boasts a high sensitivity and specificity of 95% and 90%, respectively. Pancreatitis-induced ileus can sometimes limit an ultrasonographical study due to the presence of overlying bowel gas. Furthermore, if gallstone pancreatitis is caused by microlithiasis, it is often impossible to detect the causative gallstone by ultrasound. Gallstones can be retrospectively determined to have caused an episode of acute pancreatitis when a gallstone is retrieved from feces within 10 days of the attack. The term gallbladder sludge is sometimes used to describe findings on an ultrasound. This should be considered gallstone disease, and symptomatic patients or patients who present with gallstone pancreatitis should be referred for a cholecystectomy.

Cholecystectomy

For patients suffering from symptomatic gallstone disease, surgical intervention in the form of an elective laparoscopic cholecystectomy is the most frequently recommended treatment. A cholecystectomy is the most common major abdominal procedure performed in Western countries, and there are few absolute contraindications.

Acute Cholecystitis

Laparoscopic cholecystectomy is the treatment of choice for symptomatic gallstone disease to include acute cholecystitis. This disease process accounts for 14% to 30% of cholecystectomies around the world. There are only two absolute contraindications – uncontrolled coagulopathy and end-stage liver disease. In a patient with severe refractory gallstone disease, even the latter of the absolute contraindications can be surmounted by a cholecystectomy with concurrent liver transplantation. Patients with severe obstructive pulmonary disease or congestive heart failure are at risk of increased morbidity and mortality due to decreased tolerance of the required pneumoperitoneum; however, these comorbidities are only relative contraindications.

Although consensus exists that laparoscopic cholecystectomy is correctly indicated for acute cholecystitis, the timing of operative intervention has been hotly debated. Proponents of early intervention advocate the "golden 72-hour rule," while proponents of delayed intervention advocate a "cooling off period."

The recommendation for early intervention is predicated on evidence that suggests complication rates, conversion to open cholecystectomy, length of hospital stay, and readmission rates are non-inferior or superior to patients in which intervention is delayed beyond a variably defined window. Delay is believed to unnecessarily expose patients to the risk of recurrent gallstone complications in the interval period and allow for fibrosis and adhesive disease to anatomically complicate the eventual definitive surgery. Some authors define "early" as within 24 hours, while others extend the definition to 1 week.

Advocates of delayed intervention believe that laparoscopic cholecystectomy is more technically challenging during the acute window due to active inflammation. This is primarily due to fears that early operation increases the rates of bile duct injury, a potentially life-threating condition which requires difficult and urgent corrective surgery. Even with successful repair, bile duct injury can be severely detrimental to a patient's quality of life. A perception also exists that early operation is associated with an increased risk of conversion to open cholecystectomy.

The body of evidence available since the 1970s–1980s overwhelmingly suggests that early cholecystectomy is either non-inferior or superior to delayed cholecystectomy (see Table 16.1). However, surveys worldwide still demonstrate that the number of surgeons performing early laparoscopic cholecystectomy for acute cholecystitis varies dramatically, reaching as low as

Table 16.1 Meta-analyses concerning early vs. delayed laparoscopic cholecystectomy for acute cholecystitis

Name	Year	No. patients	No. studies	Recommended timing
Papi[a, b]	2004	1255	12[c]	Early
Siddiqui[a]	2008	375	4	Early
Gurusamy[a]	2013	488	6	Early
Zhou[a]	2014	1106	7	Equivocal
Cao[a]	2015	1608	14	Early
Menahem[a]	2015	617	9	Early
Wu[a]	2015	1625	15	Equivocal
Cao[d]	2016	40,910	77	Early

[a]Randomized controlled trials
[b]Included open and laparoscopic cholecystectomy
[c]Only 3 of 12 studied laparoscopic cholecystectomy
[d]Case-control studies

11% in British general surgeons in 2004 and 33% of Japanese general surgeons in 2007.

Early Versus Delayed Laparoscopic Cholecystectomy for Acute Cholecystitis

Papi et al. were the first to summarize findings through 2004 regarding the timing of cholecystectomy for acute calculous cholecystectomy. The majority of included studies defined delayed operation as ≥8 weeks and early operation as within 7 days of onset. There was no significant difference in the rate differences of operative or perioperative complications between early and delayed cholecystectomy (open and laparoscopic); however, the laparoscopic subgroup analysis was underpowered to avoid a type 2 error due to the low complication rate. A trend toward lower rates of conversion to open cholecystectomy is reported in early versus delayed laparoscopic cholecystectomy, but the rate difference was ultimately nonsignificant. The study emphasizes that 20% of patients initially randomized to delayed surgery failed to respond to medical management and more than 50% underwent unplanned urgent surgery. Hospital stay was significantly reduced in the early versus delayed *open* cholecystectomy group and nonsignificantly reduced in the early versus delayed *laparoscopic* cholecystectomy group. For these reasons, the meta-analysis concludes by stating:

> Considering all these features, there is no argument to support delayed operation: early surgery should be considered the preferred approach for patients with uncomplicated lithiasic cholecystitis.

The most recent meta-analysis by Cao et al., published in 2016, is a meta-analysis of 77 case-control studies comprising 40,910 patients. The majority of the studies were retrospective. The results demonstrate a clear and significant benefit of early laparoscopic cholecystectomy for acute cholecystitis. Statistically significant reductions in mortality, total complication rate, bile duct leaks and injuries, wound infections, conversion to open cholecystectomy, length of hospital stay, and blood loss were associated with early laparoscopic cholecystectomy. Previous meta-analyses including only randomized controlled trials had difficulty demonstrating statistical significance in any outcome measure other than total length of hospital stay. This was likely due to the low sample sizes of randomized controlled trials and the rarity of complication events. A large sample size is the obvious benefit of case-controlled studies. This benefit comes at this increased risk of selection bias inherent in case-controlled studies. Interestingly, Cao et al. reported nonsignificant differences in length of operation time between the early and delayed group with a trend toward shorter operating times favoring early intervention. This is contrary to all previous meta-analyses in which shorter operating times were typically the only reported statistically significant benefit in favor of delayed intervention. The study also reports a 16% failure rate in the delayed intervention group requiring urgent laparoscopic cholecystectomy. Cao et al. conclude by declaring early laparoscopic cholecystectomy to be:

> clearly superior to delayed laparoscopic cholecystectomy in the management of patients presenting with acute cholecystitis and [should] now be considered to be the standard of care in the management of acute cholecystitis.

The authors recommend targeting a goal window of within 72 hours of symptom onset.

Song et al. conducted a summary of meta-analyses in 2016 and determined that – across seven meta-analyses – early laparoscopic cholecystectomy lowers the risk of wound infection; shortens hospital stay; and increases cost-effectiveness, patient satisfaction, and quality of life. It is also associated with an increase in operation time. There was no significant difference in the incidence of mortality, bile duct injury, bile leakage, overall complications, or conversion to open cholecystectomy. Using Jadad selection criteria, Cao et al. [1] and Wu et al. were determined to be the most appropriate meta-analyses with which to generate treatment recommendations on timing of laparoscopic cholecystectomy in acute cholecystitis. Song et al. summarize nearly five decades of randomized controlled trials comparing early versus late laparoscopic cholecystectomy for acute cholecystitis:

> With the best available evidence, we recommend ELC [early laparoscopic cholecystectomy] to be

the standard treatment option in treating acute cholecystitis.

Song et al. do not recommend a definition for what constitutes "early," but the majority of included randomized controlled trials define it as between 3 and 7 days of symptom onset. Therefore, it is appropriate to assume this definition. Further clarification of optimal timing is still required; however, as even studies comparing the definition of early laparoscopic cholecystectomy between as soon as possible and within 7 days have reported higher mortality and costs when delayed.

Gallstone Pancreatitis

Cholecystectomy is essential to prevent recurrence of gallstone pancreatitis. The timing of cholecystectomy is important and still debated. A laparoscopic *index cholecystectomy* – a cholecystectomy that occurs in the same admission and prior to discharge – is usually safe. An *interval cholecystectomy* – a cholecystectomy occurring after an appropriate time interval – is recommended in certain patients.

The controversy regarding timing of intervention is evident in the literature at least as early as 50 years ago. Traditionally, allowing recovery from acute pancreatitis with follow-up elective cholecystectomy 6–12 weeks later was advised. This recommendation was predicated on the fear that early operation would encounter excessive peripancreatic inflammation and result in higher rates of surgical complication. With the revelation that nearly all patients with gallstones and acute pancreatitis had demonstrable migration of stones through the common bile duct, the traditional approach was challenged. Surgeons hypothesized that the benefits of early removal of the obstructing gallstone during the index admission may outweigh the potential risk of operating around an inflamed and edematous pancreas by preventing a potentially fatal reoccurrence of pancreatitis before delayed cholecystectomy could occur. The recurrence rate of acute pancreatitis after discharge without surgical intervention ranges from 29% to 63%. In 1978, Acosta published results comparing 86 patients who underwent delayed elective biliary tract surgery to 46 patients who underwent biliary tract surgery on admission (average, 28 hours from onset of crisis). The mortality rates were 16% and 2%, respectively. Acosta et al. suggested early relief of the obstruction is critical to patient recovery.

There still remained a question about timing of the operation within the first admission. Immediate and delayed index admission cholecystectomies were, until then, found to be equivocal in terms of mortality (6–8%). Immediate cholecystectomy allowed simultaneous exploration and removal of common bile duct stones. The advent of endoscopic sphincterotomy allowed the surgeon to separate removing the gallstones and removing the gallbladder into two discrete steps; thus, the question of immediate versus delayed cholecystectomy achieved greater import.

There was early evidence that operative timing should be predicated on pancreatitis severity. In 1979, Ranson et al. conducted a retrospective study in which early (days 0–7) definitive biliary surgery was undertaken in 11 patients with "mild" pancreatitis, with 1 death (9%), and in 6 patients with "severe" pancreatitis, with 4 deaths (67%). This suggested that early correction of associated biliary disease may be undertaken safely in patients with mild acute pancreatitis but should be deferred in severe pancreatitis until pancreatitis has subsided (but still during the index admission). In 1988, Kelly et al. reported that in patients with three or fewer positive Ranson's signs, the time of surgery appeared to have little effect on the outcome. In patients with more than three positive signs, early surgery resulted in a significant increase in rates of morbidity and mortality. By the early 1990s, the consensus on the management of gallstone pancreatitis settled on allowing the acute pancreatitis to resolve with delayed cholecystectomy during the index admission and cholangiography before or during cholecystectomy to allow extraction of impacted gallstones.

The following decade of research supported this consensus and further clarified the role of grading pancreatitis severity in determining operative timing. A retrospective case series

involving 142 patients and a prospective study involving 77 patients suggested that laparoscopic cholecystectomy is safe in patients recovering from gallstone pancreatitis and early operation (within 1 week) can safely be recommended in patients with mild pancreatitis. Patients with severe pancreatitis should undergo surgery 3 weeks after admission or face increased risk of operative complications, conversion to open, and longer postoperative stays.

Most evidence arises from retrospective studies and non-randomized prospective studies; little evidence is generated from randomized controlled trials. To date, no large high-quality RCT regarding timing of intervention in severe acute pancreatitis has been published. The PONCHO study, a randomized controlled trial published, included 266 inpatients from 23 hospitals in the Netherlands recovering from mild gallstone pancreatitis. These patients were randomized to either interval cholecystectomy (25–30 days after randomization and discharge) or index admission cholecystectomy (within 3 days of randomization). The results predictably echoed earlier retrospective studies:

> Compared with interval cholecystectomy, same-admission cholecystectomy reduced the rate of recurrent gallstone-related complications in patients with mild gallstone pancreatitis, with a very low risk of cholecystectomy-related complications.

Operative Technique

Critical View of Safety

Regardless of the approach (open, laparoscopic, robotic, single-port, reduced-port, etc.), the critical view of safety must be obtained during cholecystic pedicle dissection. This is particularly important in laparoscopic compared to open cholecystectomy given that the laparoscopic procedure relies more heavily on visual identification of critical structures without the benefit of manual palpation. Visual perceptual illusion is the primary cause of error in 97% of laparoscopic bile duct injuries. Faulty technical skills are present in only 3% of injuries which likely explains why, despite improving equipment and increasing laparoscopic experience, the incidence of bile duct injury has not decreased over time (≤1.5%). This illusion can be so convincing that surgeons fail to recognize duct misidentification and erroneous transection of the duct even after it has occurred. One study reports that in 42 cases of bile duct injury, the injury was unrecognized in 70% of patients; delay of recognition even persisted into the postoperative period in 57%.

Per the original author, Strasberg et al., the critical view of safety has three requirements:

1. The triangle of Calot must be cleared of fat and fibrous tissue. The common bile duct does *not* need to be exposed.
2. The lowest part of the gallbladder must be separated from the cystic plate (liver bed of the gallbladder).
3. Two structures, and only two structures, should be seen to enter the gallbladder (cystic duct and artery).

Once these three criteria are fulfilled, the critical view of safety has been attained.

The importance of obtaining this view is demonstrated by multiple studies. If 97% of bile duct injury is due to misidentification, then it serves that the critical view of safety – if properly achieved – should significantly reduce the number of bile duct injuries in laparoscopic cholecystectomies. A study of 3042 patients undergoing laparoscopic cholecystectomy and using the critical view of safety for structural identification between 2002 and 2006 reported only one bile duct injury in an 80-year-old patient. The injury was incurred prior to achieving the view. This reported rate of injury was an order of magnitude lower than the expected 2–4 per 1000 cholecystectomies. A prospective study conducted between 2002 and 2004 involving consecutive laparoscopic cholecystectomies in which the critical view of safety was photodocumented in 97 of 100 patients reported a single postoperative cystic duct stump leak. Kaya et al. reported in 2017 that 0 of 120 patients in whom the critical view of safety was achieved suffered intraoperative or postoperative biliary complications.

Despite the well-demonstrated efficacy of the critical view of safety, a study involving ten surgeons of variable training and experience across six hospitals in North Carolina found that only two surgeons (20%) satisfactorily achieved the critical view of safety during laparoscopic cholecystectomy. Although this is an isolated study with a small sample size, it serves to remind all readers to clearly and purposefully obtain the critical view of safety.

Laparoscopic Partial Cholecystectomy and Damage Control

Performing a cholecystectomy in the acute setting can be technically challenging, and the anatomy difficult to discern. The feasibility and safety of a laparoscopic partial cholecystectomy in cases of difficult laparoscopic cholecystectomy is emerging as an alternative to open conversion. Traditionally, when the critical view of safety could not be obtained due to acute inflammation, unfamiliar anatomic variants, or any other reason, conversion to open cholecystectomy was advised. However, some surgeons may feel more comfortable operating laparoscopically. This is becoming more applicable to younger generations of surgeons who perform relatively few, if any, open procedures. There is also evidence that conversion of laparoscopic to open cholecystectomies is at increased risk of major complications compared to a planned open cholecystectomy. Therefore, conversion may no longer be the best alternative when positive identification of biliary anatomy cannot be obtained.

The first open partial cholecystectomy for management of difficult gallbladders was described in 1985 by Bornman and Terblanche. Since 1993, laparoscopic partial cholecystectomies have also been performed. The technique was developed as an alternative to conversion to open cholecystectomy in situations where injury to biliary structures or the cystic artery was at increased risk. There are different techniques described but primarily revolve around either removal or non-removal of the posterior wall and closure or non-closure of the cystic duct and gallbladder stump. The most basic definition of a partial cholecystectomy requires "some portion of the gallbladder left in continuity with the cystic duct and not resected." No parallel randomized controlled studies directly comparing techniques exist.

A systematic review conducted in 2013 reported on 625 patients and 4 different operative techniques. The review included primarily retrospective consecutive studies, but four prospective consecutive studies were also included. Of the 625 patients included, 90% of patients undergoing difficult resection safely underwent laparoscopic partial cholecystectomy. Only 10.4% of patients required conversion to open procedure. One case of major bile duct injury occurred. The most frequent complication was bile leakage from an inadequately or not closed cystic duct. Gallstone formation in the gallbladder remnant pouch is often cited as a concern in regard to partial cholecystectomy. Symptomatic gallstone disease was found to be present in only 4 of 184 patients (2.2%) who underwent partial cholecystectomy.

The authors of this systematic review suggest that:

> LPC seems to be feasible and may be a good alternative to conversion for a difficult gallbladder at LC.

However, they make no firm recommendations in regard to the method of partial cholecystectomy, but they do recommend closure of the remnant gallbladder pouch, cystic duct, or both to minimize the risk of a postoperative bile leak; this was higher in a series that did not close the gallbladder stump.

A 2015 meta-analysis – which included many of the same studies – similarly concluded that subtotal cholecystectomy, when necessary, is associated with morbidity rates in difficult gallbladders comparable to rates reported for total cholecystectomy. The authors state that:

> ...treatment in patients with complex conditions undergoing SC is managed as safely as in patient with simple conditions undergoing TC.

The authors' results suggest that laparoscopic subtotal cholecystectomy produces less risk of

subhepatic collections, retained stones, wound infections, reoperations, and mortality but more bile leaks compared with open subtotal cholecystectomy. They failed to demonstrate any significant difference between different subtotal cholecystectomy techniques and therefore make no recommendations.

Readers should note that many of the studies included in the two publications discussed above were retrospective studies with small sample sizes and of poor quality. Furthermore, the exact surgical techniques utilized varied between studies and made pooling of data difficult. Continued high-quality research is necessary.

Summary of Recommendations

Gallstone disease is more common in the elderly, women, obese, and those with poor dietary patterns. Two-thirds of patients with gallstones are asymptomatic, and only 2–3% per year of patients with asymptomatic gallstones will progress to symptomatic gallstone disease. Early laparoscopic cholecystectomy should be the standard procedure of choice for patients with acute cholecystitis. Early laparoscopic cholecystectomy during the index admission is suggested for patients presenting with mild acute gallstone pancreatitis. There is limited evidence to suggest performing laparoscopic cholecystectomy 1–3 weeks after presentation in patients with severe pancreatitis. Obtaining the critical view of safety is critical to safely performing a laparoscopic cholecystectomy. A laparoscopic partial cholecystectomy is a feasible alternative to conversion to open cholecystectomy when managing a difficult gallbladder.

References

1. Kelly TR, Wagner DS. Gallstone pancreatitis: a prospective randomized trial of the timing of surgery. Surgery. 1988;104:600–5.
2. Bornman PC, Terblanche J. Subtotal cholecystectomy: for the difficult gallbladder in portal hypertension and cholecystitis. Surgery. 1985;98:1–6.
3. Strasberg SM, Brunt LM. Rationale and use of the critical view of safety in laparoscopic cholecystectomy. J Am Coll Surg. 2010;211:132–8. https://doi.org/10.1016/j.jamcollsurg.2010.02.053.
4. Kaya B, Fersahoglu MM, Kilic F, Onur E, Memisoglu K. Importance of critical view of safety in laparoscopic cholecystectomy: a survey of 120 serial patients, with no incidence of complications. Ann Hepatobiliary Pancreat Surg. 2017;21:17–20. https://doi.org/10.14701/ahbps.2017.21.1.17.
5. Ranson JH. The timing of biliary surgery in acute pancreatitis. Ann Surg. 1979;189:654–63.
6. Acosta JM, Ledesma CL. Gallstone migration as a cause of acute pancreatitis. N Engl J Med. 1974;290:484–7. https://doi.org/10.1056/NEJM197402282900904.
7. Wu X-D, Tian X, Liu M-M, Wu L, Zhao S, Zhao L. Meta-analysis comparing early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Br J Surg. 2015;102:1302–13. https://doi.org/10.1002/bjs.9886.
8. Song G-M, Bian W, Zeng X-T, Zhou J-G, Luo Y-Q, Tian X. Laparoscopic cholecystectomy for acute cholecystitis: early or delayed?: evidence from a systematic review of discordant meta-analyses. Medicine. 2016;95:e3835. https://doi.org/10.1097/MD.0000000000003835.
9. Papi C, Catarci M, D'Ambrosio L, Gili L, Koch M, Grassi GB, Capurso L. Timing of cholecystectomy for acute calculous cholecystitis: a meta-analysis. Am J Gastroenterol. 2004;99:147–55.
10. Trowbridge RL, Rutkowski NK, Shojania KG. Does this patient have acute cholecystitis. JAMA. 2003;289:80–6.
11. Cao AM, Eslick GD, Cox MR. Early laparoscopic cholecystectomy is superior to delayed acute cholecystitis: a meta-analysis of case-control studies. Surg Endosc. 2016;30:1172. https://doi.org/10.1007/s00464-015-4325-4.

17 Choledocholithiasis and Cholangitis: Incidence, Initial Management, and Surgical Management

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Choledocholithiasis

Epidemiology

Nearly 15% of the adult population in the United States has underlying cholelithiasis [1]. Of this number, 10–20% are estimated to have concomitant non-obstructing choledocholithiasis [2, 3]. Exact figures of the prevalence of choledocholithiasis are difficult to ascertain as many stone formers may pass clinically silent stones [4]. While ductal stones typically arise in and are secreted from the gallbladder, choleliths may arise *de novo* in the biliary tree. A history of cholecystectomy, therefore, does not preclude the development of choledocholithiasis. Risk factors for primary stone formation include bile stasis (as in cystic fibrosis), periampular diverticula, and East Asian heritage [5, 6].

Clinical Presentation

Choledocholithiasis causes symptoms only when stones result in obstruction. These patients present with symptoms similar to those of biliary colic. There is crampy, intermittent right upper quadrant pain and associated nausea and vomiting. Pain typically persists for longer periods than is seen with simple biliary colic, up to several hours per episode [7]. The patient may appear jaundiced and endorse right upper quadrant tenderness to palpation. There may also be a history of acholic stools, generalized pruritus, and darkened urine secondary to altered bilirubin excretion. Patients with intermittent obstruction and subsequent passage of stones may describe a history of repeated bouts of abdominal pain associated with jaundice. A palpable gallbladder (Courvoisier's sign) has been described, but this is more commonly associated with the progressive obstruction of malignant disease than with the acute process of stone blockage [8].

If the offending stone is located distal to the junction of the common bile duct and main pancreatic duct, the presenting signs and symptoms may instead be those of pancreatitis, namely, epigastric pain with radiation to the back [9]. Though this clinical entity is a potential complication of choledocholithiasis, it will be discussed in another section.

Laboratory Findings

The earliest laboratory abnormality is a transaminitis with elevations of alanine aminotransferase

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(ALT) and aspartate aminotransferase (AST) up to 25 times the upper limit of normal, though these findings have poor specificity. A cholestatic picture then predominates with elevations of serum bilirubin, alkaline phosphatase, and gamma-glutamyl transpeptidase (GGT) [10]. Hyperbilirubinemia is seen in a broad range of hepatic and biliary derangements as well as hemolysis and therefore should not be considered a specific finding. Fractionation of the serum bilirubin allows for the determination of conjugated hyperbilirubinemia which generally supports the determination of a biliary rather than a hepatocellular source. However, conjugated hyperbilirubinemia may also be seen in Rotor syndrome and Dubin-Johnson syndrome; in these cases serum GGT and alkaline phosphatase should be normal. The presentation of acute-onset right upper quadrant pain and marked transaminitis in the absence of concomitant elevation in alkaline phosphatase, GGT, and conjugated bilirubin should raise suspicion for an acute hepatitis. In gallstone pancreatitis, lipase will be elevated.

Imaging

Ultrasonography (US) of the right upper quadrant is often obtained early in the course of the clinical presentation concerning for choledocholithiasis. Though several signs, namely, visualized stones and common bile duct dilation (Fig. 17.1), may be observed that support the diagnosis of choledocholithiasis, this modality has generally poor sensitivity and may not be relied upon to exclude the diagnosis of choledocholithiasis [11].

Normal common bile duct diameter varies depending both on the age and the surgical history of the patient [12]. Up to the 5th decade of life, 4 mm should be considered a mean measurement in the healthy population. For each decade thereafter, the average increases by 1 mm [13]. In the patient who has undergone cholecystectomy, duct diameters up to 10 mm are routinely found in patients without obstruction [14, 15]. When there is high clinical suspicion for intraductal stone based on presentation and laboratory findings, further imaging is not warranted prior to proceeding to endoscopic retrograde cholangiopancreatography (ERCP), as this intervention allows for simultaneous diagnosis and treatment. When the diagnosis of choledocholithiasis is uncertain, magnetic resonance cholangiopancreatography (MRCP) is called for and has virtually 100% sensitivity for stones large enough to be clinically significant [16]. In patients in whom cholecystectomy is indicated for symptomatic cholelithiasis or acute cholecystitis, and there is low but nonzero concern for ductal stones, intraoperative cholangiography (IOC) may be used to exclude the diagnosis of concomitant choledocholithiasis.

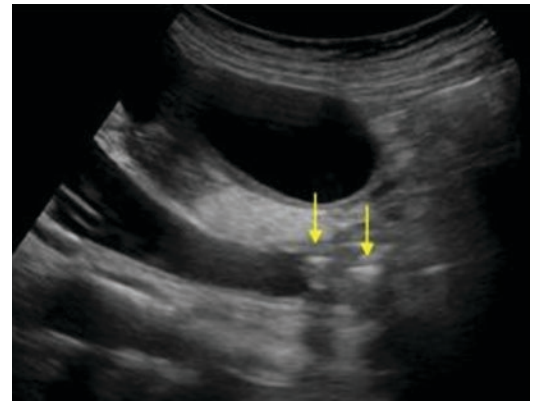

Fig. 17.1 Right upper quadrant ultrasound image demonstrating common bile duct stones (yellow arrows) visualized obstructing a dilated common bile duct. (Image used courtesy of *Dr. T.S.A. Geertsma*)

Management

Given the potential for development of cholangitis, as discussed below, all patients with confirmed choledocholithiasis require intervention. ERCP with stone extraction is indicated for clearing the offending stone. Contemporaneous sphincterotomy decreases the likelihood of recurrence; however it remains common enough that laparoscopic cholecystectomy is indicated within 72 hours of ERCP to decrease the potential for further episodes. Cases of post-sphincterotomy stenosis of the sphincter of Oddi with subsequent ascending cholangitis have also been described [17, 18].

ERCP fails in retrieving the offending stone in approximately 4.7–6% of cases depending of the volume of procedures performed at the institution in question [19]. In these cases, biliary distention may be temporized through the use of percutaneous transhepatic cholangiography (PTC), wherein the intrahepatic biliary ducts, dilated by downstream obstruction, are cannulated via a percutaneous approach. This allows for direct administration of contrast for the purposes of imaging (Fig. 17.2), as well as relieving the obstructed flow of bile. While not definitive, PTC offers relief of upstream obstruction and can greatly improve symptoms. The offending stone may then be removed either via a second attempt at ERCP or via a common bile duct exploration at the time of cholecystectomy [20, 21].

For the patient in whom ERCP is successful but comorbid conditions delay proceeding to surgery for cholecystectomy, biliary stenting at the time of ERCP can be considered [22]. Stents should also be considered if there have been repeated bouts of choledocholithiasis or if obstructing stones are removed but smaller stones remain in situ in the common bile duct. Definitive surgical therapy is still required as long-term stent placement is associated with 6–16% mortality, likely due to the stent acting as a nidus for bacterial cholangitis [23]. The stent may also serve as a nidus for the generation of further common duct stones, and for these reasons, proper patient selection is important.

Though ERCP carries with it a connotation of being a safer "nonsurgical" option in the minds of many providers, it bears the risk of several inherent complications. These include pancreatitis in 3.5% of cases, as well as bleeding and perforation in 1.3% and 0.6% of cases, respectively [24]. Additionally, the cardiovascular risks intrinsic to the induction of general anesthesia persist, including a remote risk of mortality in 0.07% of cases.

If choledocholithiasis is not discovered until IOC in the setting of cholecystectomy, intraoperative ERCP is indicated. If intraoperative ERCP is unavailable, two approaches are reasonable. Either the surgeon must elect to complete the cholecystectomy and allow for postoperative ERCP or a common bile duct exploration must be performed to remove the stone [25]. Common duct exploration will be discussed further in the section on management of cholangitis below. The decision to defer to postoperative ERCP carries with it the risk of ERCP failure and the need for a third procedure to relieve the obstruction.

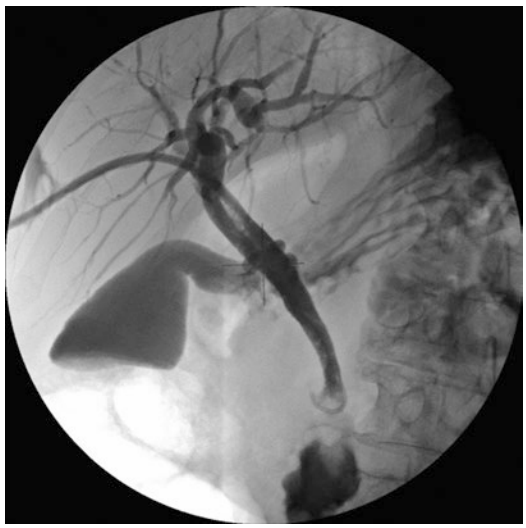

Fig. 17.2 Fluoroscopic mage taken at the time of percutaneous transhepatic cholangiography demonstrating distal obstruction of the common bile duct and proximal dilation of the intrahepatic ductal system

Cholangitis

Epidemiology

Cholangitis is the presence of infection and inflammation within the biliary tree. Cholangitis classically arises in the setting of ductal obstruction secondary to choledocholithiasis. Roughly half of cholangitis cases arise via this etiology. Possible alternative causes include biliary stricture, biliopancreatic malignancies, indwelling foreign bodies (e.g., PTC catheter or stent), and choledocal cysts.

Pathogenesis

Under normal conditions, the continuous flow of bile, IgA secretion by the biliary epithelium, and

isolation of the common bile duct from enteric contents by the sphincter of Oddi all promote sterility of the biliary tree. Regardless of the etiology of common bile duct obstruction, resultant biliary stasis and rising intraductal pressure undermine these defenses and allow the ascent of duodenal pathogens, commonly *E. Coli* and *Klebsiella* [26]. Pathogenic infection of bile and inflammation from rising pressure due to obstructed bile flow contribute to a systemic inflammatory response.

Clinical Presentation

The classic presentation associated with cholangitis is that of fever, right upper quadrant abdominal pain, and jaundice, termed Charcot's triad. Though the modified Tokyo guidelines support that Charcot's triad achieves >95% specificity in the diagnosis of cholangitis, its sensitivity is poor and captures only one quarter of patients [27]. Hypotension and altered mental status (Reynolds' pentad when found together with Charcot's triad) are late clinical findings that suggest septic shock and portend poor outcomes. Diagnosis, therefore, cannot rely on these classic findings [28].

Laboratory Findings

Findings are similar to those associated with choledocholithiasis; elevated transaminases evince hepatocellular irritation, and an obstructive pattern emerges with elevations of conjugated bilirubin, alkaline phosphatase, and GGT. Unlike choledocholithiasis, leukocytosis and a relative neutrophilia are expected.

Imaging

If acute cholangitis is suspected, diagnostic imaging should not delay therapeutic intervention. If imaging is obtained, the diagnosis is confirmed with evidence of bile duct dilation or visualized obstructing lesion such as a stone or malignancy. Thickening of the common bile duct wall is also supportive of the diagnosis (Fig. 17.3).

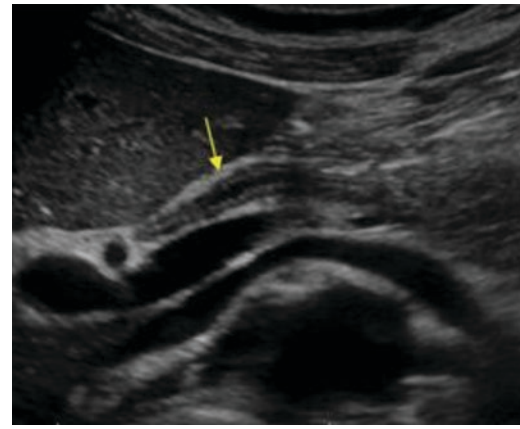

Fig. 17.3 Thickened common bile duct wall found on ultrasonography in a patient with acute cholangitis. No intraductal stones are visualized. (Image used courtesy of *Dr. T.S.A. Geertsma*)

Management

As in other etiologies of septic shock, early antibiotics and goal-directed resuscitation are vital. Blood cultures should be obtained but should not delay initiation of antimicrobial therapy. Given the ascending etiology of cholangitis, broad antibiotic therapy should be directed against gram-negative enteric organisms with an agent such as ampicillin/sulbactam or piperacillin/tazobactam [29]. In the great majority of patients, response to antimicrobial therapy is sufficient to allow a delay in ERCP up to 24 hours. If no improvement is evident and signs of suppurative cholangitis persist, emergent biliary decompression is indicated. This is ideally performed with immediate ERCP and sphincterotomy. When ERCP is unavailable or unsuccessful, biliary decompression is achieved with PTC, as discussed above.

Operative management of cholangitis should be considered as a last resort when the above interventions have failed. Choledochotomy may be attempted using a laparoscopic or open approach. The technique of a common bile duct exploration will be discussed in another chapter. The administration of glucagon may aid the surgeon in stone removal as it allows further dilation of the ductal system. The placement of a T-tube is advantageous as it allows for postopera-

tive contrasted imaging of the biliary tree as well as manipulation of the common bile duct postoperatively without the need for reoperation [30]. A more in-depth discussion of bile duct exploration occurs elsewhere in this text.

Provided the ascending infection arose in the setting of choledocholithiasis, cholecystectomy should again be performed as soon as the patient is clinically stable so as to prevent recurrence. However, in patients whose comorbidities preclude safe surgery, namely, the elderly and the frail, ERCP with sphincterotomy alone may be the best possible solution. In these patients, stents should be placed as leaving the gallbladder in situ increases the risk of recurrent episodes of choledocholithiasis and possibly subsequent cholangitis.

Conclusion

Choledocholithiasis and cholangitis represent two distinct clinical entities. Though choledocholithiasis is often to blame for the development of cholangitis, this is not always the case. In either event, clinical outcomes can be devastating without prompt recognition and intervention. Multidisciplinary management is necessary as these cases often require the involvement of surgical, endoscopic, and sometimes interventional radiology teams. With rising incidence of cholelithiasis, more cases of choledocholithiasis and subsequent cholangitis should be anticipated. Clinicians of all specialties must be familiar with the presentations of these disorders and maintain healthy suspicion in the patient with right upper quadrant pain and an obstructive biochemical laboratory pattern.

References

1. Shaffer EA. Epidemiology of gallbladder stone disease. Best Pract Res Clin Gastroenterol. 2006;20(6):981–96.
2. Everhart JE, Khare M, Hill M, Maurer KR. Prevalence and ethnic differences in gallbladder disease in the United States. Gastroenterology. 1999;117(3):632–9.
3. Tazuma S. Epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). Best Pract Res Clin Gastroenterol. 2006;20(6):1075–83.
4. Collins C, Maguire D, Ireland A, Fitzgerald E, O'Sullivan GC. A prospective study of common bile duct calculi in patients undergoing laparoscopic cholecystectomy: natural history of choledocholithiasis revisited. Ann Surg. 2004;239(1):28.
5. Chhoda A, Jain D, Singhal S. Sex-related differences in predicting choledocholithiasis using current American Society of Gastrointestinal Endoscopy risk criteria. Ann Gastroenterol. 2017;30(6):682.
6. Abboud PAC, Malet PF, Berlin JA, Staroscik R, Cabana MD, Clarke JR, Shea JA, Schwartz JS, Williams SV. Predictors of common bile duct stones prior to cholecystectomy: a meta-analysis. Gastrointest Endosc. 1996;44(4):450–7.
7. Yokoe M, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Gomi H, Pitt HA, Gouma DJ, Garden OJ, Büchler MW, Kiriyama S. New diagnostic criteria and severity assessment of acute cholecystitis in revised Tokyo guidelines. J Hepatobiliary Pancreat Sci. 2012;19(5):578–85.
8. Fitzgerald JEF, White MJ, Lobo DN. Courvoisier's gallbladder: law or sign? World J Surg. 2009;33(4):886–91.
9. Attasaranya S, Fogel EL, Lehman GA. Choledocholithiasis, ascending cholangitis, and gallstone pancreatitis. Med Clin. 2008;92(4):925–60.
10. Wang CH, Mo LR, Lin RC, Kuo JY, Chang KK. Rapid diagnosis of choledocholithiasis using biochemical tests in patients undergoing laparoscopic cholecystectomy. Hepato-Gastroenterology. 2001;48(39):619–21.
11. Einstein DM, Lapin SA, Ralls P, Halls JM. The insensitivity of sonography in the detection of choledocholithiasis. Am J Roentgenol. 1984;142(4):725–8.
12. Perret RS, Sloop GD, Borne JA. Common bile duct measurements in an elderly population. J Ultrasound Med. 2000;19(11):727–30.
13. Karamanos E, Inaba K, Berg RJ, Resnick S, Okoye O, Alexopoulos S, Chouliaras K, Demetriades D. The relationship between age, common bile duct diameter and diagnostic probability in suspected choledocholithiasis. Dig Surg. 2017;34(5):421–8.
14. Wu CC, Ho YH, Chen CY. Effect of aging on common bile duct diameter: a real-time ultrasonographic study. J Clin Ultrasound. 1984;12(8):473–8.
15. Bowie JD. What is the upper limit of normal for the common bile duct on ultrasound: how much do you want it to be. Am J Gastroenterol. 2000;95(4):897.
16. Costi R, Gnocchi A, Di Mario F, Sarli L. Diagnosis and management of choledocholithiasis in the golden age of imaging, endoscopy and laparoscopy. World J Gastroenterol: WJG. 2014;20(37):13382.
17. Sugiyama M, Atomi Y. Follow-up of more than 10 years after endoscopic sphincterotomy for choledocholithiasis in young patients. Br J Surg. 1998;85(7):917–21.
18. Yi SY. Recurrence of biliary symptoms after endoscopic sphincterotomy for choledocholithiasis in patients with gall bladder stones. J Gastroenterol Hepatol. 2000;15(6):661–4.

19. 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.
20. Salman B, Yılmaz U, Kerem M, Bedirli A, Sare M, Sakrak O, Tatlicioglu E. The timing of laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreatography in cholelithiasis coexisting with choledocholithiasis. J Hepatobiliary Pancreat Sci. 2009;16(6):832–6.
21. Pitt HA. Role of open choledochotomy in the treatment of choledocholithiasis. Am J Surg. 1993;165(4):483–6.
22. Moreira VF, Arribas R, Sanroman AL, Larena C, Garcia M, Torres G. Choledocolithiasis in cirrhotic patients: is endoscopic sphincterotomy the safest choice? Am J Gastroenterol. 1991;(8):86, 1006.
23. Bergman JJ, Rauws EA, Tijssen JG, Tytgat GN, Huibregtse K. Biliary endoprostheses in elderly patients with endoscopically irretrievable common bile duct stones: report on 117 patients. Gastrointest Endosc. 1995;42(3):195–201.
24. Andriulli A, Loperfido S, Napolitano G, Niro G, Valvano MR, Spirito F, Pilotto A, Forlano R. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Am J Gastroenterol. 2007; 102(8):1781.
25. Rojas-Ortega S, Arizpe-Bravo D, López ERM, Cesin-Sánchez R, Reed-San Roman G, Gómez C. Transcystic common bile duct exploration in the management of patients with choledocholithiasis. J Gastrointest Surg. 2003;7(4):492–6.
26. Sung JY, Costerton JW, Shaffer EA. Defense system in the biliary tract against bacterial infection. Dig Dis Sci. 1992;37(5):689–96.
27. Kimura Y, Takada T, Kawarada Y, Nimura Y, Hirata K, Sekimoto M, Yoshida M, Mayumi T, Wada K, Miura F, Yasuda H. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo guidelines. J Hepatobiliary Pancreat Sci. 2007;14(1):15–26.
28. Lee JG. Diagnosis and management of acute cholangitis. Nat Rev Gastroenterol Hepatol. 2009;6(9):533.
29. van den Hazel SJ, Speelman P, Tytgat GN, Dankert J, van Leeuwen DJ. Role of antibiotics in the treatment and prevention of acute and recurrent cholangitis. Clin Infect Dis. 1994;19(2):279–86.
30. Pérez G, Escalona A, Jarufe N, Ibáñez L, Viviani P, García C, Benavides C, Salvadó J. Prospective randomized study of T-tube versus biliary stent for common bile duct decompression after open choledochotomy. World J Surg. 2005;29(7):869–72.

18 Endoluminal Therapy for Choledocholithiasis and Cholangitis

Aditya Gutta and Mark A. Gromski

Introduction

Choledocholithiasis is the presence of stones within the bile ducts. They can be classified into either primary, which develop de novo in the bile ducts, or secondary from the passage of gallstones from the gallbladder. About 85% of choledocholithiasis is secondary to passage of gallstones from the gallbladder into the common bile duct (CBD). Gallstones represent a failure to maintain a balance of biliary solutes (cholesterol, calcium salts, bile acids) leading to either cholesterol stones (70–80%) or pigment stones consisting of unconjugated bilirubin. The pigment stones are primarily black (20–30% of all stones) and are formed due to deposition of bilirubin as polymers of calcium bilirubinate. Brown pigment stones are formed due to bacterial infection or overgrowth from stasis leading to deconjugation of bilirubin and subsequent precipitation and represent about 30–90% of gallstones in Asian populations. The formation of primary stones in the CBD is mostly due to bile stasis from diseases such as benign biliary strictures, choledochal cysts, cystic fibrosis, or peri-ampullary diverticula (Fig. 18.1). Recurrent or persistent infections from primary sclerosing cholangitis or recurrent pyogenic cholangiohepatitis seen in the East Asian population (termed "oriental cholangitis") can also lead to intraductal stone formation as well [1].

Obstruction of the bile duct can lead to an infection of biliary tree (acute cholangitis), primarily by translocation of bacteria from the duodenum and rarely from the portal venous system [2]. In addition to an obstructing stone, other causes of biliary obstruction leading to

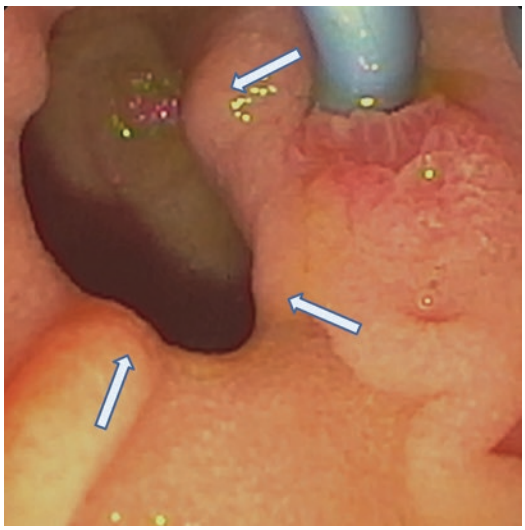

Fig. 18.1 Peri-ampullary diverticulum (arrows)

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cholangitis may include biliary stricture, pancreatic head mass, or extrinsic compression on the bile duct (Mirizzi syndrome or bulky lymphadenopathy).

Clinical Presentation

The typical presentation of choledocholithiasis is usually biliary colic, where the patient reports epigastric and/or right upper quadrant (RUQ) abdominal pain. The pain radiates to the back and is associated with autonomic symptoms of nausea and non-bloody emesis that may resolve after 1–2 hours. Tenderness may or may not be elicited in the RUQ [1, 3, 4]. A typical cholestatic pattern is seen in the liver chemistries with elevation in alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and bilirubin (conjugated predominant), far exceeding a rise in aspartate transaminase (AST) and alanine transaminase (ALT) [1, 5–7]. Charcot's triad is the combination of a fever (>100.4 °F), persistent RUQ pain, and clinical jaundice; and it raises the suspicion of acute cholangitis. Often there will be a significant elevation of ALP, GGT, and bilirubin (conjugated predominant) as well as elevation of the WBC and a leftward shift in the granulocytes in the setting of acute cholangitis. If underlying sepsis becomes severe with development of encephalopathy and hypotension, Reynaud's pentad for acute cholangitis is met, which reflects the severe and systemic manifestation of acute suppurative cholangitis [1, 8–10]. Rarely, AST and ALT can be elevated to >1000 when there is associated hepatocyte necrosis due to spread of infection into the liver parenchyma, leading to microabscesses [10]. In the setting of choledocholithiasis, patients may also develop pancreatitis due to obstruction of the pancreatic duct by a stone at the level of the ampulla, leading to elevation of lipase greater than three times the upper limit of normal as well as elevation of ALT greater than three times upper limit of normal [1, 10–13]. An ALT greater than three times the upper limit of normal is the most specific laboratory abnormality found in acute biliary pancreatitis [14].

Diagnosis

Ultrasound (US) of the abdomen is usually the first diagnostic study that is undertaken to assess the biliary tree and gallbladder, although it is operator-dependent and has varied sensitivity and specificity [15–17]. Based on the clinical presentation, laboratory data, and the transabdominal US, the American Society for Gastrointestinal Endoscopy (ASGE) has proposed a set of guidelines in 2010 to stratify the risk of a patient with symptomatic cholelithiasis of having choledocholithiasis and to determine the next step in management (Table 18.1) [18].

Based on the risk assessment, an algorithm for the management of symptomatic cholelithiasis with regard to the likelihood of choledocholithiasis has been proposed (Fig. 18.2, modified from Tse et al. [19]).

In regard to the choice of imaging, meta-analyses have found that endoscopic ultrasound (EUS) has a 94% sensitivity and a 95% specificity for detecting choledocholithiasis [13, 20, 21], while systematic reviews have shown that magnetic resonance cholangiopancreatography

Table 18.1 ASGE 2010 Guidelines in determining the likelihood for choledocholithiasis based on clinical, laboratory, and imaging predictors

Very strong predictors
CBD stone on transabdominal US Ascending cholangitis (Charcot's triad or Raynaud's pentad) Total bilirubin > 4 mg/dL
Strong predictors
CBD diameter > 6 mm on transabdominal US with GB in situ Total bilirubin 1.8–4 mg/dL
Moderate predictors
Abnormal liver chemistries (AST, ALT, ALP) other than bilirubin Age > 55 years Gallstone pancreatitis
High likelihood of choledocholithiasis
Any one very strong predictor Two strong predictors
Low likelihood of choledocholithiasis
No predictors
Intermediate likelihood of choledocholithiasis
All others

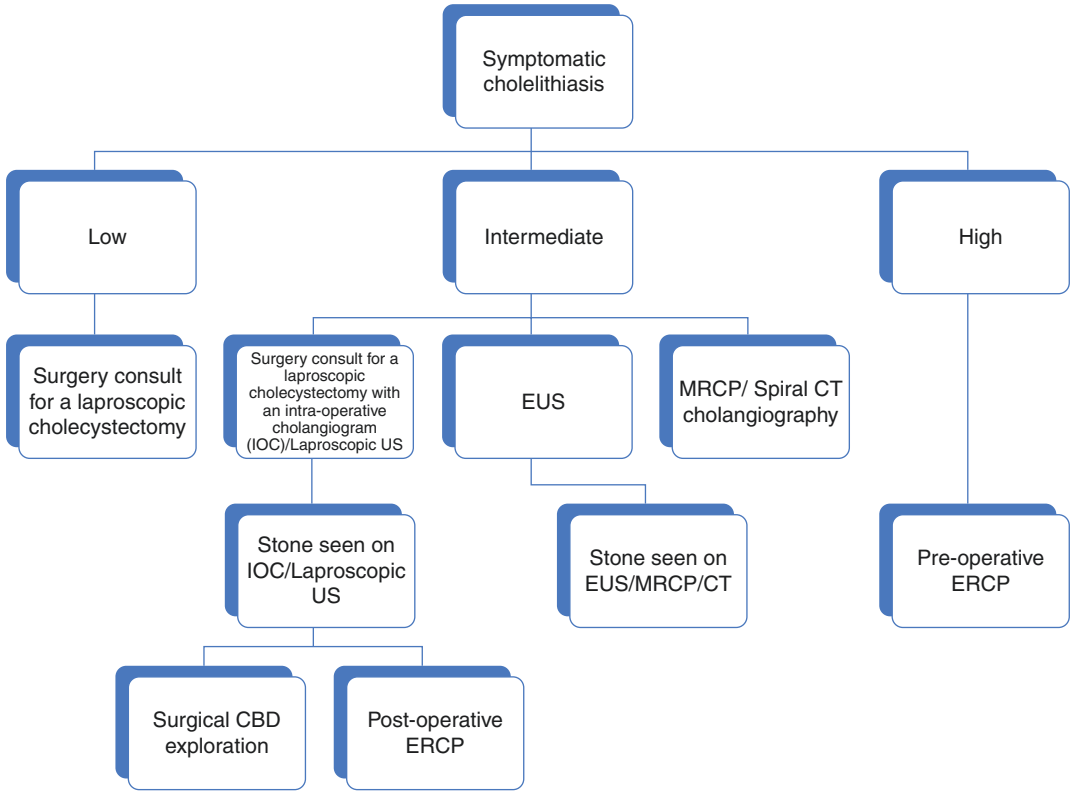

Fig. 18.2 Algorithm for the management of symptomatic cholelithiasis based on the likelihood of choledocholithiasis

(MRCP) has a 93% sensitivity and a 94% specificity [22]. Systematic reviews of studies comparing EUS and MRCP show no significant difference in the accuracy of the two modalities to detect choledocholithiasis [23–25]. However, the accuracy of MRCP to detect stones <6 mm in size may be slightly inferior [26].

EUS has the benefit of a subsequent endoscopic retrograde cholangiopancreatography (ERCP) in tandem during the same procedure, if a stone is detected. But this service is not available at all institutions and is dependent of the availability and expertise of the operator.

Literature suggests the presence of CBD stones in 9–11% of patient undergoing cholecystectomy with intraoperative cholangiogram (IOC). IOC technical success rate has been previously described to be 88–100%, with a sensitivity of 68–100% and a specificity of 92–100% [27, 28]. An alternative approach is an intraoperative US, which has a sensitivity of 90% and does not have the small risk of bile duct injury that an IOC carries, as there is no cannulation of the bile duct [27, 29, 30]. This is not a skill, however, that most general surgeons have.

Diagnostic ERCP to detect bile duct stones in patients with a low or intermediate likelihood of choledocholithiasis is rarely undertaken due to the higher risk of this procedure and the availability of other diagnostic modalities with a reasonably high level of accuracy [31, 32]. For patients with low or intermediate likelihood of having choledocholithiasis, studies have indicated that an EUS-first approach, when available, carries a high negative predictive value with a very small number of patients subsequently developing pancreatobiliary symptoms from choledocholithiasis on follow-up, without the associated mortality and morbidity associated with ERCP. It has also been found to be a cost-effective approach [33–36].

Treatment

The definitive treatment of choledocholithiasis is extraction of the stone – either with an endoscopic approach using an ERCP, via percutaneous transhepatic cholangiography (PTHC), or via surgical exploration of the CBD at the time of cholecystectomy. Studies have suggested that it is not emergent to relieve obstruction from choledocholithiasis and can be done electively in the absence of cholangitis [37–39]. However, if the patient manifests signs of acute cholangitis, achieving source control and removal of the obstruction via an ERCP within 48 hours has been shown to improve mortality and to decrease the length of hospital stay [40–42]. Generally, in the patient with suspected cholangitis, we recommend ERCP promptly as soon as the patient has achieved clinical stability after initial resuscitation after presentation (within the first 48 hours). If the patient is actively clinically decompensating despite optimal resuscitation in an intensive care unit and may not tolerate anesthesia for an ERCP, then drainage via PTHC is required to stabilize the patient prior to undergoing definitive management with ERCP.

As with any cause of sepsis, obtaining blood cultures, fluid resuscitation, and initiation of antibiotics to cover gram-negative enteric organisms as well as enterococcus species is of paramount importance, with a plan for an ERCP once resuscitation and a reasonable level of hemodynamic stability have been achieved [43–45].

Most often, extraction of choledocholithiasis is achieved with ERCP. A number of ERCP approaches can be utilized for biliary access and stone extraction. Following cannulation of the major papilla, a cholangiogram is performed by injecting a contrast agent into the biliary tree, thereby facilitating identification of choledocholithiasis (Fig. 18.3a, b). If cholangitis is suspected, often injection is limited to minimize the intraductal pressure and risk of disseminating infection retrograde into the liver. In this case, aspiration of biliary contents can confirm biliary location and enable the bile to be sent for culture and sensitivity testing. Once cholangitis or a biliary stone is identified, an endoscopic biliary sphincterotomy is usually performed to help relieve the resistance offered by the sphincter of Oddi and enable stone extraction (Fig. 18.4). Rarely, the biliary tree is unable to be cannulated, sometimes due to impaction of the stone at the ampulla. In this case, a "precut" papillotomy may be performed using a freehand technique or over a pancreatic duct stent, to gain access into the biliary tree (Fig. 18.5a–c) [46]. After biliary sphincterotomy, most CBD stones < 15 mm in size can be extracted with either a stone extraction balloon or a stone extraction basket (Fig. 18.6).

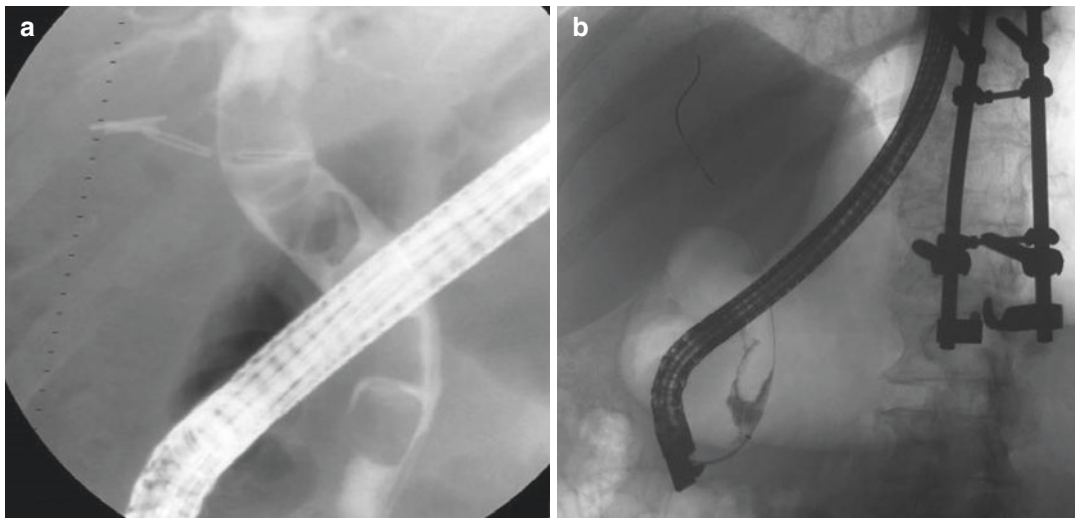

Fig. 18.3 (**a**) Multiple stacked stones identified at time of ERCP in the CBD and common hepatic duct. (**b**) Single large stone identified at time of ERCP in the CBD

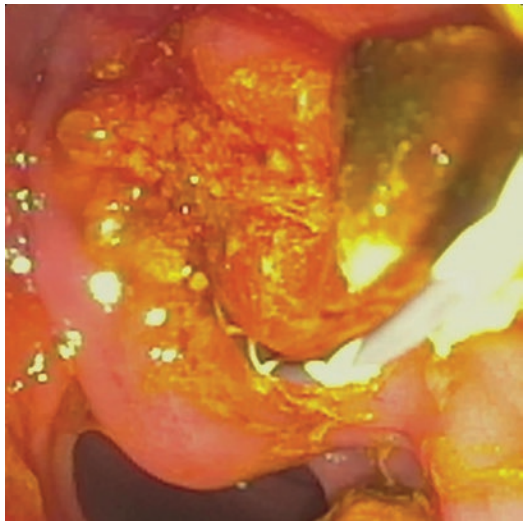

Fig. 18.4 Extraction of stones after conventional biliary sphincterotomy

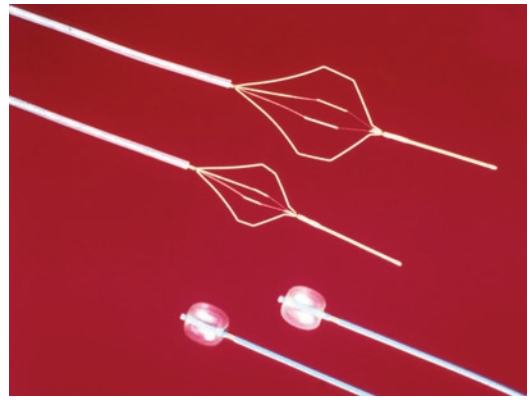

Fig. 18.6 Endoscopic stone extraction balloons and baskets

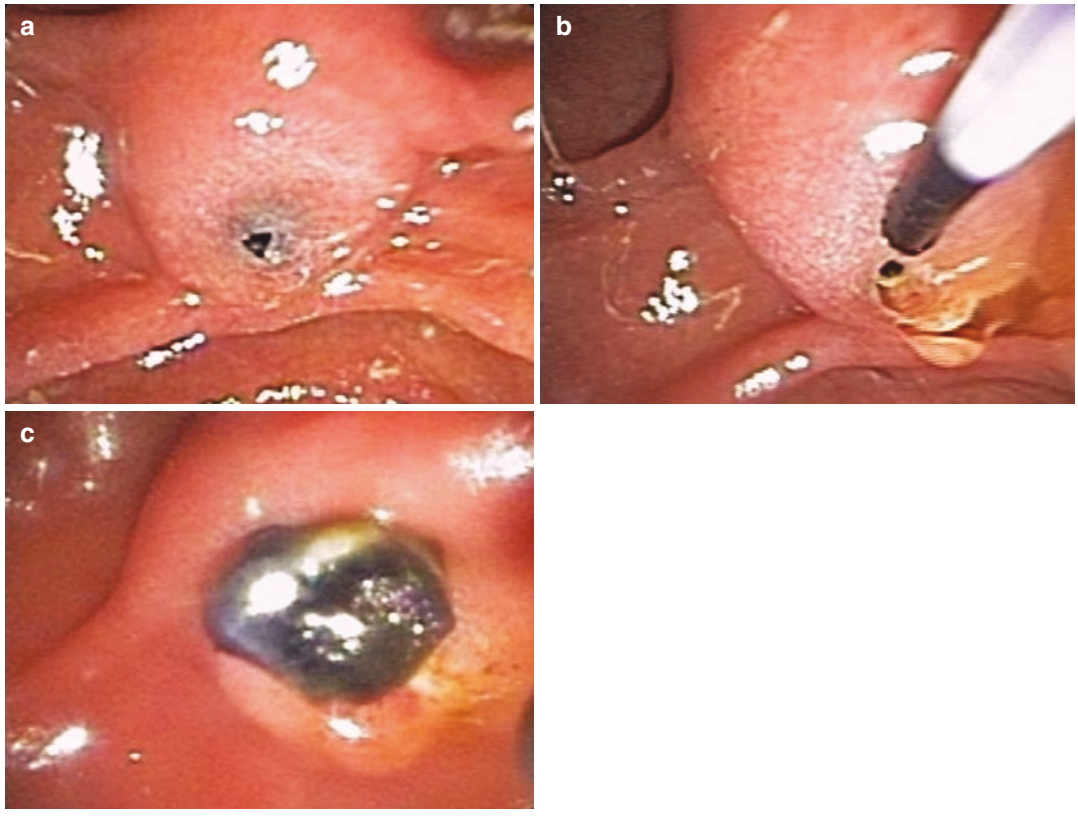

Fig. 18.5 (**a**) Stone apparent at the biliary orifice of the major papilla. (**b**) Precut biliary access using freehand needle-knife technique. (**c**) Extraction of stone after precut sphincterotomy

ERCP with sphincterotomy in the setting of choledocholithiasis is associated with periprocedural (<30 days) complications of approximately 10% that include bleeding (1%), pancreatitis (5%), perforation (1%), and cholangitis (1%), with a mortality rate of 0.1% [47–50]. Certain factors, such as pain during the procedure, indication of the procedure, and procedural factors, increase the risk of immediate complications [51]. The peri-procedure administration of rectal indomethacin and/or protective pancreatic duct stenting have been shown to reduce the risk of pancreatitis in selected patients [52]. Long-term complications from sphincterotomy include development of papillary stenosis in about 6–24%, leading to recurrence of stone formation and cholangitis rarely, with no evidence of increased risk of cholangiocarcinoma [53–57].

If a sphincterotomy is contraindicated due to presence of anticoagulants and/or antiplatelet agents or due to abnormal anatomy, a balloon sphincteroplasty can be performed using a dilation balloon to dilate the biliary orifice [58]. A Cochrane review [59] of available literature suggests that a balloon sphincteroplasty is less efficacious in extracting a CBD stone compared to a sphincterotomy (90% vs 95%); and it required more frequent use of repeat procedures and mechanical lithotripsy for stone clearance. Balloon sphincteroplasty without sphincterotomy is also associated with a higher risk of post-ERCP pancreatitis (8.6% vs 4.3%). However, there was no increase in mortality related to pancreatitis. The sphincteroplasty method, however, was associated with a lower risk of short-term (2.5% vs 5.0%) and long-term infections (2.4% vs 5.8%), as well as a lower risk of bleeding (0.1% vs 4.8%). Overall, there was no difference in the rates of perforation and overall mortality [59].

In the case of large stones and a tapering distal CBD, where conventional extraction maneuvers may fail, a combination technique such as dilation-assisted stone extraction (DASE), which incorporates balloon dilation of the sphincter orifice after a biliary sphincterotomy is performed, has shown to be more effective than a sphincterotomy alone, particularly with a decreased need for lithotripsy and no increased risk of ERCP-related short-term or long-term complications [60, 61].

In 10–15% of cases, stones cannot be removed with standard ERCP techniques described above. This generally occurs if the stone is >15 mm, located above a stricture, or is impacted [1]. In this case, more complex endoscopic interventions such as laser lithotripsy (LL), electrohydraulic lithotripsy (EHL), or mechanical lithotripsy can be employed to fracture the stone into fragments and subsequently extract them. In the case of mechanical lithotripsy, through-the-scope lithotripters are available to grasp the stone at any level in the biliary tree and crush into fragments with mechanical force. A mechanical winch attached to the device increases the pressure within the lithotripter [62–66]. LL or EHL is used predominantly to fragment large stones in the common duct or impacted intrahepatic stones. The lithotripsy probes are advanced under fluoroscopic guidance and direct visualization using a digital single-operator cholangioscope (D-SOC) [67] (Figs. 18.7 and 18.8a–c). EHL consists of a bipolar lithotripsy catheter probe that discharges high-pressure hydraulic pressure waves in an aqueous medium with the tip of the probe positioned within 2 mm of the stone. The energy is delivered in pulses over 1–2 s and continued until stone fragmentation is

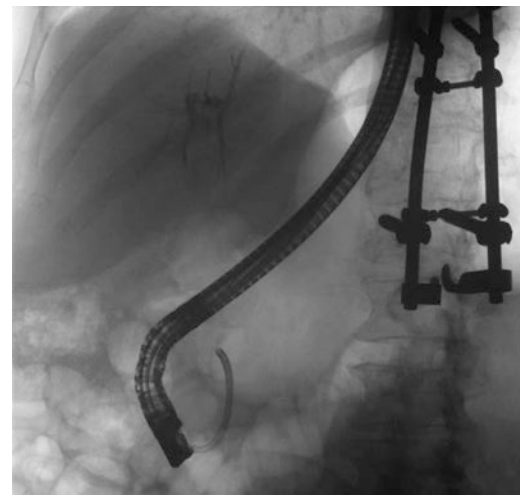

Fig. 18.7 Digital single-operator cholangioscope visualized under fluoroscopy

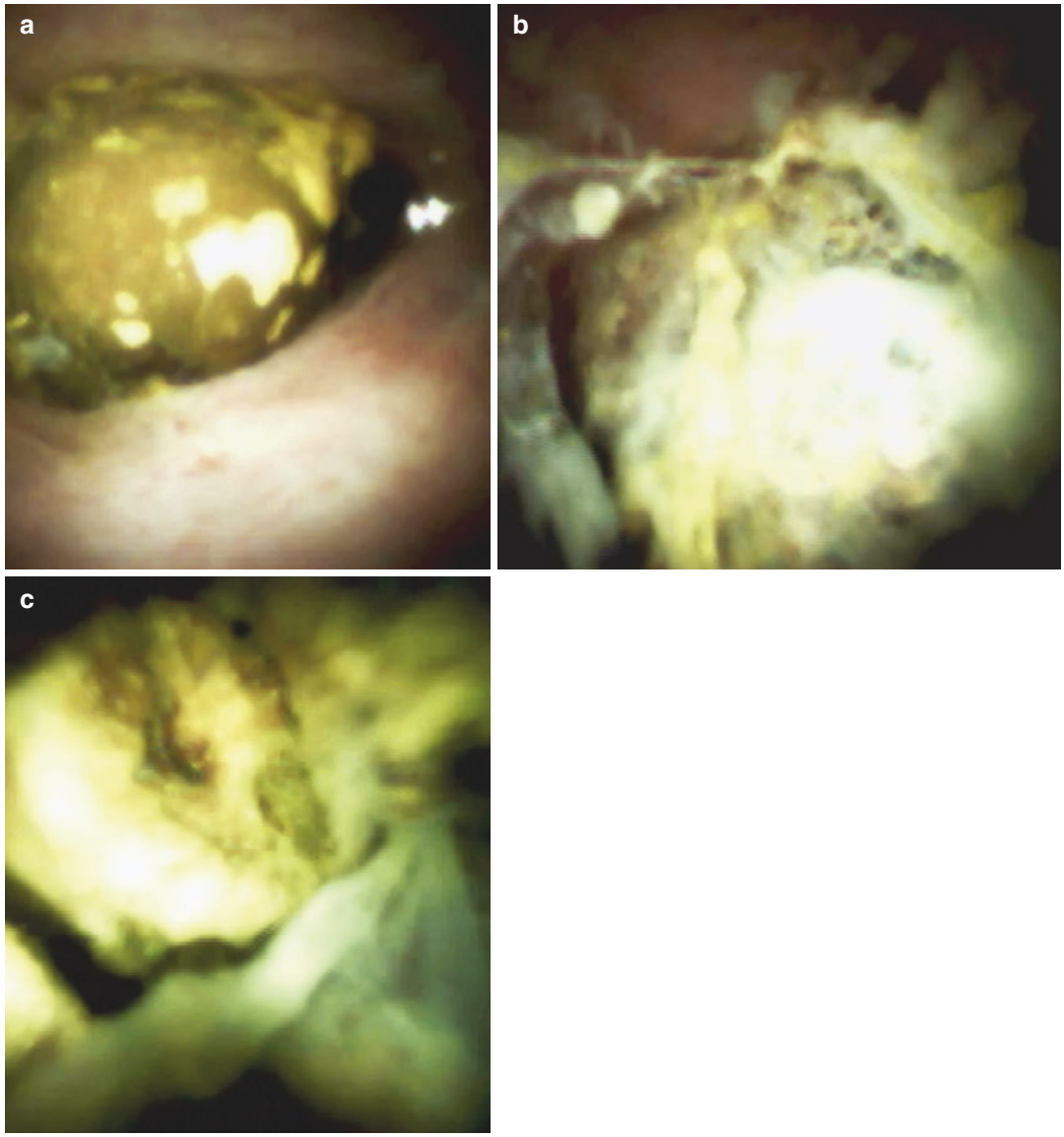

Fig. 18.8 (**a**) Pigmented CBD stone visualized with digital single-operator cholangioscope. (**b**) CBD stone visualized with digital single-operator cholangioscope. (**c**) CBD stone visualized with digital single-operator cholangioscope

achieved, with subsequent extraction of the fragments using conventional techniques (Fig. 18.9a, b) [68]. It has a demonstrated success rate greater than 97% in the fragmentation and extraction of stones over 1–4 sessions, with most requiring just one session (77%) [68–72]. In the case of LL, YAG laser-induced pulsed shock waves are directed precisely to target the biliary stones without damaging the biliary epithelium under direct visualization using a single-operator cholangioscopy (SOC) and further assisted by a radiopaque marker for fluoroscopic control. It is reported to have a similar efficacy to EHL but with a shorter procedure time (73.9 ± 33.5 min vs 49.9 ± 32.4 min). It does, however, require the practitioner to undergo special training to utilize the therapeutic laser. The risk of adverse events for EHL/LL is similar to

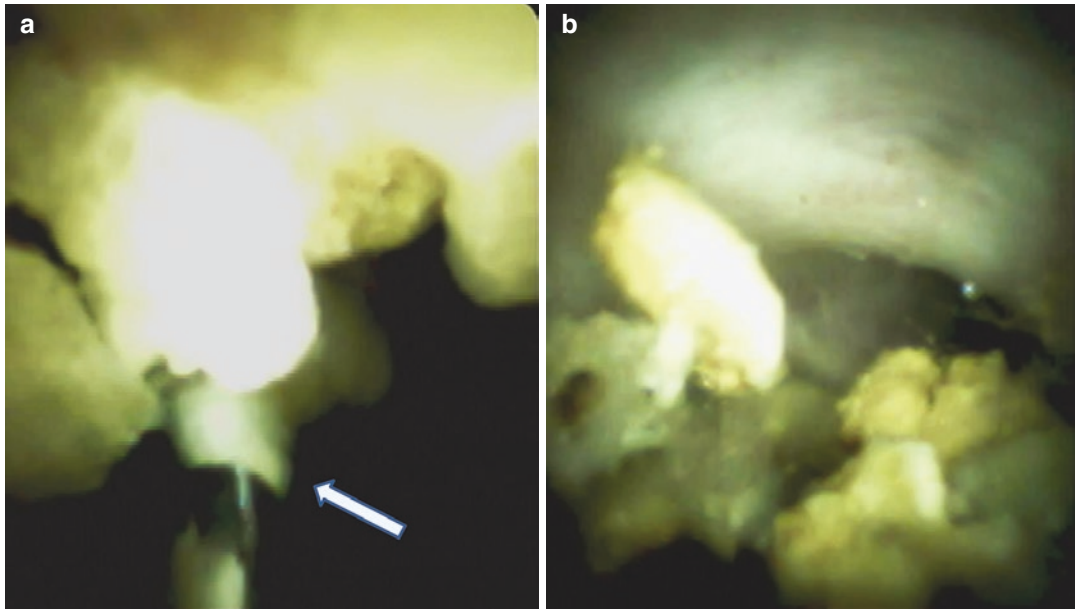

Fig. 18.9 (**a**) EHL probe (arrow) directed fragmentation of a CBD stone under direct visualization with a digital single-operator cholangioscope. (**b**) Fragments of CBD stone after EHL probe under direct visualization with a digital single-operator cholangioscope

conventional ERCP, with technical failure related to failure of cannulation of the CBD [68, 73–75].

In the setting of suspected cholangitis, we recommend aspiration of bile at the time of ERCP to evaluate the bile for presence of microorganisms. If the cultures are positive, they should be sent for microbial antibiotic sensitivity to help direct clinical care of the infection [44, 76]. If there is significant purulence seen in the bile duct following cannulation (Fig. 18.10a, b), to reduce the risk of spreading the infection retrograde to the liver, forceful biliary injection of contrast is not recommended. Once the obstruction is identified, a biliary stent traversing the obstruction should be placed [77], with or without a biliary sphincterotomy or sphincteroplasty. After adequate treatment with antibiotics and aforementioned biliary drainage, a subsequent ERCP can then be performed to treat the obstruction stone or lesion definitively.

Furthermore, with postsurgical anatomy or in the rare case that ERCP fails in the setting of choledocholithiasis or cholangitis, an EUS-guided rendezvous technique can be employed, a percutaneous transhepatic biliary drain (and subsequent therapy) can be attempted by interventional radiology, or a surgical common bile duct exploration and clearance may be pursued [78].

After removal of choledocholithiasis, a cholecystectomy is recommended in surgical candidates, to reduce the risk of recurrence of choledocholithiasis, cholangitis, or gallstone pancreatitis. Studies show an increased risk of recurrent pancreatobiliary events in those who were managed expectantly without cholecystectomy, which is higher when compared to groups who had a cholecystectomy – with the recurrence as high as 47% [79]. Also, patients who underwent early cholecystectomy within 72 hours of presentation had a lower rate of recurrent biliary events compared with those who delayed cholecystectomy up to 6–8 weeks (2% vs 36%) [80]. On the other hand, a systematic review of studies which included patients of both Asian and Western populations that were at a high risk of surgical complications from cholecystectomy (e.g., elderly patients, patients with cardiopulmonary comorbidities, cancer, or cirrhosis) showed an

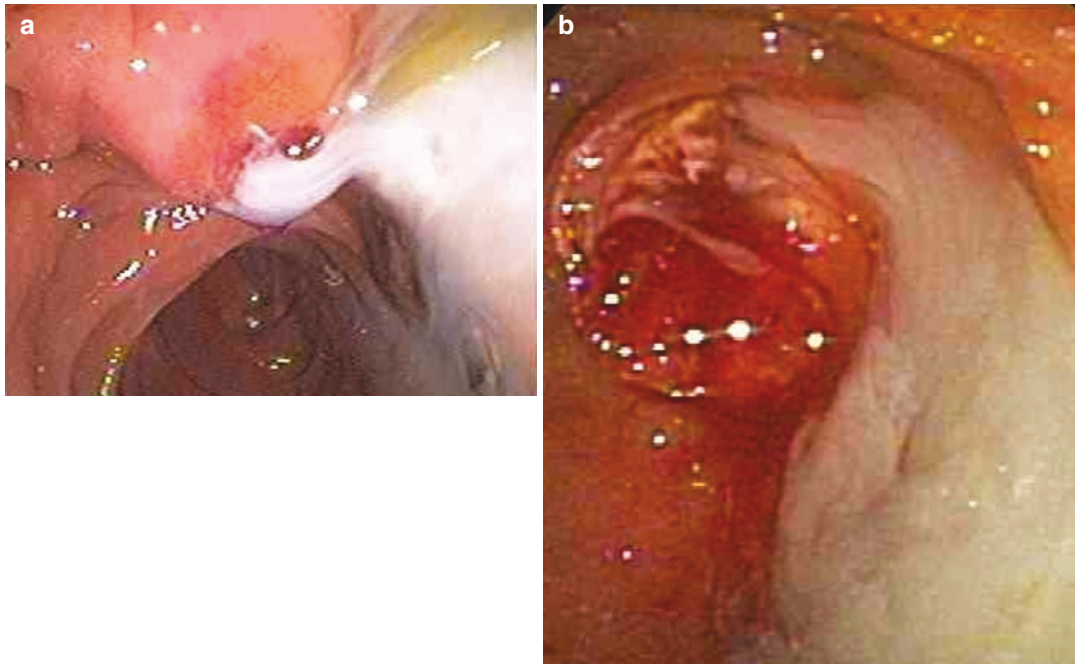

Fig. 18.10 (**a**) Purulent material exiting biliary orifice . (**b**) Purulent material exiting biliary orifice status post-biliary sphincterotomy

increased risk of biliary events but no difference in mortality with expectant management of choledocholithiasis after a biliary sphincterotomy when compared to receiving a subsequent cholecystectomy [81]. These findings are corroborated by a recent retrospective [82] and outcome study [83]. Ultimately, however, the determination of risk versus benefit of subsequent cholecystectomy of high-risk patients should be determined by the surgeon and the patient. It is not unreasonable for high-risk patients with underlying chronic disease such as cardiopulmonary disease or cirrhosis to be referred to a tertiary care center for multidisciplinary consultation.

Conclusion

ERCP is the first-line treatment for choledocholithiasis and should be performed within 48 hours in patients who are suspected of having cholangitis or pancreatitis. Consideration should be made for even earlier intervention in patients who present with septic shock due to the cholangitis. There are several techniques available for the endoscopist who has advanced endoscopic skills, all with similar outcomes and risks. In general, successful stone extraction should be followed by cholecystectomy within 72 hours. For the frail patient who is high risk for general anesthesia, consideration can be made for sphincterotomy alone with expectant management for any future biliary-pancreatic symptoms.

References

1. Fogel EL, Sherman S. In: Goldman L, Schafer AI, editors. Goldman-Cecil medicine e-book. 25th ed. Burlington: Elsevier Health Sciences; 2015. p. 1038–48.
2. Kimura Y, Takada T, Kawarada Y, et al. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. J Hepato-Biliary-Pancreat Surg. 2007;14:15–26.
3. Diehl AK, Sugarek NJ, Todd KH. Clinical evaluation for gallstone disease: usefulness of symptoms and signs in diagnosis. Am J Med. 1990;89:29–33.
4. Easler JJ, Sherman S. Endoscopic retrograde cholangiopancreatography for the management of common

bile duct stones and gallstone pancreatitis. Gastrointest Endosc Clin N Am. 2015;25:657–75.
5. Yang MH, Chen TH, Wang SE, et al. Biochemical predictors for absence of common bile duct stones in patients undergoing laparoscopic cholecystectomy. Surg Endosc. 2008;22:1620–4.
6. Abboud PA, Malet PF, Berlin JA, et al. Predictors of common bile duct stones prior to cholecystectomy: a meta-analysis. Gastrointest Endosc. 1996;44:450–5.
7. Prat F, Meduri B, Ducot B, Chiche R, Salimbeni-Bartolini R, Pelletier G. Prediction of common bile duct stones by noninvasive tests. Ann Surg. 1999;229:362–8.
8. Kiriyama S, Takada T, Strasberg SM, et al. TG13 guidelines for diagnosis and severity grading of acute cholangitis (with videos). J Hepatobiliary Pancreat Sci. 2013;20:24–34.
9. Mosler P. Diagnosis and management of acute cholangitis. Curr Gastroenterol Rep. 2011;13:166–72.
10. Attasaranya S, Fogel EL, Lehman GA. Choledocholithiasis, ascending cholangitis, and gallstone pancreatitis. Med Clin North Am. 2008;92:925–60, x.
11. Anderson K, Brown LA, Daniel P, Connor SJ. Alanine transaminase rather than abdominal ultrasound alone is an important investigation to justify cholecystectomy in patients presenting with acute pancreatitis. HPB (Oxford). 2010;12:342–7.
12. Moolla Z, Anderson F, Thomson SR. Use of amylase and alanine transaminase to predict acute gallstone pancreatitis in a population with high HIV prevalence. World J Surg. 2013;37:156–61.
13. Vaynshtein J, Sabbag G, Pinsk I, Rahmani I, Reshef A. Predictors for choledocholitiasis in patients undergoing endoscopic ultrasound. Scand J Gastroenterol. 2018;53:1–5.
14. Fogel EL, Sherman S. ERCP for gallstone pancreatitis. N Engl J Med. 2014;370:150–7.
15. Gurusamy KS, Giljaca V, Takwoingi Y, et al. Ultrasound versus liver function tests for diagnosis of common bile duct stones. Cochrane Database Syst Rev. 2015;(2):Cd011548.
16. Einstein DM, Lapin SA, Ralls PW, Halls JM. The insensitivity of sonography in the detection of choledocholithiasis. AJR Am J Roentgenol. 1984;142:725–8.
17. Laing FC, Jeffrey RB, Wing VW. Improved visualization of choledocholithiasis by sonography. AJR Am J Roentgenol. 1984;143:949–52.
18. Maple JT, Ben-Menachem T, Anderson MA, et al. The role of endoscopy in the evaluation of suspected choledocholithiasis. Gastrointest Endosc. 2010;71:1–9.
19. Tse F, Barkun JS, Barkun AN. The elective evaluation of patients with suspected choledocholithiasis undergoing laparoscopic cholecystectomy. Gastrointest Endosc. 2004;60:437–48.
20. Garrow D, Miller S, Sinha D, et al. Endoscopic ultrasound: a meta-analysis of test performance in suspected biliary obstruction. Clin Gastroenterol Hepatol. 2007;5:616–23.
21. Tse F, Liu L, Barkun AN, Armstrong D, Moayyedi P. EUS: a meta-analysis of test performance in suspected choledocholithiasis. Gastrointest Endosc. 2008;67:235–44.
22. Romagnuolo J, Bardou M, Rahme E, Joseph L, Reinhold C, Barkun AN. Magnetic resonance cholangiopancreatography: a meta-analysis of test performance in suspected biliary disease. Ann Intern Med. 2003;139:547–57.
23. Giljaca V, Gurusamy KS, Takwoingi Y, et al. Endoscopic ultrasound versus magnetic resonance cholangiopancreatography for common bile duct stones. Cochrane Database Syst Rev. 2015;(2):Cd011549.
24. Verma D, Kapadia A, Eisen GM, Adler DG. EUS vs MRCP for detection of choledocholithiasis. Gastrointest Endosc. 2006;64:248–54.
25. Ledro-Cano D. Suspected choledocholithiasis: endoscopic ultrasound or magnetic resonance cholangiopancreatography? A systematic review. Eur J Gastroenterol Hepatol. 2007;19:1007–11.
26. Zidi SH, Prat F, Le Guen O, et al. Use of magnetic resonance cholangiography in the diagnosis of choledocholithiasis: prospective comparison with a reference imaging method. Gut. 1999;44:118–22.
27. Machi J, Tateishi T, Oishi AJ, et al. Laparoscopic ultrasonography versus operative cholangiography during laparoscopic cholecystectomy: review of the literature and a comparison with open intraoperative ultrasonography. J Am Coll Surg. 1999;188:360–7.
28. Videhult P, Sandblom G, Rasmussen IC. How reliable is intraoperative cholangiography as a method for detecting common bile duct stones?: a prospective population-based study on 1171 patients. Surg Endosc. 2009;23:304–12.
29. Machi J, Johnson JO, Deziel DJ, et al. The routine use of laparoscopic ultrasound decreases bile duct injury: a multicenter study. Surg Endosc. 2009;23:384–8.
30. Machi J, Oishi AJ, Tajiri T, Murayama KM, Furumoto NL, Oishi RH. Routine laparoscopic ultrasound can significantly reduce the need for selective intraoperative cholangiography during cholecystectomy. Surg Endosc. 2007;21:270–4.
31. Gurusamy KS, Giljaca V, Takwoingi Y, et al. Endoscopic retrograde cholangiopancreatography versus intraoperative cholangiography for diagnosis of common bile duct stones. Cochrane Database Syst Rev. 2015;(2):Cd010339.
32. Prat F, Amouyal G, Amouyal P, et al. Prospective controlled study of endoscopic ultrasonography and endoscopic retrograde cholangiography in patients with suspected common-bileduct lithiasis. Lancet (London, England). 1996;347:75–9.
33. Karakan T, Cindoruk M, Alagozlu H, Ergun M, Dumlu S, Unal S. EUS versus endoscopic retrograde cholangiography for patients with intermediate probability of bile duct stones: a prospective randomized trial. Gastrointest Endosc. 2009;69:244–52.
34. Lee YT, Chan FK, Leung WK, et al. Comparison of EUS and ERCP in the investigation with sus-

pected biliary obstruction caused by choledocholithiasis: a randomized study. Gastrointest Endosc. 2008;67:660–8.
35. Liu CL, Fan ST, Lo CM, et al. Comparison of early endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in the management of acute biliary pancreatitis: a prospective randomized study. Clin Gastroenterol Hepatol. 2005;3:1238–44.
36. Polkowski M, Regula J, Tilszer A, Butruk E. Endoscopic ultrasound versus endoscopic retrograde cholangiography for patients with intermediate probability of bile duct stones: a randomized trial comparing two management strategies. Endoscopy. 2007;39:296–303.
37. Adler DG, Baron TH, Davila RE, et al. ASGE guideline: the role of ERCP in diseases of the biliary tract and the pancreas. Gastrointest Endosc. 2005;62:1–8.
38. Cohen S, Bacon BR, Berlin JA, et al. National Institutes of Health State-of-the-Science Conference Statement: ERCP for diagnosis and therapy, January 14–16, 2002. Gastrointest Endosc. 2002;56:803–9.
39. Lee HS, Chung MJ, Park JY, et al. Urgent endoscopic retrograde cholangiopancreatography is not superior to early ERCP in acute biliary pancreatitis with biliary obstruction without cholangitis. PLoS One. 2018;13:e0190835.
40. Hui CK, Lai KC, Yuen MF, Ng M, Lai CL, Lam SK. Acute cholangitis–predictive factors for emergency ERCP. Aliment Pharmacol Ther. 2001;15:1633–7.
41. Parikh MP, Wadhwa V, Thota PN, Lopez R, Sanaka MR. Outcomes associated with timing of ercp in acute cholangitis secondary to choledocholithiasis. J Clin Gastroenterol. 2018;52(10):e97–102.
42. Salek J, Livote E, Sideridis K, Bank S. Analysis of risk factors predictive of early mortality and urgent ERCP in acute cholangitis. J Clin Gastroenterol. 2009;43:171–5.
43. Doi A, Morimoto T, Iwata K. Shorter duration of antibiotic treatment for acute bacteraemic cholangitis with successful biliary drainage: a retrospective cohort study. Clin Microbiol Infect. 2018;24:1184.
44. Rerknimitr R, Fogel EL, Kalayci C, Esber E, Lehman GA, Sherman S. Microbiology of bile in patients with cholangitis or cholestasis with and without plastic biliary endoprosthesis. Gastrointest Endosc. 2002;56:885–9.
45. van den Hazel SJ, Speelman P, Tytgat GN, Dankert J, van Leeuwen DJ. Role of antibiotics in the treatment and prevention of acute and recurrent cholangitis. Clin Infect Dis. 1994;19:279–86.
46. Lopes L, Dinis-Ribeiro M, Rolanda C. Early precut fistulotomy for biliary access: time to change the paradigm of "the later, the better"? Gastrointest Endosc. 2014;80:634–41.
47. Andriulli A, Loperfido S, Napolitano G, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Am J Gastroenterol. 2007;102:1781–8.
48. Freeman ML, Nelson DB, Sherman S, et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med. 1996;335:909–18.
49. Williams EJ, Taylor S, Fairclough P, et al. Risk factors for complication following ERCP; results of a large-scale, prospective multicenter study. Endoscopy. 2007;39:793–801.
50. Wang P, Li ZS, Liu F, et al. Risk factors for ERCP-related complications: a prospective multicenter study. Am J Gastroenterol. 2009;104:31–40.
51. Ho KY, Montes H, Sossenheimer MJ, et al. Features that may predict hospital admission following outpatient therapeutic ERCP. Gastrointest Endosc. 1999;49:587–92.
52. Elmunzer BJ, Scheiman JM, Lehman GA, et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. N Engl J Med. 2012;366:1414–22.
53. Hawes RH, Cotton PB, Vallon AG. Follow-up 6 to 11 years after duodenoscopic sphincterotomy for stones in patients with prior cholecystectomy. Gastroenterology. 1990;98:1008–12.
54. Oliveira-Cunha M, Dennison AR, Garcea G. Late complications after endoscopic sphincterotomy. Surg Laparosc Endosc Percutan Tech. 2016;26:1–5.
55. Prat F, Malak NA, Pelletier G, et al. Biliary symptoms and complications more than 8 years after endoscopic sphincterotomy for choledocholithiasis. Gastroenterology. 1996;110:894–9.
56. Sugiyama M, Atomi Y. Follow-up of more than 10 years after endoscopic sphincterotomy for choledocholithiasis in young patients. Br J Surg. 1998;85:917–21.
57. Wojtun S, Gil J, Gietka W, Gil M. Endoscopic sphincterotomy for choledocholithiasis: a prospective single-center study on the short-term and long-term treatment results in 483 patients. Endoscopy. 1997;29:258–65.
58. Teoh AY, Cheung FK, Hu B, et al. Randomized trial of endoscopic sphincterotomy with balloon dilation versus endoscopic sphincterotomy alone for removal of bile duct stones. Gastroenterology. 2013;144:341–5. e1.
59. Weinberg BM, Shindy W, Lo S. Endoscopic balloon sphincter dilation (sphincteroplasty) versus sphincterotomy for common bile duct stones. Cochrane Database Syst Rev. 2006;(4):Cd004890.
60. Ersoz G, Tekesin O, Ozutemiz AO, Gunsar F. Biliary sphincterotomy plus dilation with a large balloon for bile duct stones that are difficult to extract. Gastrointest Endosc. 2003;57:156–9.
61. Li G, Pang Q, Zhang X, et al. Dilation-assisted stone extraction: an alternative method for removal of common bile duct stones. Dig Dis Sci. 2014;59:857–64.
62. Cipolletta L, Costamagna G, Bianco MA, et al. Endoscopic mechanical lithotripsy of difficult common bile duct stones. Br J Surg. 1997;84:1407–9.
63. Cohello R, Bordas JM, Guevara MC, et al. Mechanical lithotripsy during retrograde cholangiography in choledocholithiasis untreatable by conventional

endoscopic sphincterotomy. Gastroenterol Hepatol. 1997;20:124–7.
64. Garg PK, Tandon RK, Ahuja V, Makharia GK, Batra Y. Predictors of unsuccessful mechanical lithotripsy and endoscopic clearance of large bile duct stones. Gastrointest Endosc. 2004;59:601–5.
65. Hintze RE, Adler A, Veltzke W. Outcome of mechanical lithotripsy of bile duct stones in an unselected series of 704 patients. Hepato-Gastroenterology. 1996;43:473–6.
66. Sorbi D, Van Os EC, Aberger FJ, et al. Clinical application of a new disposable lithotripter: a prospective multicenter study. Gastrointest Endosc. 1999;49:210–3.
67. Stefanidis G, Christodoulou C, Manolakopoulos S, Chuttani R. Endoscopic extraction of large common bile duct stones: a review article. World J Gastrointest Endosc. 2012;4:167–79.
68. Brewer Gutierrez OI, Bekkali NLH, Raijman I, et al. Efficacy and safety of digital single-operator cholangioscopy for difficult biliary stones. Clin Gastroenterol Hepatol. 2017;16:918.
69. Binmoeller KF, Bruckner M, Thonke F, Soehendra N. Treatment of difficult bile duct stones using mechanical, electrohydraulic and extracorporeal shock wave lithotripsy. Endoscopy. 1993;25:201–6.
70. Josephs LG, Birkett DH. Electrohydraulic lithotripsy (EHL) for the treatment of large retained common duct stones. Am Surg. 1990;56:232–4.
71. Sheen-Chen SM, Chou FF. Intraoperative choledochoscopic electrohydraulic lithotripsy for difficulty retrieved impacted common bile duct stones. Arch Surg (Chicago, Ill: 1960). 1995;130:430–2.
72. Yucel O, Arregui ME. Electrohydraulic lithotripsy combined with laparoscopy and endoscopy for managing difficult biliary stones. Surg Laparosc Endosc. 1993;3:398–402.
73. Jakobs R, Pereira-Lima JC, Schuch AW, Pereira-Lima LF, Eickhoff A, Riemann JF. Endoscopic laser lithotripsy for complicated bile duct stones: is cholangioscopic guidance necessary? Arq Gastroenterol. 2007;44:137–40.
74. Patel SN, Rosenkranz L, Hooks B, et al. Holmium-yttrium aluminum garnet laser lithotripsy in the treatment of biliary calculi using single-operator cholangioscopy: a multicenter experience (with video). Gastrointest Endosc. 2014;79:344–8.
75. Sauer BG, Cerefice M, Swartz DC, et al. Safety and efficacy of laser lithotripsy for complicated biliary stones using direct choledochoscopy. Dig Dis Sci. 2013;58:253–6.
76. Gromski MA, Gutta A, Fogel EL, et al. Microbiology of Ercp bile aspirates in patients with suspected cholangitis. Gastroenterology. 2018;154:S-303.
77. Hui CK, Lai KC, Yuen MF, et al. Does the addition of endoscopic sphincterotomy to stent insertion improve drainage of the bile duct in acute suppurative cholangitis? Gastrointest Endosc. 2003;58:500–4.
78. Lai EC, Tam PC, Paterson IA, et al. Emergency surgery for severe acute cholangitis. The high-risk patients. Ann Surg. 1990;211:55–9.
79. McAlister VC, Davenport E, Renouf E. Cholecystectomy deferral in patients with endoscopic sphincterotomy. Cochrane Database Syst Rev. 2007;(4):Cd006233.
80. Reinders JS, Goud A, Timmer R, et al. Early laparoscopic cholecystectomy improves outcomes after endoscopic sphincterotomy for choledochocystolithiasis. Gastroenterology. 2010;138:2315–20.
81. Khan MA, Khan Z, Tombazzi CR, Gadiparthi C, Lee W, Wilcox CM. Role of cholecystectomy after endoscopic sphincterotomy in the management of choledocholithiasis in high-risk patients: a systematic review and meta-analysis. J Clin Gastroenterol. 2018;52:579–89.
82. Huang RJ, Barakat MT, Girotra M, Banerjee S. Practice patterns for cholecystectomy after endoscopic retrograde cholangiopancreatography for patients with choledocholithiasis. Gastroenterology. 2017;153:762–71.e2.
83. Elmunzer BJ, Noureldin M, Morgan KA, Adams DB, Cote GA, Waljee AK. The impact of cholecystectomy after endoscopic sphincterotomy for complicated gallstone disease. Am J Gastroenterol. 2017;112:1596–602.

19 Percutaneous Transhepatic Cholangiography and the Role of Interventional Radiology in Biliary Obstructions

Jonathan Marshall

The biliary tree is a network of branching ducts responsible for draining the bile produced in the liver. Bile is created by the hepatocytes and altered through resorption and secretion by the biliary epithelium. Bile is 95% water and contains bile salts, cholesterol, amino acids, steroids, bilirubin phospholipids, enzymes, porphyrins, vitamins, heavy metals, and environmental toxins [1]. Bile functions to excrete bile salts and other substances too large to be readily excreted by the kidney. Bile salts emulsify dietary fats to aid absorption in the intestines. Bile is also a major source of the excretion of cholesterol, hormones, IgA, and pheromones. Furthermore, the exocrine pancreas secretes pancreatic enzymes and bicarbonate that break down carbohydrates, protein, and fat. Any traumatic, infectious, benign obstructive, or malignant alteration in the creation and excretion of bile can lead to a profound disruption in the function of the hepatobiliary system.

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Anatomy and Imaging of the Hepatobiliary System

The liver is composed of nine functional segments (left liver, II, III, IVA, IVB; right liver, I, V, VI, VII, VIII). Classically, the celiac artery branches into the splenic and common hepatic artery. Beyond the gastroduodenal artery, the proper hepatic artery branches into right and left hepatic branches. For the hepatic venous system, there are typically right (drains segments V, VI, and VII), left (drains segments II and III), and middle (drains segments IV, V, and VIII) hepatic veins which drain into the intrahepatic IVC. The caudate lobe (segment 1) typically drains directly into the IVC. In normal portal venous anatomy, the main portal vein bifurcates in the porta hepatis into right and left intrahepatic branches. The right portal vein branches into anterior and posterior branches [2].

Normal biliary tree anatomy occurs in approximately 58% of patients [3]. Anterior (segments VI and VII) and posterior (segments V and VIII) sectoral ducts drain the right liver into the right hepatic duct, while the left hepatic duct drains the left liver. The left and right hepatic ducts form the common hepatic duct. The cystic duct drains into the common hepatic duct to form the common bile duct.

The pancreatic duct most typically takes on a linear descending course but can have a sigmoid, vertical, or loop configuration. The most common

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configuration of the pancreatic duct is a bifid main pancreatic duct with dominant drainage through the duct of Wirsung and the sphincter of Oddi and minor drainage through the accessory duct of Santorini [4].

Malignant Biliary Obstruction

Malignant biliary obstruction occurs as a result of cholangiocarcinoma, pancreatic adenocarcinoma, hepatocellular carcinoma (HCC), gallbladder carcinoma, porta hepatis lymphadenopathy, duodenal carcinoma, and an ampullary carcinoma. Patients with biliary obstruction typically present with painless jaundice, scleral icterus, weight loss, nausea, and pruritus. A potentially catastrophic consequence of biliary obstruction is cholangitis presenting with leukocytosis, sepsis, and hemodynamic instability.

Imaging of biliary obstruction typically begins with right upper quadrant ultrasound which leads to cross-sectional imaging with contrast-enhanced CT if a biliary duct mass is suspected. MRCP and gadolinium-enhanced MRI of the abdomen continue to represent mandatory modalities in the preprocedure evaluation of the biliary system. When differentiating between benign and malignant strictures, MRCP is 96% sensitive and 85% specific [5, 6].

Percutaneous interventions usually represent second-line therapies when endoscopic interventions are technically unfeasible or complicated as with a history of Roux-en-Y gastric bypass. The choice between percutaneous biliary drainage and endoscopic biliary drainage remains controversial but has similar technical and therapeutic success rates. Drainage can be performed with pure external biliary bag drainage or internal-external stent drainage when the small bowel can be accessed. As a result of catheter dislodgement, clogging of the catheters, and cholangitis, the catheters should be assessed and changed every 3 months (Figs. 19.1 and 19.2).

A hepaticogastrostomy which connects the hepatic duct to the stomach is a worthwhile option in patients with complete central or common bile duct obstruction and the inability to pass a wire into the duodenum. The cause of obstruction may be the result of iatrogenic bile duct injury during cholecystectomy or hepatectomy, a therapy which has become more frequent in the treatment

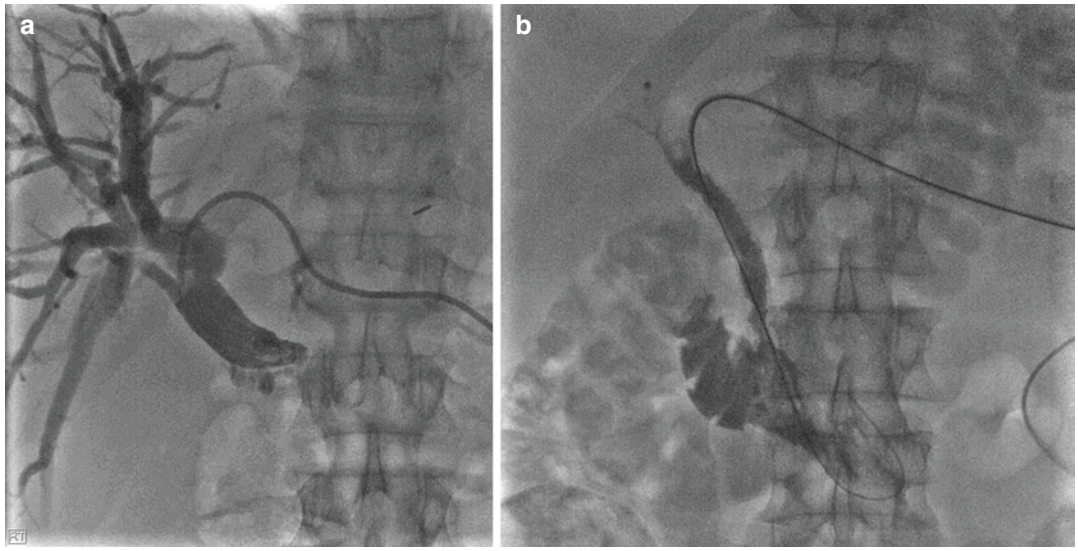

Fig. 19.1 (**a**) The image on the left demonstrates a left-sided approach for percutaneous biliary drainage using ultrasound guidance. There is complete obstruction of the distal common bile duct as a result of advanced gastric carcinoma. (**b**) Wire access to the duodenum and deployment of a self-expanding bare-metal stent

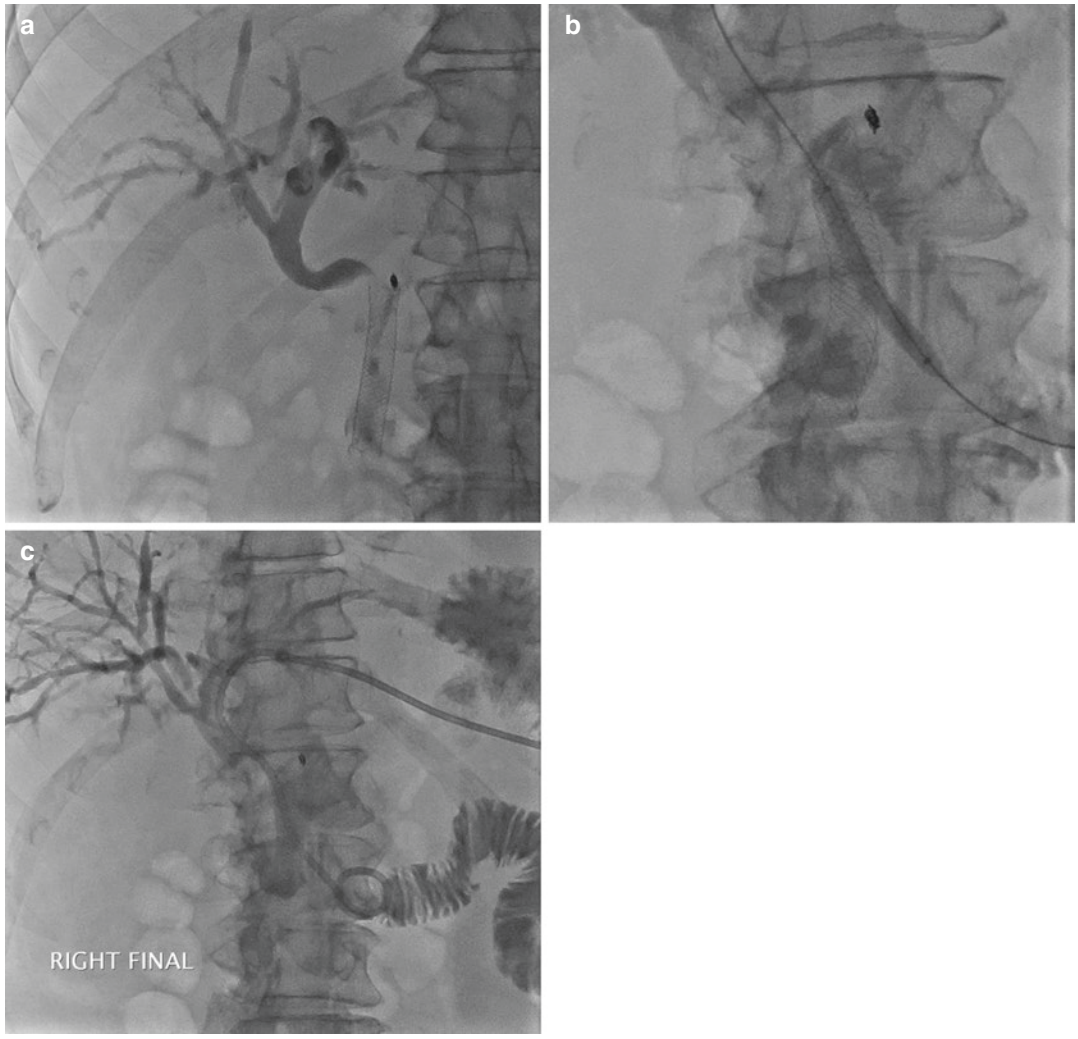

Fig. 19.2 (**a**) Occluded and migrated bare-metal stent previously placed endoscopically for malignant pancreatic carcinoma. (**b**) Wire access to the duodenum through the interstices of the stent was obtained, and they were ballooned open. (**c**) Internal-external biliary drainage catheter placement maintaining access in the event a tube change is required. The internal-external drain provides the characteristics of a metal stent while maintaining access

of metastatic colorectal carcinoma, or a central malignancy. The procedure can be done both endoscopically with EUS guidance and percutaneously, and it allows the biliary tree to drain into the stomach.

To perform a hepaticogastrostomy, a percutaneous biliary drain is initially placed, and CT cholangiogram is subsequently performed to evaluate for a straight segment III bile duct adjacent to the lesser curvature of the stomach. A nasogastric tube is placed to insufflate the stomach. Using CT guidance, a percutaneous, transhepatic pexy suture (similar to those placed during simple gastrostomy) is deployed within the stomach. Using the previously placed percutaneous biliary access, a TIPS needle is inserted through a sheath into the segment III bile duct. A needle is used to puncture through the wall of the stomach, and a wire is passed into the gastric lumen. An internal-external biliary drain can then be inserted over the wire similar to drainage into the duodenum. Once the tract has matured after 4–6 weeks,

a self-expanding stent can be deployed into the hepaticogastric tract, and the percutaneous drain can be removed. In small-numbered studies, the mean patency was 234 days with jaundice-free rates of 100%, 96%, 93%, and 80% at 1-, 3-, 6-, and 12-month follow-up. The reintervention rate was approximately 14% [7].

The absence of intestinal bile can play a role in the development of septic complications in these patients [8]. Additionally, the rate of renal dysfunction can be as high as 25% in patients receiving external biliary bag drainage which may be the result of altered hemodynamics and dehydration or the nephrotoxic effects of increased serum bilirubin in the circulation [9]. Furthermore, percutaneous biliary drains can be associated with pain and discomfort which can significantly affect a patient's quality of life.

The complication rates of percutaneous and endoscopic interventions range from 4% to 7%. The risks include sepsis, bleeding, pancreatitis, and pneumothorax (which can lead to biliary pleural fistulae). Care is taken during biliary access and drainage of the biliary system under pressure as a result of obstruction due to the risk of intraprocedural sepsis and hypotension. Percutaneous biliary drainage can lead to bile peritonitis and subcapsular liver abscess. Hemobilia following percutaneous biliary drainage is suggestive of a fistulous communication between the biliary tree and hepatic vasculature. Angiography of the liver requires removal of the drain over a wire to remove the tamponade effect of the catheter which can obscure the culprit bleeder. Once the arterial bleed is identified, embolization can be performed.

Stenting

Across multiple studies, the patency rate for metal stents lies within a 5-month range which matches survival rates for metastatic pancreatic adenocarcinoma [10]. Furthermore, the higher reintervention rate seen with plastic stents makes metal stents desirable for maintaining biliary patency.

Preservation of the sphincter of Oddi is important when possible to maintain sphincteric integrity and to avoid reflux of small bowel contents which can lead to ascending cholangitis. Different configurations of stent deployment can be used: isolated common bile duct, Y-shaped, and inline stent deployment to preserve the functioning lobe contralateral to a lobe with significant cirrhotic change. Care should be given not to "jail" biliary tributaries when placing covered stents. Exopolysaccharide matrices and intestinal microbes can form a biofilm which on self-expanding bare-metal stents can create a configuration similar to covered stents further contributing to stent failure and biliary obstruction [11].

Benign Biliary Obstruction

There are multiple potential causes of benign biliary strictures. Benign biliary strictures are iatrogenic from orthoptic liver transplantation or cholecystectomy 80% of the time; but other causes include primary sclerosing cholangitis, IgG4 cholangitis, HIV cholangiopathy, recurrent pyogenic cholangitis, chronic or autoimmune pancreatitis, and chemotherapy-induced cholangitis [12]. Biliary stricture can occur in 0.2–0.89% of laparoscopic cholecystectomies [13]. The Bismuth classification is used to characterize benign biliary strictures. Type I biliary strictures occur 2 cm from the hepatic confluence, Type II occur within the confluence, Type III involve the confluence, Type IV disrupt the confluence, and Type V extend into an aberrant right hepatic duct branch.

Endoscopic management includes the use of balloon angioplasty, plastic stents, and covered stents. In 43% of cases, restenosis occurs following balloon angioplasty [14–16]. Uncovered bare-metal stents are rarely used due to the risk of becoming embedded as a result of epithelial hyperplasia [17].

Postoperative changes in the GI anatomy may preclude treatment via an endoscopic approach. Aside from irreversible coagulopathy, there are no contraindications to percutaneous biliary access. Occasionally, a *rendezvous* procedure can be performed in collaboration with the endoscopists [18]. After obtaining wire access across a benign stricture, balloon dilation and placement of an internal-external biliary drain can be performed. Similar to the endoscopic approach, stones can be retrieved or pushed through the sphincter of Oddi using cutting balloons to perform a sphincter-

otomy. In some tertiary care centers, cholangioscopes can be inserted through a dilated antegrade percutaneous tract [19]. Ballooning of a postoperative anastomosis should not be performed in the perioperative period since this can result in further damage and a biliary leak. In cases of complete occlusion, sharp recanalization techniques can be employed using TIPS needles, the back end or a stiff wire, or an RF wire [20]. Sequential cholangiograms with upsizing of the biliary drains for a period of 6–12 months can lead to drain removal. The 1-year patency rate using this technique reaches 84%, 5-year patency rate of 74%, and 10-year patency of 67% [21]. When placed percutaneously, fully covered common bile duct stents have a 1-year patency rate of 91% [22]. The downfalls of both endoscopically and percutaneously placed stents include stent migration and restenosis at each end of the stent. Retrievable biliary stents have gained favor in the treatment of benign biliary strictures. In a study by Gwon et al., 100% of the stents were retrieved, and repeat stent placement for recurrent strictures was performed in 9% of the patients [23] (Fig. 19.3).

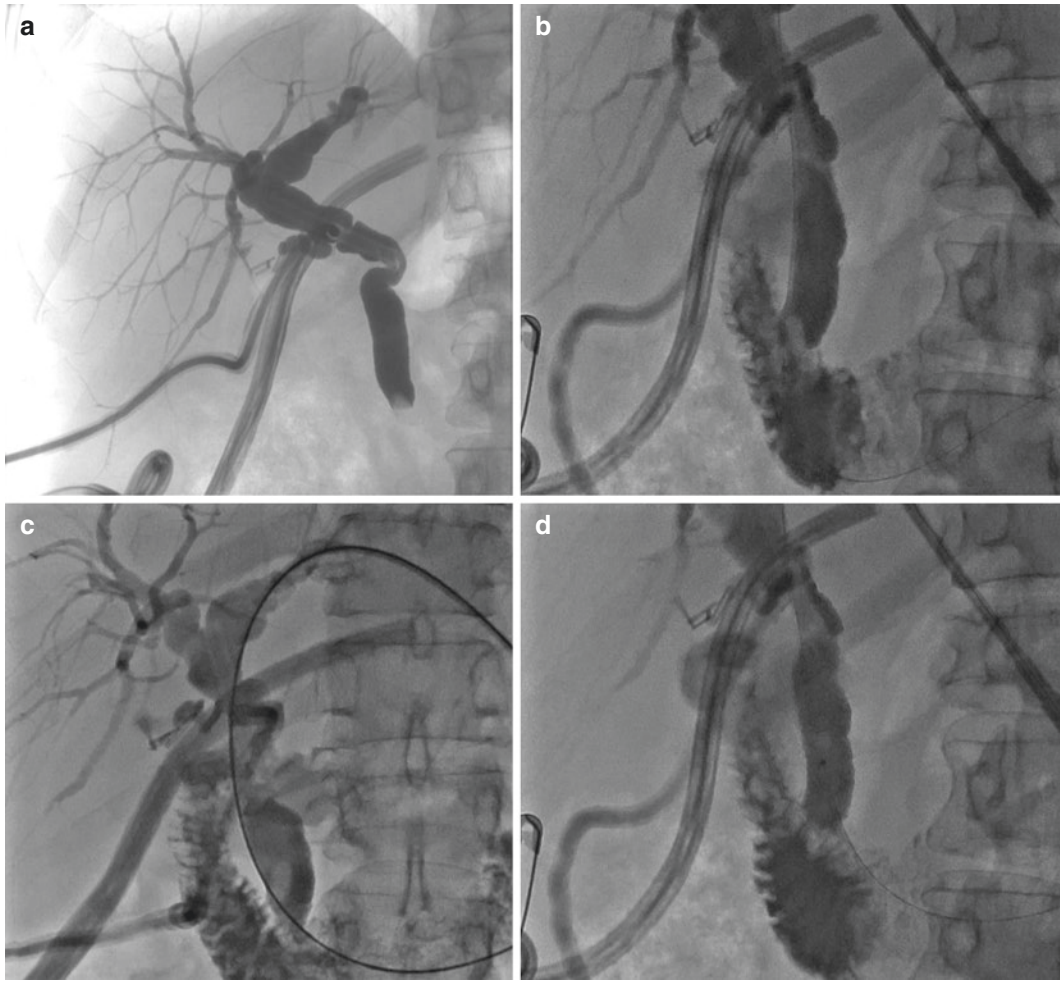

Fig. 19.3 (**a**) T-tube cholangiogram in a 28-year-old female following cholecystectomy at an outlying facility. An obstructive stone is noted in the distal common bile duct. The patient's past medical history is significant for previous gastric bypass precluding endoscopic treatment. (**b**) Left-sided biliary access was obtained. (**c**) Access to the duodenum was subsequently obtained, and a sphincterotomy was performed using a cutting balloon. (**d**) Completion images demonstrate absence of the stone and patency of the distal common bile duct

Future Therapies

Magnetic compression anastomosis (MCA) is a compelling technique that can be used in short inline anastomoses. MCA functions by placing high strength magnets both percutaneously and endoscopically on either side of the obstruction. Over time, the magnets attract one another, and through necrosis of the tissues between magnets, a biliobiliary fistula is formed [24].

On the horizon, biodegradable biliary stents may represent the future in the treatment of benign biliary strictures. Studies performed mostly in Europe have shown that the placement of biodegradable biliary stents is safe and feasible; however additional studies are required [25, 26].

Conclusions

The role of interventional radiology is crucial in the treatment of acute cholangitis to relieve the obstructed common bile duct, especially if the biliary tree cannot be accessed by endoscopic means. Hemodynamically unstable patients should be addressed with the utmost urgency if the unstability is thought to be due to the ascending cholangitis from an acute obstruction. But IR therapy can also play an important role in the relief of biliary obstruction due to malignancies, strictures, or pancreatitis. IR maneuvers can be utilized to help decompress the biliary tree, and new techniques using magnets are also being deployed to bypass the obstructed segment. The endoscopic and IR therapies can prevent the use of technically demanding surgeries in the acute setting and allow for transfer from the acute care surgeon's care to a hepatobiliary specialist, who is probably better suited to performing a biliary-enteric anastomosis.

References

1. Boyer JL. Bile formation and secretion. Compr Physiol. 2013;3(3):1035–78. https://doi.org/10.1002/cphy.c120027.
2. Tani K, Shindoh J, Akamatsu N, et al. Venous drainage map of the liver for complex hepatobiliary surgery and liver transplantation. HPB (Oxford). 2016;18(12):1031–8. https://doi.org/10.1016/j.hpb.2016.08.007.
3. Catalano A, Singh A, Uppot R, Hahn P, Ferrone C, Sahani D. Vascular and biliary variants in the liver: implications for liver surgery. Radiographics. 2008;28:359–78.
4. Türkvatan A, Erden A, Türkoğlu MA, Yener Ö. Congenital variants and anomalies of the pancreas and pancreatic duct: imaging by magnetic resonance cholangiopancreatography and multidetector computed tomography. Korean J Radiol. 2013;14(6):905–13. https://doi.org/10.3348/kjr.2013.14.6.905.
5. Suthar M, Purohit S, Bhargav V, Goyal P. Role of MRCP in differentiation of benign and malignant causes of biliary obstruction. J Clin Diagn Res. 2015;9(11):TC08–12.
6. Xu MM, Sethi A. Diagnosing biliary malignancy. Gastrointest Endosc Clin N Am. 2015;25(4):677–90.
7. Soulez G, et al. Left hepaticogastrostomy for biliary obstruction: long-term results. Radiology. 1997;204:780–6.
8. Kamiya S, Nagino M, Kanazawa H, et al. The value of bile replacement during external biliary drainage: an analysis of intestinal permeability, integrity, and microflora. Ann Surg. 2004;239(4):510–7. https://doi.org/10.1097/01.sla.0000118594.23874.89.
9. Parildar Z, Cinar C, Barutcuoglu B, Basol G, Parildar M. Effects of percutaneous transhepatic biliary drainage on renal function in patients with obstructive jaundice. Diagn Interv Radiol. 2011;17:74–9.
10. Kayahara M, Nagakawa T, Ueno K, Ohta T, Takeda T, Miyazaki I. An evaluation of radical resection for pancreatic cancer based on the mode of recurrence as determined by autopsy and diagnostic imaging. Cancer. 1993;72(7):2118–23.
11. Vaishanavi C, et al. Characterization of biofilms in biliary stents and potential factors involved in occlusion. World J Gastroenterol. 2018;24(1):112.
12. Shanbhogue AKP, Tirumani SH, Prasad SR, Fasih N, McInnes M. Benign biliary strictures: a current comprehensive clinical and imaging review. Am J Roentgenol. 2011;197:W295–306.
13. MacFadyen BV Jr, Vecchio R, Ricardo AE, Mathis CR. Bile duct injury after laparoscopic cholecystectomy: the United States experience. Surg Endosc. 1998;12:315–21.
14. Chan CH, Telford JJ. Endoscopic management of benign biliary strictures. Gastrointest Endosc Clin N Am. 2012;22(3):511–37.
15. Smith MT, Sherman S, Lehman GA. Endoscopic management of benign strictures of the biliary tree. Endoscopy. 1995;27(3):253–66.
16. Foutch PG, Sivak MV Jr. Therapeutic endoscopic balloon dilatation of the extrahepatic biliary ducts. Am J Gastroenterol. 1985;80(7):575–80.
17. Ferreira R, Loureiro R, Nunes N, et al. Role of endoscopic retrograde cholangiopancreatography in the management of benign biliary strictures: what's new? World J Gastrointest Endosc. 2016;8(4):220–31.
18. Scapa E, Peer A, Witz E, Eshchar J. "Rendezvous" procedure (RVP) for obstructive jaundice. Surg Laparosc Endosc. 1994;4:82–5.

19. Lee JH, Kim HW, Kang DH, et al. Usefulness of percutaneous transhepatic cholangioscopic lithotomy for removal of difficult common bile duct stones. Clin Endosc. 2013;46(1):65–70. https://doi.org/10.5946/ce.2013.46.1.65.
20. Guimaraes MA, et al. Successful recanalization of bile duct occlusion with a radiofrequency puncture wire technique. J Vasc Intervent Radiol JVIR. 2010;21(2):289–94.
21. DePietro DM, Shlansky-Goldberg RD, Soulen MC, et al. Long-term outcomes of a benign biliary stricture protocol. J Vasc Interv Radiol. 2015;26(7):1032–9.
22. Gwon DI, Ko GY, Ko HK, Yoon HK, Sung KB. Percutaneous trans- hepatic treatment using retrievable covered stents in patients with benign biliary strictures: mid-term outcomes in 68 patients. Dig Dis Sci. 2013;58(11):3270–9.
23. Gwon DI, Shim HJ, Kwak BK. Retrievable biliary stent-graft in the treatment of benign biliary strictures. J Vasc Interv Radiol. 2008 Sep;19(9):1328–35.
24. Itoi T, Yamanouchi E, Ikeuchi N, Kasuya K, Iwamoto H, Tsuchida A. Magnetic compression duct-to-duct anastomosis for biliary obstruction in a patient with living donor liver transplantation. Gut Liver. 2010;4(Suppl. 1):S96.
25. Giménez ME, et al. Biodegradable biliary stents: a new approach for the management of hepaticojejunostomy strictures following bile duct injury. Prospective study. Arq Bras Cir Dig ABCD. 2016;29(2):112–6. PMC. Web. 20 Mar. 2018.
26. Mauri G, Michelozzi C, Melchiorre F, Poretti D, Tramarin M, Pedicini V, Solbiati L, Cornalba G. Luca Maria Sconfienz. Biodegradable biliary stent implantation in the treatment of benign bilioplastic-refractory biliary strictures: preliminary experience. Eur Radiol. 2013;23(12):3304–10.

Common Bile Duct Exploration

20

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Epidemiology/Diagnosis

As stated in previous chapters, about 10–20% of patients with cholelithiasis present with choledocholithiasis [1]. 1–2% of patients who undergo a cholecystectomy will present with retained stones postoperatively if intraoperative cholangiography is not done [2]. Open common bile duct (CBD) exploration was the conventional method of stone extraction in the operating room; however, with the advent of laparoscopic surgery, newer options have been developed [3]. CBD stones can present anywhere along a spectrum from silent (incidentally noted), to biliary colic, to obstruction of the ampulla of Vater, and all the way to obstructive jaundice and ascending cholangitis [2].

A patient's laboratory analysis can be abnormal with elevated liver enzymes and elevated bilirubin. If there is an infection, they can present with a leukocytosis. Ultrasound may show choledocholithiasis or may just show dilation of the biliary ducts (intrahepatic or common bile duct). Choledocholithiasis is highly suggested in patients with biliary pain, cholelithiasis, jaundice, and a dilated bile duct >8 mm [2]. MRCP (magnetic resonance cholangiopancreatography) is almost 100% specific and >90% sensitive for common bile duct stones and is noninvasive; however, once choledocholithiasis is found, intervention is still needed [2]. Endoscopic retrograde cholangiopancreatography (ERCP) can also diagnose choledocholithiasis and can clear stones in about 75% of patients during their first ERCP and about 90% after repeat ERCP [2].

Ultrasound is routinely used for the evaluation of biliary disease, while MRCP and ERCP are employed more selectively. Ultrasound has been noted to have a sensitivity of only 32% for CBD stones making MRCP an important adjunct [4]. ERCP is a great option for patients with cholangitis and biliary pancreatitis or if the surgeon has limited experience with duct exploration. Otherwise, cholangiography during laparoscopic cholecystectomy is a good option [2]. However, one study found that if cholangiography is employed on all patients intraoperatively, 1/3rd of the CBD stones found will pass spontaneously within 6 weeks of surgery; and therefore it may be more prudent to employ selective intraoperative cholangiography [5]. While there are many signs and symptoms of choledocholithiasis, about 40–50% of patients with choledocholithiasis will be asymptomatic [6] (Fig. 20.1).

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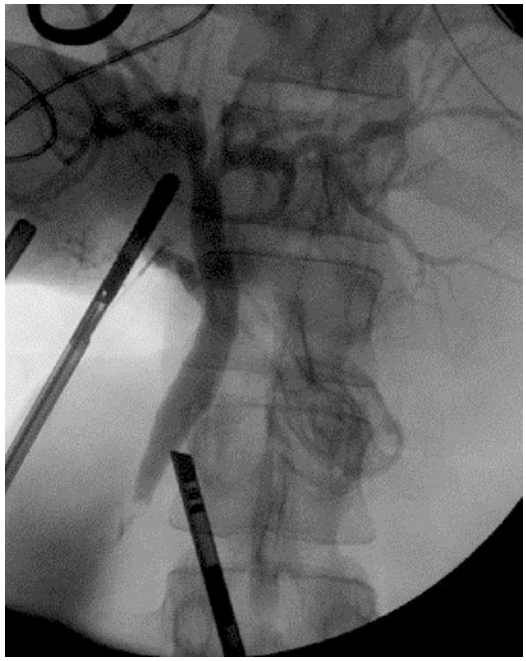

Fig. 20.1 Choledocholithiasis seen on intraoperative cholangiogram. There is a positive meniscus sign at the common bile duct stone and absence of filling of the small bowel

Treatment Options

Treatment options include preoperative ERCP, PTHC (Percutaneous Transhepatic Cholangiogram), laparoscopic cholecystectomy with laparoscopic common bile duct exploration, open bile duct exploration, and postoperative ERCP. Smaller stones (usually <4 mm) are likely to pass on their own or to flush easily after administration of 1–2 mg of IV glucagon intraoperatively [6]. ERCP is a good option for patients with difficult anatomy, and it is still an option in those who have had a Roux-en-Y gastric bypass though it may require surgical assistance for access through the remnant stomach [7]. 86% of providers noted they would choose ERCP if the CBD stones are found preoperatively, while 30% would choose laparoscopic common bile duct exploration (LCBDE) if the stones are found intraoperatively [8, 9]. There are a few contraindications to laparoscopic common bile duct exploration to include a hostile porta hepatis, lack of technical skill, and the absence of common bile duct pathology [6]. In the hands of an experienced provider, laparoscopic common bile duct exploration has a success rate of about 90% [6]. A meta-analysis from 2006 looked at ERCP vs LCBDE vs open common bile duct exploration and found that open surgery resulted in significantly reduced number of retained stones compared to ERCP, while ERCP and LCBDE were similar [10]. However, this study used data from the early days of endoscopy. Laparoscopic CBD exploration has shown comparable stone extraction rates to ERCP; however, the length of hospital stay is shorter, and physician fees are lower in patients who undergo stone extraction via common duct exploration at the time of cholecystectomy [11–13]. A retrospective study from 2017 showed that laparoscopic cholecystectomy with postoperative ERCP was more successful at stone clearance than LCBDE (98% vs 88.6%); however, the LCBDE group had a fewer number of procedures (1.1 vs 2.0; $P < 0.001$) per patient [14]. The laparoscopic transductal approach to LCBDE has shown a higher clearance rate than the transcystic approach and ERCP (100% vs 93.7% vs 92.3%), respectfully [12]. One study attempted to identify factors that predict converting to an open common bile duct exploration from a laparoscopic exploration, and they found that prior antibiotic use, previous ERCP attempt, and abnormal biliary anatomy had a 90% likelihood of failed laparoscopic common bile duct exploration [15].

Laparoscopic Common Bile Duct Exploration

Once an intraoperative cholangiogram is done to confirm the presence of stones in the common bile duct, a decision can be made on whether or not a common bile duct exploration needs to be done. Some of the decisions can be based on size of the ducts, locations of the stones, and size of the stones (see Table 20.1). 1–3 mm stones that are few in number can often be managed by duct irrigation and glucagon administration, which relaxes the sphincter of Oddi. A second cholan-

Table 20.1 Contraindications

Transcystic	Larger stones (>6 mm), intrahepatic stones, cystic duct <4 mm, cystic duct entrance to CBD posterior or distal
Transcholedochal	Small CBD <6 mm, marked inflammation, poor suturing ability of the provider
Either approach appropriate	One or multiple small stones, cystic duct >4 mm, CBD >6 mm, cystic duct entrance to CBD is lateral, and mild inflammation

giogram should be done to ensure that the stone or stones have cleared the duct and that contrast enters the duodenum. If this fails or if the stones are >4 mm, then a formal CBD exploration is needed. One should prepare for a CBD exploration preoperatively by ensuring all of the equipment to do an exploration is in the room. As this is not a commonly performed procedure, trying to find the proper equipment intraoperatively will only serve to cause delays and frustration. The equipment needed are:

- Choledochoscope with saline bag to flush the scope and allow better visualization
- 0.028 or 0.035 inch guidewire
- Over the wire dilators or balloon dilators
- Wire baskets
- Balloon catheters (4*f* Fogarty embolectomy catheters can be used)

There are two access points for laparoscopic CBD exploration: the transcystic approach and the transcholedochal approach. As stated before, there are several factors that have been identified that can influence your approach to a LCBDE, whether it be transcystic or transcholedochal (Figs. 20.2, 20.3, and 20.4, imaging courtesy of Dr. Franklin Goldwire, TAMC GI Department) [6, 7].

Using a cystic ductotomy, the transcystic approach is accomplished passing the guidewire down into the common bile duct using fluoroscopic guidance. Next a balloon or bougie-type dilator is placed over the guidewire to dilate the cystic duct to about 4 mm. The dilator is removed, and the choledochoscope is introduced over a wire or freely by pushing it into the duct after dilation [6]. Through the working port of the choledochoscope, the stones can then be removed with a wire basket or a Fogarty balloon catheter. There is a risk of dragging stones into the common hepatic duct or pushing stones through the sphincter of Oddi and causing trauma (injury, pancreatitis, bleeding, etc.) [6]. A wire basket can also be used to ensnare the stone once it is found. Once the stone is captured in the basket, both the basket with the stone

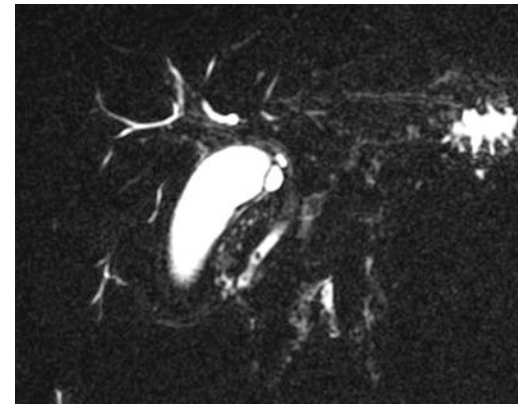

Fig. 20.2 This MRCP shows a patient with choledocholithiasis with at least two stones in the distal common bile duct with minimal inflammation. The common bile duct on this study measured 6 mm. She is likely a good candidate for either approach (large CBD size, mild inflammation, multiple small stones)

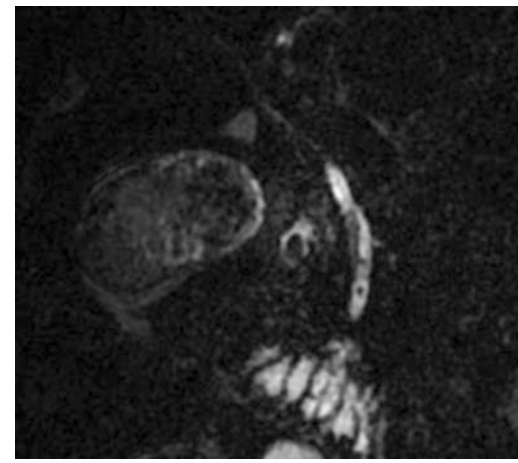

Fig. 20.3 This MRCP shows a patient with choledocholithiasis with multiple distal common bile duct stones. He was found to have a non-dilated common bile duct with the largest diameter being 4 mm. He would be a better candidate for a transcystic approach due to the small CBD size

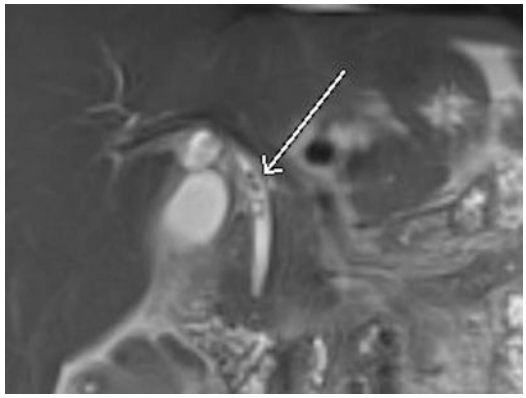

Fig. 20.4 This MRCP shows a patient with choledocholithiasis with multiple small stones in the proximal common bile duct. Her common bile duct measured 7 mm. She is likely a better candidate for a transcholedochal approach because of the size of her CBD and the possibility of more proximal stones. (Imaging courtesy of Dr. Franklin Goldwire, TAMC GI Department)

and the choledochoscope are removed together [2]. This approach is not appropriate for stones in the common hepatic duct above the cystic duct insertion point [2]. This approach may require an additional port placed halfway between the subxiphoid and right subcostal ports; this port needs to be valveless in order to pass the choledochoscope [6]. Sometimes a stay suture placed into the cystic duct distal to the ductotomy, if there is room, can help to manipulate the duct allowing easier passage of the guidewire, choledochoscope, and other instruments. A liver retractor can also be place to hold the liver as well as the biliary tree in place, freeing up an instrument arm for the surgeon or assistant. Finally this can also be attempted under fluoroscopic guidance only and not through the choledochoscope. However this will likely cause more exposure to radiation and contrast.

For a transcholedochal approach, an incision is made on the CBD. This is best when the transcystic approach is contraindicated as noted in Table 20.1 and the anatomy is easily identifiable laparoscopically. A longitudinal incision is made in order to prevent damage to the blood supply to the CBD which are located at the 3 and 9 o'clock positions along the duct [6]. The length of the incision should be at least as large as the largest stone within the duct. Stones will usually fall out of the duct at this time, but flushing may help extract additional stones [6]. The choledochoscope is then fed distally to look for additional stones which can be removed using the techniques discussed in the transcystic approach. The choledochoscope can also be used to examine the hepatic ducts if stones are noted there. Complete clearance of the CBD with flow going into the duodenum should again be confirmed by cholangiogram or by the choledochoscope being seen in the duodenum. The choledochal incision is then closed with 4-0 or 5-0 absorbable sutures. Placement of a T-tube, biliary drains, or a biliary stent is controversial, but a meta-analysis has shown a lower complication rate if T-tubes are not placed and no additional benefit with drain or stent placement [6, 16]. Primary duct closure has shown fewer overall complications compared to T-tube placement, especially with bile peritonitis, and thus, it is recommended to be the preferred option due to increased risk of infection [17, 18]. T-tube placement is recommended to decompress the CBD if there is a distal obstruction or if the CBD diameter is small, <8 mm, in order to decrease the risk of bile duct stricture [4, 16]. Drain placement is not necessary unless there is concern for increased pressure (stricturing, edema of the papilla, inflammation, retained stones, etc.) and a closed suction drain is really only necessary if one is worried about a bile leak [6, 16, 19–21].

Impacted stones can present a unique challenge. If they are not able to be extracted with the above techniques, fragmentation can be attempted by laser or electrohydraulic lithotripsy if that is available [6]. Cholangioscopy-guided laser lithotripsy has increased the rate of stone extraction in those with stones larger than 1 cm [22]. Another option is postoperative ERCP. Hepatic duct stones are another challenging entity, and they cannot be managed with a transcystic approach due to the difficulty making the upward turn from the cystic duct to the hepatic ducts. A transcholedochal approach is favored; however, if the CBD is too small, ERCP is a safer option [6]. Finally, if the ducts cannot be cleared at the time of surgery, an antegrade ampullary stent can be placed

to allow for decompression and to facilitate a postoperative ERCP. While converting to an open bile duct exploration in this scenario is an option, it is discouraged if the cholecystectomy can be done laparoscopically and a postoperative ERCP is available as the latter has less morbidity than an open exploration [6].

Open Common Bile Duct Exploration

This is a good option for patients already undergoing an open cholecystectomy and those with impacted stones at the ampulla, which pose a difficult problem for endoscopy and laparoscopic routes. Either a right upper quadrant subcostal incision or a midline incision can be utilized. The liver is retracted superiorly and the duodenum inferiorly, and a Kocher maneuver is performed to better visualize the distal CBD. A longitudinal incision is made on the duct for the same reasons as for the laparoscopic approach. Most stones will fall out on their own or with some manual manipulation. Saline irrigation and a Fogarty catheter can be used if stones still remain. As with the laparoscopic approach, if these maneuvers fail, choledochoscopy and basket retrieval can be used. The choledochotomy can be closed primarily or over a T-tube for the same reasons as the laparoscopic approach.

If the CBD exploration fails to remove the impacted stones, one can perform lithotripsy or a duodenotomy with sphincterotomy of the ampulla of Vater. Again, the main point of all of these explorations is to decompress the biliary tree and control the cholangitis, if present. This can also be done with T-tube placement into the CBD. Additionally this can be considered a stabilizing maneuver, and one who is not experienced with an anastomosis involving the CBD can stop here. If the biliary tree is dilated, drainage can be accomplished through a choledochoenterostomy with either a choledochoduodenostomy or a Roux-en-Y choledochojejunostomy [2]. This, however, should be done by someone with good experience performing hepatobiliary surgery.

Postoperative Management

LFTs should not be checked postoperatively unless the patient is having symptoms because the levels can remain elevated over a week after the procedure [23]. A cholangiogram is done at 24–48 hours postoperatively if a T-tube was placed during the procedure. If the cholangiogram is clear, the drain is clamped but typically remains in place for 10–14 days. Note that silastic T-tubes tend to cause less of a reaction than do latex ones; as such they may not be amenable to removing within 14 days. If the cholangiogram is abnormal (stones are present), leave the drain open for 1–2 weeks, and repeat the cholangiogram. If that cholangiogram is normal, the T-tube can be removed; however, if it is still abnormal, interventional radiology can be consulted to perform a percutaneous transhepatic cholangiogram, or an ERCP can be done [6].

Complications

For LCBDE, retained stones occur in about 0–5% [20]. This is lower when biliary endoscopy is used as compared to using the basket blindly. Bile leaks occur in about 2.3–16.7% of patients [6]. Bile duct strictures occur in about 0–0.8% of patients, pancreatitis occurs in about 0–3% of patients, and there is a risk of postoperative infections as well [6, 9, 24]. T-tube drainage complications include fluid and electrolyte disturbances, inconvenience of carrying the drainage bag, local pain, bile leakage once removed, biliary peritonitis, premature dislodgement, and wound infection [4].

Conclusion

Laparoscopic common bile duct explorations are not routinely performed by many general surgeons, but competency in this skill can be helpful when ERCP and PTHC are not readily available or when these modalities fail. Preparation is key to success. There are two generally accepted

ways to approach a CBD exploration: either the transcystic or transcholedochal approach. Stone size, stone location, and duct morphology will dictate which approach to take. Completion cholangiography should always be done.

Resources

1. Senthilnathan P, et al. Laparoscopic choledochoduodenostomy as a reliable rescue procedure for complicated bile duct stones. Surg Endosc. 2018;32:1828–33.
2. Chapter 55: Biliary system. In: Townsend CM, et al., editors. Sabiston textbook of surgery, 19th ed. Philadelphia: Elsevier Sanders; 2012, p. 1476–514.
3. Ying-chao Gao MM, et al. Efficacy and safety of laparoscopic bile duct exploration versus endoscopic sphincterotomy for concomitant gallstones and common bile duct stones: a meta-analysis of randomized controlled trials. Medicine. 2017;96:37.
4. Liu W-S, et al. Laparoscopic exploration can salvage recurrent common bile duct stone after cholecystectomy. Am Surg. 2017;83(12):1343–6.
5. Tarantino G, et al. Surgery in biliary lithiasis: from the traditional "open" approach to laparoscopy and the "rendezvous" technique. Hepatobiliary Pancreat Dis Int. 2017;16(6):595–601.
6. Zerey M, et al. Laparoscopic common bile duct exploration. Surg Endosc. 2018;32(6):2603–12.
7. Petelin JB. Techniques and cost of common bile duct exploration. Semin Laparosc Surg. 1997;4(1):23–33.
8. Baucom RB, et al. Surgeons, ERCP, and laparoscopic common bile duct exploration: do we need a standard approach for common bile duct stones? Surg Endosc. 2016;30:414–23.
9. Wang X, et al. Endoscopic retrograde cholangiopancreatography versus laparoscopic exploration for common bile duct stones in post-cholecystectomy patients: a retrospective study. Oncotarget. 2017;8(47):82114–22.
10. Dasari BVM, et al. Surgical versus endoscopic treatment of bile duct stones (review). Cochrane Database Syst Rev. 2013;12:CD003327.
11. Rogers SJ, et al. Prospective randomized trial of LC+LCBDE vs ERCP/S+LC for common bile duct stone disease. Arch Surg. 2010;145:28–33.
12. Zhou Y, et al. Three modalities on management of choledocholithiasis: a prospective cohort study. Int J Surg. 2017;44:269–73.
13. Costi R, Gnocchi A, Di Mario F, Sarli L. Diagnosis and management of choledocholithiasis in the golden age of imaging, endoscopy and laparoscopy. World J Gastroenterol. 2014;20(37):13382–401.
14. Al-Temimi MH, et al. Laparoscopic common bile duct exploration versus endoscopic retrograde cholangiopancreatography for choledocholithiasis found at time of laparoscopic cholecystectomy: analysis of a large integrated health care system database. Am J Surg. 2017;214:1075–9.
15. Chue KM, et al. A predictive nomogram to identify factors influencing the success of a concomitant laparoscopic cholecystectomy with common bile duct exploration for choledocholithiasis. Hepato-Pancreato-Biliary. 2017;20:313–20.
16. Yin Z, et al. Is the end of the T-tube drainage era in laparoscopic choledochotomy for common bile duct stones is coming? A systematic review and meta-analysis. Ann Surg. 2013;257(1):54–66.
17. Zhang W, Li G, Chen Y. Should T-tube drainage be performed for choledocholithiasis after laparoscopic common bile duct exploration? A systematic review and meta-analysis of randomized controlled trials. Surg Laprosc Endosc Percutan Tech. 2017;27(6):415–23.
18. Parra-Membrives P, Marinez-Baena D, Lorente-Herce J, Jimenez-Riera G. Comparative study of three bile duct closure methods following laparoscopic common bile duct exploration for choledocholithiasis. J Laparoendosc Adv Surg Tech. 2018;28(2):145–51.
19. Gurusamy KS, Koti R, Davidson BR. T-tube drainage versus primary closure after laparoscopic common bile duct exploration. Cochrane Database Syst Rev. 2013;6:CD005641.
20. Khaled YS, et al. Laparoscopic bile duct exploration via choledochotomy followed by primary duct closure is feasible and safe for the treatment of choledocholithiasis. Surg Endosc. 2013;27(11):4164–70.
21. Lyon M, et al. Use of biliary stent in laparoscopic common bile duct exploration. Surg Endosc. 2015;29(5):1094–8.
22. Buxbaum J, et al. Randomized trial of cholangioscopy-guided laser lithotripsy versus conventional therapy for large bile duct stones. Gastrointest Endosc. 2018;87(4):1050–60.
23. Saber AA, et al. Changes in liver function tests after laparoscopic cholecystectomy: not so rare, not always ominous. Am Surg. 2000;66(7):699.
24. Li K-Y, et al. Advantages of laparoscopic common bile duct exploration in common bile duct stones. Wien Klin Wochenschr. 2018;130:100–4.

Part VII

Diverticulitis

Diverticulitis: Incidence and Initial Management

21

Dominic M. Forte and Andrew T. Schlussel

Introduction

Diverticulitis is one of the most common benign colonic disorders. The severity of the disease is highly variable, with mild cases managed on an outpatient basis with volume repletion and antibiotics, while complicated or severe diverticulitis may require emergent surgical therapy. Given the variability in presentation and the corresponding clinical consequences, an algorithmic approach should be utilized to guide medical and surgical treatment (Fig. 21.1).

Incidence

Diverticulosis is a modern disease. Initially described in the early 1800s as a rare curiosity, this condition has become increasingly common [1]. The risk of developing diverticulosis increases with age, with a prevalence of less than 10% in those younger than 40 and approximately 70% in individuals 80 years or older [2, 3]. Left-sided diverticular disease is more common in Western culture, where right-sided disease is more frequently seen in the Asian population and a younger cohort [4]. Previous literature has described a 10–25% risk of developing complications related to diverticulosis; however; modern population-based studies utilizing colonoscopic screening suggest only 1–4% of patients will progress to symptomatic disease [2, 5–7].

Diverticular disease places a substantial impact on the US healthcare system. Cost estimates from 2015 demonstrated that complications arising from this condition accounted for $2.6 billion in spending, with 333,464 emergency department visits, 216,560 hospital admissions, 4567 deaths, and 2.3 million outpatient visits. These national statistics have increased markedly since 2012, and as the nation's population ages, an increase in disease burden is anticipated [8, 9].

Initial Management

History and Physical Exam

Uncomplicated diverticulitis is defined by inflammation of the colon in association with diverticula. The triad of left lower quadrant abdominal pain, fever, and leukocytosis is present in approximately 40% of patients [10]. Abdominal pain can be right sided or suprapubic in case of cecal diverticulitis or a redundant sigmoid colon [11–13]. Patients often have a change in bowel habits including constipation (34.8%), diarrhea (18.6%),

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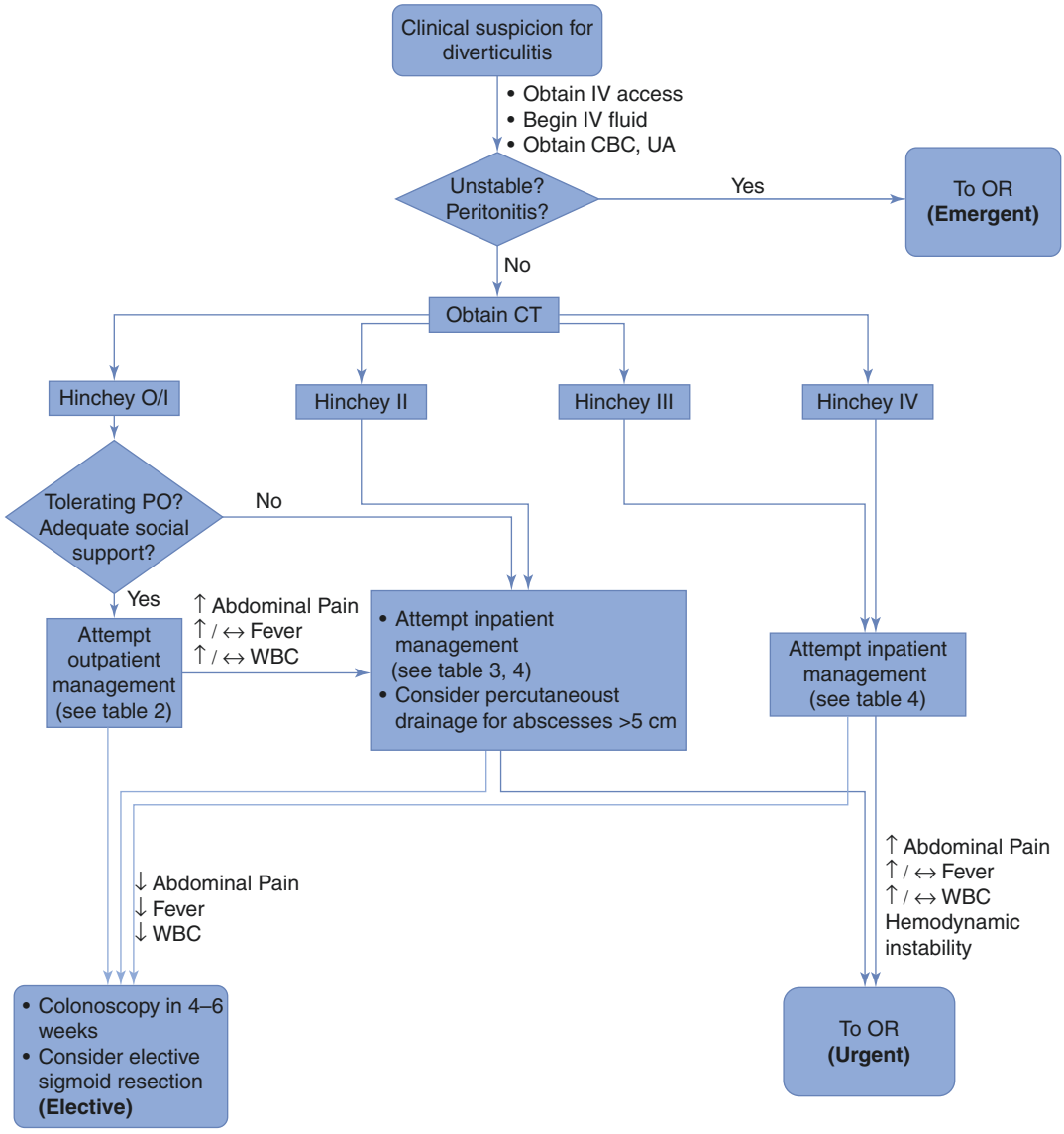

Fig. 21.1 Medical management algorithm

or a combination of both (8.6%) [14]. Nausea, vomiting, and anorexia may be present in up to 20% and can signify the presence of an ileus or bowel obstruction [13, 14]. Urinary symptoms consisting of dysuria, frequency, and urgency are seen in as many 13% of patients and may be associated with sterile pyuria. Hematochezia is rare and mild when present with diverticulitis, and significant bleeding should raise concern for alternative diagnoses such as an underlying neoplastic process [13].

Complicated diverticulitis is defined by the presence of a pericolonic or pelvic abscess, fistula, bowel obstruction, or free perforation. An intra-abdominal abscess may develop in approximately 15–20% of patients requiring hospital admission [15, 16]. Symptoms suggestive of an abscess include high fever, malaise, or a palpable mass on either abdominal, pelvic, or rectal examination [14]. Fistula formation is most likely to be present in those with repeated episodes of diverticulitis. The development of a diverticular fistula

varies based on gender and surgical history, with the most common including colovesical (65%), colovaginal (25%), coloenteric (6.5%), and colouterine (3%). Colovesical fistulae occur more commonly in men and are associated with dysuria, fecaluria, pneumaturia, and a history of recurrent cystitis. A colovaginal fistula is more common in women who have had a hysterectomy and present clinically as foul vaginal discharge or frank passage of feces from the vagina [17]. A large bowel obstruction in the sigmoid colon may occur as a result of chronic recurrent inflammation or secondary to a fibrotic stricture. In addition, a small bowel obstruction can result from the effects of pericolonic inflammation [14]. Free perforation is rare, but rates may be increasing [18]. This manifests as peritonitis, high fever, and hypotension. When present, perforation can rapidly progress to intra-abdominal sepsis and multisystem organ failure [19].

Laboratory Evaluation

A complete blood count, basic metabolic panel, and urinalysis are the most useful labs when assessing patients with known or suspected diverticulitis [20]. In addition, there has been increased interest in evaluating the role of C-reactive protein (CRP) in the management of acute diverticulitis. A CRP value ≥150 mg/L has been demonstrated to have a sensitivity (Sn) of 85% and specificity (Sp) of 65% in distinguishing complicated from uncomplicated diverticulitis [21]. This is of uncertain clinical relevance given the widespread use of cross-sectional imaging and a poor negative predictive value of CRP. Makela and colleagues reported over 35% of patients with a CRP ≤150 mg/L were found to have complicated disease on imaging [22]. The trend of CRP in the first 24 hours has not been found to be predictive of response to treatment; however, this may play a role in identifying failure of treatment without antibiotics [23]. Stool testing for bacteria or parasites should only be implemented when there is concern for infectious diarrhea as an alternative explanation for abdominal pain.

Imaging

Computed tomography (CT) is the preferred diagnostic imaging modality for the diagnosis of acute diverticulitis [20]. The sensitivity of CT imaging in the identification of diverticulitis is 94% with a specificity of 99% [24, 25]. Findings suggestive of diverticulitis on CT include bowel wall thickening (>4 mm), pericolonic fat stranding, presence of a fluid collection or air fluid levels, extraluminal gas, abscess, stricture, fistula, or a pericolonic soft tissue density (phlegmon) [20, 26]. The modified Hinchey classification is the most common CT-based grading scale for complicated diverticulitis (Table 21.1 and Fig. 21.2) [27–29]. Representative CT slices are shown in Figs. 21.3, 21.4, 21.5, and 21.6. The Hinchey grade can aid in determining the appropriate management for these patients (Fig. 21.1).

Table 21.1 Comparison of Hinchey and modified Hinchey classifications

Hinchey classification, 1978 [27]		Modified Hinchey classification, 1997 [28]		Modified Hinchey classification, 1999 [29]	
I	Pericolic abscess or phlegmon	I	Pericolic abscess	Ia	Phlegmon
				Ib	Pericolic abscess
II	Pelvic, intra-abdominal, or retroperitoneal abscess	IIa	Pelvic abscess or phlegmon amenable to drainage	II	Pelvic abscess
		IIb	Complex abscess associated not amenable to drainage, presence of fistula		
III	Generalized purulent peritonitis	III	Generalized purulent peritonitis	III	Purulent peritonitis
IV	Generalized fecal peritonitis	IV	Fecal peritonitis	IV	Fecal peritonitis

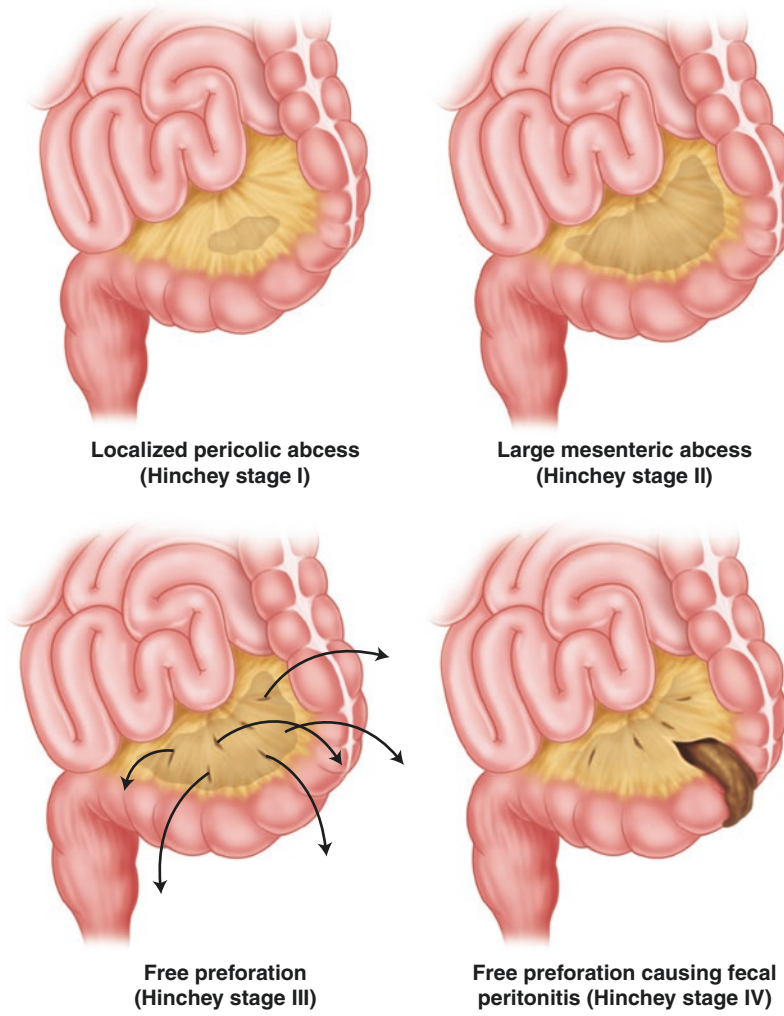

Fig. 21.2 Hinchey classification

While CT is favored, magnetic resonance imaging (MRI) and graded compression ultrasound are potential alternatives. MRI has a similar sensitivity (>94%), but lower specificity (88%) than CT in the diagnosis of diverticulitis [30]. Although MRI offers the benefit of avoiding radiation exposure, the increased cost, decreased availability, and decreased expedience limit its utilization. Graded compression ultrasound offers a sensitivity of 92% and specificity of 90% [24]. The drawbacks of ultrasound in the diagnosis of diverticulitis include high inter-user variability, decreased utility in obese patients, and a decreased ability to identify alternative diagnoses. The American Society of Colon and Rectal Surgeons (ASCRS) clinical practice guidelines only acknowledge ultrasound's capability to aid in diagnosis, whereas European professional organizations either have no preference between US and CT or recommend the use of CT only if ultrasound is unavailable or findings are equivocal [31].

Endoscopy

Colonoscopy does not have a diagnostic role in the acute setting. Tissue friability, severe

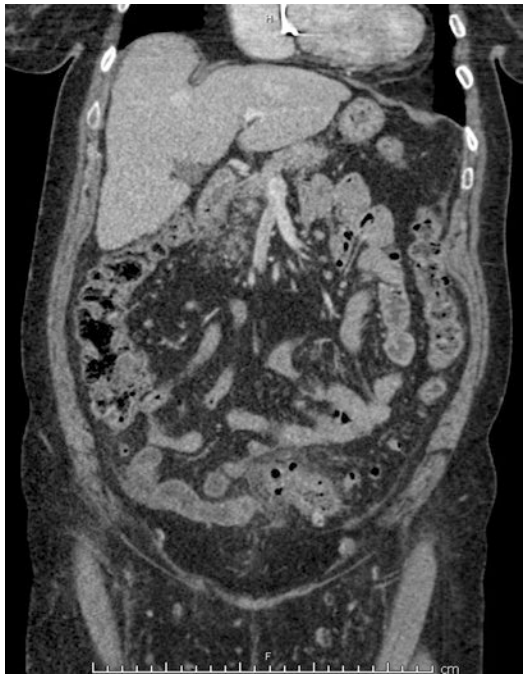

Fig. 21.3 Uncomplicated diverticulitis: pericolonic inflammation without perforation or free air

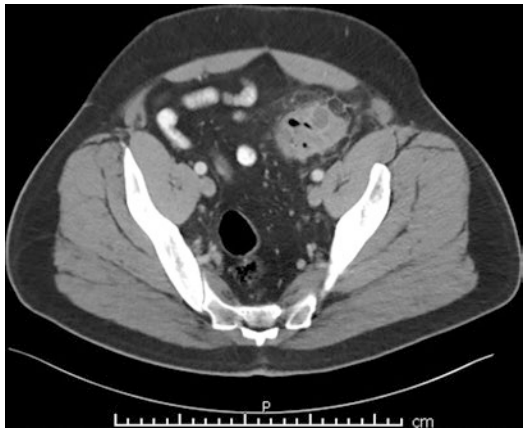

Fig. 21.4 Hinchey Ib: localized pericolonic abscess

inflammation, and potential pre-existing perforation make attempting colonoscopy dangerous. Given low utility and high risk, it is not recommended as part of the initial management. Colonoscopy is recommended 4–6 weeks following successful management of acute diverticulitis to evaluate for an underlying malignancy [20].

Medical Management

Medical management alone should be considered in all patients without generalized peritonitis or obstruction. This may be carried out either on an inpatient or outpatient basis. Regardless, all patients receiving nonsurgical therapy should be frequently reassessed for treatment failure.

Outpatient Management

Outpatient management should be considered for mild uncomplicated diverticulitis. This is appropriate in patients who are able to tolerate an oral diet, have adequate social support, and demonstrate an appropriate response with initial resuscitation [32, 33]. Predictors of failure include female gender and free fluid on CT scan. Age, white blood cell count, CRP trend, comorbidities, and duration of antibiotic therapy have not been found to be significantly associated with outpatient treatment failures [23, 34].

Administration of antibiotics is the standard of care for uncomplicated diverticulitis in the United States. However, two multicenter randomized controlled trials have demonstrated equivalent outcomes with and without antibiotics [35, 36]. While acknowledging the poor evidence for antibiotic use in uncomplicated diverticulitis, the most current ASCRS practice parameters strongly recommend the use of oral or intravenous antibiotics [20]. Current American Gastroenterological Association Institute Guidelines advocate for the selective use of antibiotics; however, they provide no guidance regarding patient selection [37]. A Dutch retrospective cohort study assessed patients with uncomplicated diverticulitis treated without antibiotics for predictors of treatment failure, which was defined as (re)admittance, disease progression, requirement of a procedural intervention, or mortality. Significant predictors of failure included an elevated CRP on presentation, ASA > 2, and greater mean age (63 vs. 58 year old; $p = 0.02$). A CRP level > 170 mg/L was associated with a sensitivity of 20% and specificity of 91% in predicting treatment failure [38].

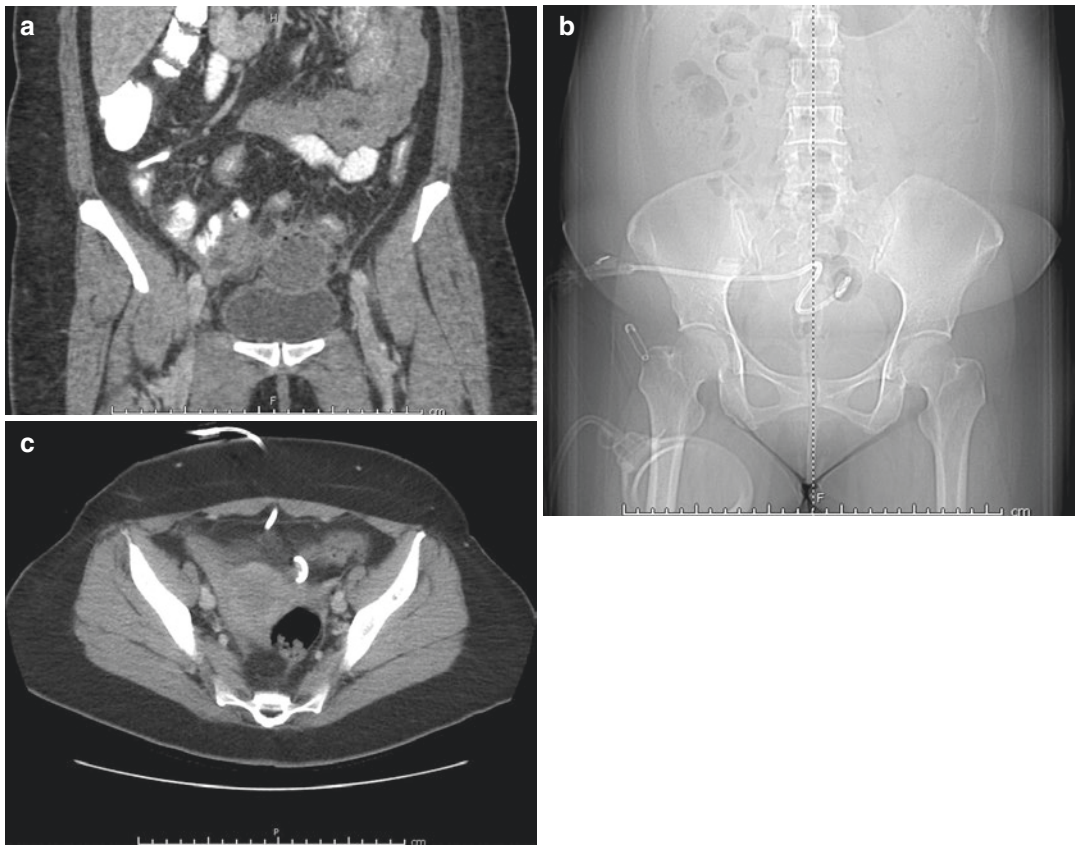

Fig. 21.5 (**a**) Hinchey IIa: pelvic abscess. (**b**) Pelvic abscess following placement of pigtail drain (scout). (**c**) Pelvic abscess with pigtail drain

Antibiotic regimens should target gram-negative and anaerobic bacteria [20, 39]. Possible oral regimens per Infectious Disease Society of America (IDSA) guidelines are outlined in Table 21.2 [40]. Multiple studies have demonstrated non-inferiority of oral antibiotics when compared to intravenous antibiotics [32, 41, 42]. The duration of treatment is typically 7–10 days, although limited evidence suggests shorter courses may be equally effective [43, 44]. A local antibiogram should be utilized prior to prescribing fluoroquinolones given the increased rates of *Escherichia coli* resistance to this class of medications [45].

There is no evidence that dietary modifications affect the course of mild uncomplicated diverticulitis. If desired, a patient can be placed on a clear liquid diet initially with a transition to a low residue diet while recovering [43]. Following recovery, the patient should be transitioned to high-fiber diet [20].

Patients managed on an outpatient basis should be frequently reassessed in the acute period to determine if they require admission. The optimal interval for initial assessment is dependent on whether a patient is at increased risk for failure. In general, patients should be evaluated 1–3 days following the commencement of therapy. Treatment failure should be recognized by the development of fever, worsening pain, and inability to tolerate a diet.

Inpatient Management

Inpatient management is appropriate for patients with clinical evidence or radiographic findings to suggest complicated disease. This includes a high

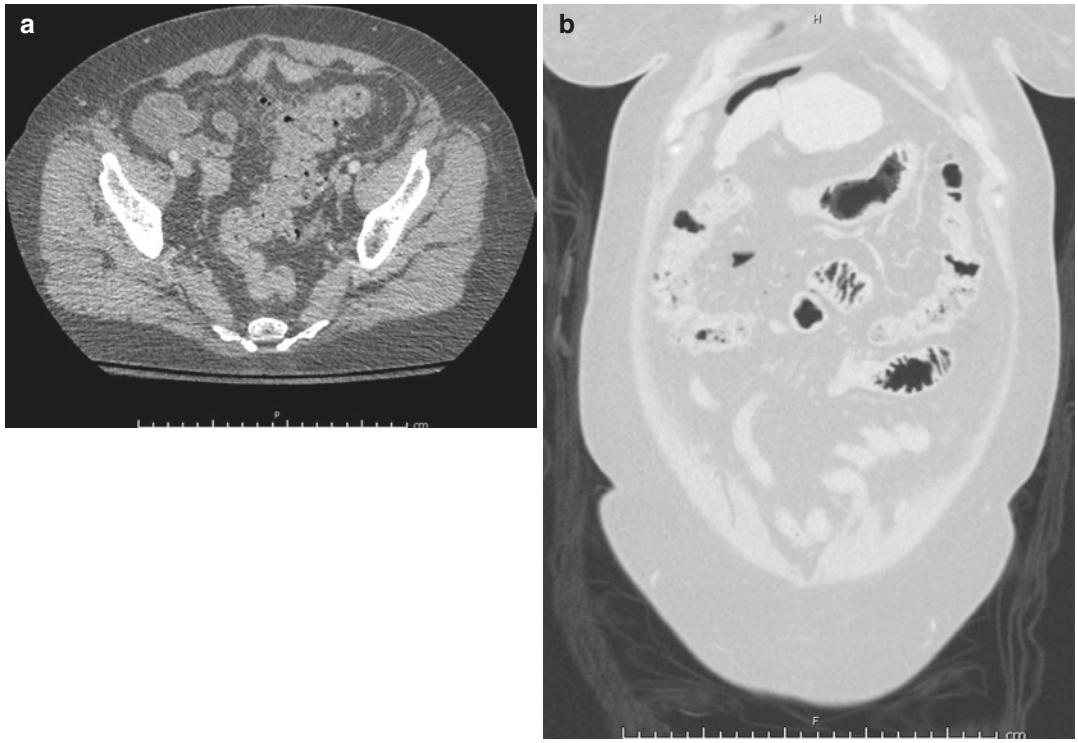

Fig. 21.6 (**a**) Hinchey III: localized free air surrounding the inflamed colon. (**b**) Diverticulitis with distant free air present above the liver

Table 21.2 Oral Antibiotic Regimens for Diverticulitis [40]

Medication	Dose
Single agent	
Amoxicillin-clavulanic acid	875 mg/125 mg PO every 12 hours
Moxifloxacin	400 mg every 24 hours
Combination regimens	
Metronidazole	500 mg every 8 hours
and	
Ciprofloxacin	500 mg PO every 12 hours
or	
Levofloxacin	750 mg every 24 hours
or	
Cefazolin	1–2 g every 8 hours
or	
Cefuroxime	1.5 g every 8 hours

fever, marked leukocytosis, hemodynamic instability, and peritonitis. In addition, inpatient management should be considered for the treatment of uncomplicated diverticulitis when patients lack social support and have an inability to tolerate an oral diet, in the setting of pregnancy, or those who are immunocompromised. Patients should be counseled and educated on their expected hospital course. Non-operative management is often successful, even in the setting of an intra-abdominal abscess and pneumoperitoneum, with greater than >90% of patients avoiding surgical therapy during their initial hospitalization [46].

Once inpatient management is initiated, any oral intake should be avoided until the requirement of surgical intervention or percutaneous drainage is determined. The patient should receive intravenous volume resuscitation and antibiotics [20]. Tables 21.3 and 21.4 outline IDSA recommended intravenous antibiotic regimens for mild to moderate and severe disease, respectively [40].

Diverticular Abscess

Diverticular abscesses >5 cm should be considered for percutaneous drainage in addition to

Table 21.3 Intravenous antibiotic regimens for mild to moderate diverticulitis [40]

Medication	Dose
Single agent	
Cefoxitin	2 g every 6 hours
Ertapenem	1 g every 24 hours
Moxifloxacin	400 mg every 24 hours
Tigecycline	100 mg initial dose, then 50 mg every 12 hours
Ticarcillin-clavulanic acid	3.1 g every 6 hours (200–300 mg/kg/day divided to be dosed every 6 hours)
Combination regimens	
Metronidazole	500 mg every 8 hours
and	
Cefazolin	1–2 g every 8 hours
or	
Cefuroxime	1.5 g every 8 hours
or	
Ceftriaxone	2 g every 24 hours
or	
Cefotaxime	2 g every 24 hours
or	
Ciprofloxacin	400 mg every 12 hours
or	
Levofloxacin	750 mg every 24 hours

Table 21.4 Intravenous antibiotic regimens for severe diverticulitis [40]

Medication	Dose
Single agent	
Imipenem-cilastatin	500 mg every 6 hours
Meropenem	1 g every 8 hours
Doripenem	500 mg every 8 hours
Piperacillin-tazobactam	4.5 g every 6 hours
Combination regimens	
Metronidazole	500 mg every 8 hours
and	
Cefepime	2 g every 8 hours
or	
Ceftazidime	2 g every 8 hours
or	
Ciprofloxacin	400 mg every 12 hours
or	
Levofloxacin	750 mg every 24 hours

intravenous antibiotics (Fig. 21.5a–c). The objective of drainage is to temporize the acute infectious process in order to defer surgical intervention to the elective setting. This avoids the high morbidity and mortality associated with emergent operations. Although there is variability in size criteria, current consensus guidelines recommend the drainage of any "large" abscess (ranging from at least 2 to 5 cm on CT scan). These recommendations stem from the findings that an abscess >5 cm is unlikely to be successfully managed with antibiotics alone [20, 31, 47].

CT-guided drainage is successful at controlling sepsis and preventing need for emergent surgery in 66–93.8% of cases [48–50]. A pelvic abscess has a greater risk of requiring surgical intervention as compared to mesocolic abscesses during the initial hospitalization despite percutaneous drainage (39% vs. 15%, $p = 0.04$). However, there is no difference in the rate of an elective sigmoid resection between a pelvic and mesocolic abscess when successfully drained during the initial hospitalization (32% vs. 36% at a median of 43 months) [51]. The risk of recurrent complicated disease following successful drainage is relatively frequent at 71%, suggesting that CT-guided drainage should only be viewed as an effective tool for deferring surgery, not as a substitute [48].

Failure of Medical Management

Medical management with or without CT-guided drainage is considered to have failed when the patient develops worsening abdominal pain, fevers, peritonitis, leukocytosis, or hemodynamic instability despite maximal therapy or interventions. These patients will require surgery during their initial hospitalization. The surgical decision-making process and operative interventions will be addressed in a subsequent chapter.

Special Considerations

Immunosuppression

A high level of suspicion must be maintained to accurately diagnose diverticulitis in the immunosuppressed (IMS) patient. Limited ability to mount an inflammatory response can minimize the typical radiographic findings of diverticulitis

[20]. These patients require inpatient management to facilitate close observation and expedite intervention if needed. The IMS patient is at an increased risk of clinically decompensating even during an episode of uncomplicated acute diverticulitis (OR 4.34, $p = 0.04$) [52]. These patients are more likely to require emergent or urgent surgery than immunocompetent patients (31.3% vs. 21%, $p = 0.004$), and perioperative mortality is significantly higher (33.3% vs. 15.9%, $p = 0.004$) [53]. Furthermore, immunocompromised patients receiving chemotherapy were more likely to present with a complicated recurrence (87.5% vs. 29.4%, $p = 0.01$) and require surgery for their recurrence (75% vs. 23.5%, $p = 0.03$), with an increased risk of diversion at the time of that surgery (100% vs. 25%, $p = 0.03$) [54].

Right-Sided Diverticulitis

Right-sided or cecal diverticulitis is frequently mistaken for appendicitis [55]. Historically, the diagnosis was made at the time of surgery, but modern cross-sectional imaging often this entity. Right-sided disease is more prevalent in the Asian population; however, a recent study utilizing the National Inpatient Sample found 67% of cases in the United States occurred in Caucasian patients [56]. When properly identified, the management of right-sided diverticulitis is primarily conservative with bowel rest and intravenous antibiotics. The requirement for operative intervention is similar to left-sided disease [57]. Although data is limited, recurrence appears to be low with only 9 of 153 patients managed nonoperatively experiencing recurrence when followed for 60 months [55].

Conclusion

As the nation's population ages, acute diverticulitis has become more prevalent in our healthcare system. Although the progression from diverticulosis to an infectious process is only 1 in 50, the management of this disease may be complex. A CT scan remains the diagnostic mainstay given its ability to determine the presence or absence of complicated disease or demonstrate an alternative diagnosis. Uncomplicated diverticulitis in an otherwise healthy, reliable patient can be safely managed with a 7-day course of oral antibiotics. Complicated diverticulitis is best managed in the hospital with percutaneous drainage being utilized in the appropriate setting. Regardless of the therapies implemented, the primary goal of medical management is to avoid surgical therapy in the acute setting.

References

1. Painter NS, Burkitt DP. Diverticular disease of the colon: a deficiency disease of Western civilization. Br Med J. 1971;2(5759):450–4.
2. Shahedi K, et al. Long-term risk of acute diverticulitis among patients with incidental diverticulosis found during colonoscopy. Clin Gastroenterol Hepatol. 2013;11(12):1609–13.
3. Warner E, et al. Fourteen-year study of hospital admissions for diverticular disease in Ontario. Can J Gastroenterol. 2007;21(2):97–9.
4. Kang JY, Melville D, Maxwell JD. Epidemiology and management of diverticular disease of the colon. Drugs Aging. 2004;21(4):211–28.
5. Heise CP. Epidemiology and pathogenesis of diverticular disease. J Gastrointest Surg. 2008;12(8):1309–11.
6. Salem TA, Molloy RG, O'Dwyer PJ. Prospective, five-year follow-up study of patients with symptomatic uncomplicated diverticular disease. Dis Colon Rectum. 2007;50(9):1460–4.
7. Parks TG. Natural history of diverticular disease of the colon. Clin Gastroenterol. 1975;4(1):53–69.
8. Peery AF, et al. Burden of gastrointestinal, liver, and pancreatic diseases in the United States. Gastroenterology. 2015;149(7):1731–41 e3.
9. Peery AF, et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology. 2012;143(5):1179–87 e1–3.
10. Iyer R, et al. Acute colonic diverticulitis: diagnostic evidence, demographic and clinical features in three practice settings. J Gastrointestin Liver Dis. 2014;23(4):379–86.
11. Sugihara K. Diverticular disease of the colon in Japan. Ann Acad Med Singap. 1987;16(3):504–8.
12. Markham NI, Li AK. Diverticulitis of the right colon–experience from Hong Kong. Gut. 1992;33(4):547–9.
13. Stollman N, Raskin JB. Diverticular disease of the colon. Lancet. 2004;363(9409):631–9.
14. Parks TG. Natural history of diverticular disease of the colon. A review of 521 cases. Br Med J. 1969;4(5684):639–42.

15. Bahadursingh AM, et al. Spectrum of disease and outcome of complicated diverticular disease. Am J Surg. 2003;186(6):696–701.
16. Beckham H, Whitlow CB. The medical and nonoperative treatment of diverticulitis. Clin Colon Rectal Surg. 2009;22(3):156–60.
17. Woods RJ, et al. Internal fistulas in diverticular disease. Dis Colon Rectum. 1988;31(8):591–6.
18. Makela J, Kiviniemi H, Laitinen S. Prevalence of perforated sigmoid diverticulitis is increasing. Dis Colon Rectum. 2002;45(7):955–61.
19. Nagorney DM, Adson MA, Pemberton JH. Sigmoid diverticulitis with perforation and generalized peritonitis. Dis Colon Rectum. 1985;28(2):71–5.
20. Feingold D, et al. Practice parameters for the treatment of sigmoid diverticulitis. Dis Colon Rectum. 2014;57(3):284–94.
21. Makela JT, et al. The role of C-reactive protein in prediction of the severity of acute diverticulitis in an emergency unit. Scand J Gastroenterol. 2015;50(5):536–41.
22. Makela JT, Klintrup K, Rautio T. The role of low CRP values in the prediction of the development of acute diverticulitis. Int J Color Dis. 2016;31(1):23–7.
23. Kechagias A, Rautio T, Makela J. The early C-reactive protein trend does not have a role in monitoring acute diverticulitis progression. Chirurgia (Bucur). 2016;111(1):43–7.
24. Lameris W, et al. Graded compression ultrasonography and computed tomography in acute colonic diverticulitis: meta-analysis of test accuracy. Eur Radiol. 2008;18(11):2498–511.
25. Ambrosetti P, et al. Computed tomography in acute left colonic diverticulitis. Br J Surg. 1997;84(4):532–4.
26. Morris J, et al. The utility of computed tomography in colonic diverticulitis. Ann Surg. 1986; 204(2):128–32.
27. Hinchey EJ, Schaal PG, Richards GK. Treatment of perforated diverticular disease of the colon. Adv Surg. 1978;12:85–109.
28. Sher ME, et al. Laparoscopic surgery for diverticulitis. Surg Endosc. 1997;11(3):264–7.
29. Wasvary H, et al. Same hospitalization resection for acute diverticulitis. Am Surg. 1999;65(7):632–5; discussion 636.
30. Heverhagen JT, et al. Prospective evaluation of the value of magnetic resonance imaging in suspected acute sigmoid diverticulitis. Dis Colon Rectum. 2008;51(12):1810–5.
31. Vennix S, et al. Systematic review of evidence and consensus on diverticulitis: an analysis of national and international guidelines. Color Dis. 2014;16(11):866–78.
32. Alonso S, et al. Outpatient treatment of patients with uncomplicated acute diverticulitis. Colorectal Dis. 2010;12(10 Online):e278–82.
33. Biondo S, et al. Outpatient versus hospitalization management for uncomplicated diverticulitis: a prospective, multicenter randomized clinical trial (DIVER Trial). Ann Surg. 2014;259(1):38–44.
34. Etzioni DA, et al. Outpatient treatment of acute diverticulitis: rates and predictors of failure. Dis Colon Rectum. 2010;53(6):861–5.
35. Chabok A, et al. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. Br J Surg. 2012;99(4):532–9.
36. Daniels L, et al. Randomized clinical trial of observational versus antibiotic treatment for a first episode of CT-proven uncomplicated acute diverticulitis. Br J Surg. 2017;104(1):52–61.
37. Stollman N, et al. American Gastroenterological Association Institute guideline on the management of acute diverticulitis. Gastroenterology. 2015;149(7):1944–9.
38. Bolkenstein HE, et al. Treatment of acute uncomplicated diverticulitis without antibiotics: risk factors for treatment failure. Int J Color Dis. 2018;33:863.
39. Brook I, Frazier EH. Aerobic and anaerobic microbiology in intra-abdominal infections associated with diverticulitis. J Med Microbiol. 2000;49(9):827–30.
40. Solomkin JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. Clin Infect Dis. 2010;50(2):133–64.
41. Ribas Y, et al. Prospective randomized clinical trial assessing the efficacy of a short course of intravenously administered amoxicillin plus clavulanic acid followed by oral antibiotic in patients with uncomplicated acute diverticulitis. Int J Color Dis. 2010;25(11):1363–70.
42. Ridgway PF, et al. Randomized controlled trial of oral vs intravenous therapy for the clinically diagnosed acute uncomplicated diverticulitis. Color Dis. 2009;11(9):941–6.
43. Schechter S, Mulvey J, Eisenstat TE. Management of uncomplicated acute diverticulitis: results of a survey. Dis Colon Rectum. 1999;42(4):470–5; discussion 475–6.
44. Schug-Pass C, et al. Prospective randomized trial comparing short-term antibiotic therapy versus standard therapy for acute uncomplicated sigmoid diverticulitis. Int J Color Dis. 2010;25(6):751–9.
45. Johnson JR, et al. Intensity and mechanisms of fluoroquinolone resistance within the H30 and H30Rx subclones of *Escherichia coli* sequence type 131 compared with other fluoroquinolone-resistant *E. coli*. Antimicrob Agents Chemother. 2015;59(8):4471–80.
46. Dharmarajan S, et al. The efficacy of nonoperative management of acute complicated diverticulitis. Dis Colon Rectum. 2011;54(6):663–71.
47. Kumar RR, et al. Factors affecting the successful management of intra-abdominal abscesses with antibiotics and the need for percutaneous drainage. Dis Colon Rectum. 2006;49(2):183–9.
48. Devaraj B, et al. Medically treated diverticular abscess associated with high risk of recurrence and disease complications. Dis Colon Rectum. 2016;59(3):208–15.
49. Brandt D, et al. Percutaneous CT scan-guided drainage vs. antibiotherapy alone for Hinchey II diver-

ticulitis: a case-control study. Dis Colon Rectum. 2006;49(10):1533–8.
50. Durmishi Y, et al. Results from percutaneous drainage of Hinchey stage II diverticulitis guided by computed tomography scan. Surg Endosc. 2006;20(7):1129–33.
51. Ambrosetti P, et al. Long-term outcome of mesocolic and pelvic diverticular abscesses of the left colon: a prospective study of 73 cases. Dis Colon Rectum. 2005;48(4):787–91.
52. Jaung R, et al. Uncomplicated acute diverticulitis: identifying risk factors for severe outcomes. World J Surg. 2017;41(9):2258–65.
53. Biondo S, et al. Recurrence and virulence of colonic diverticulitis in immunocompromised patients. Am J Surg. 2012;204(2):172–9.
54. Samdani T, et al. Colonic diverticulitis in chemotherapy patients: should operative indications change? A retrospective cohort study. Int J Surg. 2014;12(12):1489–94.
55. Tan KK, Wong J, Sim R. Non-operative treatment of right-sided colonic diverticulitis has good long-term outcome: a review of 226 patients. Int J Color Dis. 2013;28(6):849–54.
56. Schlussel AT, et al. Right-sided diverticulitis requiring colectomy: an evolving demographic? A review of surgical outcomes from the National Inpatient Sample Database. J Gastrointest Surg. 2016;20(11):1874–85.
57. Komuta K, et al. Toward therapeutic guidelines for patients with acute right colonic diverticulitis. Am J Surg. 2004;187(2):233–7.

Acute Diverticulitis: Imaging and Percutaneous Drainage

22

J. Matthew Meadows

Introduction

Diverticular disease is an increasingly common condition, particularly in the western hemisphere responsible for over 300,000 hospital admissions and $2.5 billion in healthcare costs annually. While diverticular disease alone is not necessarily symptomatic, acute diverticulitis frequently results in patients seeking medical attention, and from 1998 to 2005, there was a 26% increase in acute diverticulitis cases seen in the United States [1]. Acute diverticular disease presentations vary from mild colonic inflammation to complicated cases with phlegmon, abscess formation, fistulas, bowel perforation, and generalized peritonitis [2, 3]. Mild forms of disease are typically treated effectively as outpatients, while more severe forms may require IV antibiotics, intensive care unit (ICU) admission, and surgery for definitive management [4]. The majority of diverticular disease involves the descending and sigmoid colon; however 5% of cases will involve the right colon and cecum [5]. Complicated forms of disease are seen in 15–30% of cases [4, 6–9], most commonly in the setting of pericolonic abscess formation [10, 11]. Studies have shown that there has been an increase in diverticular abscesses from 1991 to 2005 from 5.9% to 9.6%, respectively, and patients who present with complicated forms of disease will do so on their initial presentation [2, 12].

Treatment strategies of acute diverticulitis depend on the stage of the disease at presentation, patient comorbidities, and general clinical condition (Fig. 22.1). There is much discussion in the literature with regard to which acute therapies if any may reduce chronic disease complications and need for surgery. Historically uncomplicated acute diverticulitis was treated with antibiotics, and the treatment for acute complicated diverticular disease involved a three-stage surgical approach to include a diverting proximal colostomy, sigmoid colectomy and anastomosis, and colostomy takedown [13]. Modern advances in medicine and surgical procedures have evolved these treatment strategies so that now uncomplicated diverticulitis can be managed with supportive care on an outpatient basis, and complicated cases can be treated with a one-stage elective surgery in most patients after the acute complication has been controlled. The purpose of this chapter is to discuss the role of radiology in diagnosing and treating acute diverticulitis. Chronic forms of diverticular disease and the management of such are a separate issue and beyond the scope of this chapter.

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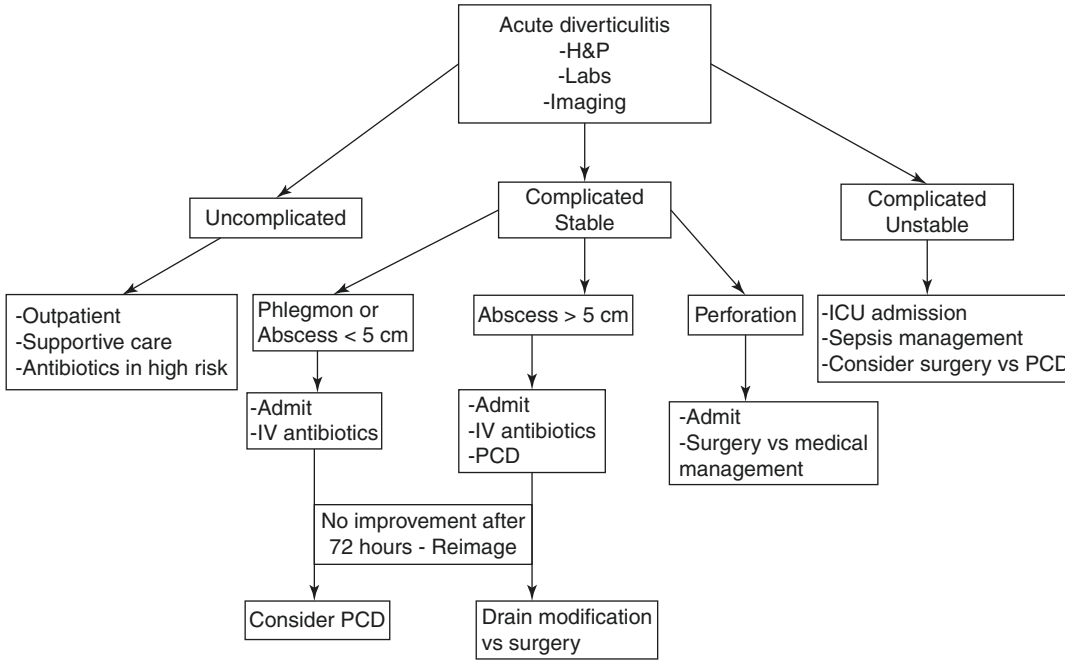

Fig. 22.1 Treatment algorithm for acute diverticulitis

Clinical Presentation and Evaluation

Patients with acute diverticular disease classically present with symptoms of left lower quadrant or lower abdomen/pelvis pain and tenderness, fever, and inability to tolerate oral intake. Patients who may be immunocompromised due to underlying malignancy, corticosteroid use, transplant patients, chronic kidney disease, and others are considered at high risk for complicated disease, and a high index of suspicion should be maintained [2, 9]. Laboratory studies should include a complete blood count, basic metabolic panel, urinalysis, and pregnancy test in females of childbearing age [4]. A basic metabolic panel to include serum creatinine and estimated glomerular filtration rate (eGFR) is obtained as a routine lab as many radiology departments require this prior to administering intravenous (IV) contrast as part of their contrast administration policies.

Imaging

Radiological studies play a vital role in diagnosing acute diverticular disease, providing information on severity and extent of disease, and sometimes provide alternative diagnoses giving healthcare providers the information they need to choose the most appropriate course of action for treatment. The American College of Radiology (ACR) has published a collection of Appropriateness Criteria ® to serve as guidelines generated from expert panels on recommended imaging studies for a variety of clinical conditions. In the setting of left lower quadrant pain, suspected to be the result of diverticular disease, computed tomography (CT) has been recognized as the gold standard imaging modality (Fig. 22.2). CT has proven to be nearly 100% sensitive and specific, with an overall accuracy of 99% in the diagnosis of diverticular disease, giving detailed

American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: **Left lower quadrant pain — suspected diverticulitis**

Variant 1: **Typical clinical presentation for diverticulitis, suspected complications or atypical presentations.**

Radiologic procedure	Rating	Comments	RRL*
CT abdomen and pelvis with IV contrast	9	For this procedure oral and/or colonic contrast may be helpful for bowel luminal visualization.	☢☢☢☢
CT abdomen and pelvis without IV contrast	6		☢☢☢☢
CT abdomen and pelvis without and with IV contrast	5		☢☢☢☢
MRI abdomen and pelvis without IV contrast	5		○
MRI abdomen and pelvis without and with IV contrast	5		○
X-ray contrast enema	4		☢☢☢
US abdomen transabdominal graded compression	4		○
X-ray abdomen and pelvis	4		☢☢☢
US pelvis transvaginal	2		○
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative radiation level**

Fig. 22.2 ACR appropriateness criteria for radiologic evaluation of left lower quadrant pain

information on the severity and extent of disease to include small perforations, distant abscesses, and providing alternative diagnoses [5, 14–16]. Intravenous (IV) contrast is encouraged and should be given in all cases unless there is a contraindication such as severe allergy to iodinated contrast or impaired renal function. Luminal contrast (oral, rectal) administration practices vary among institutions, and many facilities do not routinely administer these. Although it has been shown that the absence of luminal contrast does not significantly limit the ability to correctly diagnose an episode of acute diverticulitis, oral contrast can be extremely helpful in thin patients and for procedural planning (i.e., percutaneous drainage) to distinguish between an abscess cavity and normal fluid-filled intestine [15].

In the setting of acute diverticulitis, CT will demonstrate colonic diverticula associated with segmental bowel wall thickening (>3 mm) within the involved portion of colon and fat stranding in the adjacent mesentery and peritoneal fat. Diverticulosis and bowel wall thickening can also be seen in chronic diverticular disease due to muscular hypertrophy; however inflammatory fat stranding would not be present in this case. Complicated features of diverticulitis include:

1. Phlegmon: Heterogeneously enhancing soft tissue mass near the inflamed colon
2. Abscess: Rim-enhancing fluid collection with or without internal air. May be pericolonic or at distant sites such as the liver, lung, or adnexa
3. Perforation: May be contained pockets of air or gross pneumoperitoneum detected as extraluminal collections of air within the peritoneal cavity or retroperitoneum

CT can also reveal fistulas, obstructions, alternative diagnoses, and other ancillary findings

such as appendicitis, epiploic appendagitis, malignancy, inflammatory bowel disease, infectious/ischemic/pseudomembranous colitis, tubo-ovarian abscess, and pylephlebitis (septic thrombophlebitis) within the mesenteric and portal venous systems [5, 9, 10].

Abdominal radiographs are commonly ordered in the acute setting; however their utility in diagnosing diverticular disease is limited. When bowel perforation is present, radiographs may detect free air as pneumoperitoneum; however small and contained perforations and retroperitoneal air may not be visible [5]. Radiographs may reveal other information such as the presence of pathological calcifications in the abdomen, ileus, and bowel obstructions; however this often leads to advanced imaging to further evaluate the underlying etiology.

Abdominal ultrasound (US) and magnetic resonance imaging (MRI) can be used in select cases where there is intent to avoid ionizing radiation to the patient, such as females during pregnancy. US has a reported sensitivity of 77–98% and specificity of 80–99% but is operator dependent and not as reliable as CT in providing alternative diagnoses. The colon can be evaluated adequately in thin patients, demonstrating noncompressible diverticula with thickened hypoechoic walls and hyperechoic mesenteric fat; however, visualization is limited in overweight patients and in the presence of bowel gas. MRI has a reported sensitivity and specificity of 88–92% and 80–99%, respectively but has its own limitations in availability, increased time to acquire images, bowel motion and bowel gas artifact, and reduced resolution compared to CT. Other modalities such as CT colonography, single- and double- contrast barium, should not be a part of the imaging workup in acute diverticular disease [5, 9, 14, 15].

Classification

Since the late 1970s, there have been numerous classification systems developed with regard to the surgical, radiologic, and clinical features of acute diverticular disease, originating with the *Hinchey Classification* in 1978 based on the extent of disease at the time of surgery [2, 3, 17]. Following the increased use of CT in the 1980s and 1990s, Kaiser et al. published the *Modified Hinchey Classification* (Table 22.1) incorporating CT findings with the original Hinchey system based on findings of *Wasvery* et al. More recently the World Society of Emergency Surgery (WSES)

Table 22.1 Comparison of original Hinchey classification from 1978 with modified Hinchey classification taking CT findings into account in 1999

Stage	Original Hinchey classification (1978)	Stage	Modified Hinchey classification (1999)	Comments
		0	Mild clinical diverticulitis	LLQ pain, elevated WBC, fever, no confirmation by imaging or surgery
I	Pericolic abscess or phlegmon	**Ia**	Confined pericolic inflammation – phlegmon	
II	Pelvic, intraabdominal, or retroperitoneal abscess	**Ib**	Confined pericolic abscess	
		II	Pelvic, distant intraabdominal, or retroperitoneal abscess	
III	Generalized purulent peritonitis	**III**	Generalized purulent peritonitis	No open communication with bowel lumen
IV	Generalized fecal peritonitis	**IV**	Fecal peritonitis	Free perforation, open communication with bowel lumen
		Fistula	Colovesical/colovaginal/ coloenteric/colocutaneous	
		Obstruction	Large and/or small bowel obstruction	

proposed an updated classification also based on imaging findings, separating the system into uncomplicated and complicated forms of disease. Each system is intended to better stratify the disease presentation, guide therapy, and predict outcomes [3, 18].

WSES CT-Guided Classification System of Left Colon Acute Diverticulitis (2015)

- Stage 0: Uncomplicated

Complicated

- Stage 1a: Pericolonic air bubbles or little pericolic fluid without abscess (within 5 cm from inflamed bowel segment)
- Stage 1b: Abscess ≤ 4 cm
- Stage 2: Abscess ≥ 4 cm
- Stage 2b: Distant air (>5 cm from inflamed bowel segment)
- Stage 3: Diffuse fluid
- Stage 4: Diffuse fluid with distant free air

Sallinen et al. has produced the only classification system to date that may be used to predict mortality rate, need for surgery, and ICU level of care based on retrospective clinical, radiologic, and physiologic data of 631 patients (Table 22.2). Independent risk factors associated with poor patient outcome were organ dysfunction, abscess size >6 cm, and peritonitis [19].

Percutaneous Drainage of Abscess

The initial treatment of acute diverticulitis and complications may require a multidisciplinary approach with a general surgeon, an endoscopist, and an interventional radiologist. The medical management is discussed in another chapter. Most cases of complicated diverticulitis present with an abscess formation. Abscesses have been shown to be associated with a 25.7% chance of needing an urgent operation, which may carry significant morbidity [27]. With the development and increased use of CT during the 1980s and 1990s, percutaneous drainage procedures have become a mainstay of treatment for *Modified Hinchey Ib and II* disease [2, 28, 29]. The rate of percutaneous drainage (PCD), typically performed by interventional radiologists, nearly doubled from 1998 to 2005, while the rate of surgery during that same time declined from 17.4% to 14.4% suggesting a paradigm shift in the management of diverticular abscess [1]. Although PCD is now frequently considered the first-line treatment for diverticular abscess, it should be noted that there is no clear consensus as to which patients should undergo this procedure, who can be medically managed, and who requires surgery. The patient's overall condition plays an important role in treatment decisions and the timeliness as to when they should occur.

Patient selection can be challenging when deciding who should and should not be a considered for PCD. It has been shown that although PCD is successful 71–100% of the time resolving

Table 22.2 Classification proposed by *Sallinen* et al [19]

Classification of acute diverticulitis based on radiologic, clinical, and physiologic parameters – *Sallinen* et al. [19]							
Stage	Complicated	Abscess > 6 cm or distant air	Generalized peritonitis	Organ dysfunction	ICU admission	Operative treatment	30-Day mortality
1	N	–	–	–	0%	1%	0%
2	Y	N	N	–	0%	7%	1%
3	Y	Y	N	–	8%	54%	3%
4	Y	Y	Y	N	12%	98%	5%
5	Y	Y	Y	Y	58%	100%	37%

Distant air defined as >5 cm from affected bowel segment
Organ dysfunction defined as:
MAP <70 mmHg
GCS < 15
PaO_2/FIO_2 (P/F) ratio < 400 – corresponds well with O_2 saturation < 90%
Y = yes or present, N = no or absent

acute episodes of diverticular abscess [7, 8, 18, 27, 30–32], recurrence rates for diverticulitis following PCD remain high at 42–68% [7, 8, 27, 33, 34]. For this reason PCD is indicated as a temporizing measure to achieve source control and stabilize the patient in order to avoid emergent surgery, increasing chances of a one-stage elective surgery for definitive management typically 4-6 weeks following an acute attack [1, 2, 7, 18, 27–29, 35, 36]. In the cases where PCD is unsuccessful, there can be up to 75% mortality and 80% rate of colostomy [37].

Factors to consider when deciding on PCD include clinical stability, patient comorbidities, abscess size, and abscess location. Throughout the literature, it has been shown that abscesses up to 5 cm and sometimes even larger can be effectively treated with antibiotics alone [7, 10, 29, 33, 35]. Studies have also shown that medical management is more likely to be unsuccessful for patients with an *American Society of Anesthesiologists* (ASA) score ≥ 3, hemoglobin level ≤ 11.2 mg/dL, abscess size ≥6.5 cm, and temperature of ≥101.2 °F on initial presentation [26, 38]. A prospective study by *Ambrosetti* et al. that is cited regularly in the literature showed that mesocolic abscesses are more likely to respond to antibiotic therapy when compared to pelvic abscesses, but the rate of PCD was increased for abscesses >5 cm [11]. When clinical signs of SIRS or sepsis are present in the setting of abscess, source control is paramount. A universal standard on the timing of source control is a topic of debate [25, 28, 35, 36]; however the *Surgical Infection* Society recommends source control within 24 hours of establishing a diagnosis, but states exceptions can be made for more stable patients on a case-by-case basis. Septic patients, conversely, are more likely to require urgent interventions, while otherwise clinically stable patients can be drained within the 24-hour window [25].

The *Society for Interventional Radiology* (SIR) practice parameters for image-guided percutaneous drainage of abscesses and fluid collections provide indications and contraindications for percutaneous abscess drainage and fluid aspiration and are listed in Table 22.3. With regard to coagulation status, the SIR guidelines classify percutaneous abscess drainage as having a moderate risk of bleeding with the following parameters before performing a percutaneous drainage procedure [39]. Newer anticoagulants such as apixaban, a direct factor Xa inhibitor, are not included in the SIR anticoagulant guidelines. This drug has a 12 h half life, and should generally be held for 2–3 days in most patients, but should be held up to 5 days in patients with poor renal function defined as a creatinine clearance of < 30 mL/min [47, 48].

- INR < 1.5
- Platelets > 50,000/mL
- aPTT: no consensus but trend toward correcting values >1.5× control
- Clopidogrel: hold for 5 days
- Low molecular weight heparin: hold one dose prior to procedure
- Aspirin: does not need to be withheld

The size of an abscess that requires drainage has yet to be studied on a large-scale prospective

Table 22.3 Indications and contraindication for percutaneous abscess drainage from the SIR

Indications and contraindications for percutaneous abscess drainage
Indications
Suspected infected fluid collection or fluid collection related to a fistula
Aspiration of fluid is needed for diagnostic purposes
Suspicion that abscess/fluid is causing adverse physiologic effects such as sepsis or organ dysfunction
Absolute contraindications
None
Relative contraindications
Uncorrectable coagulopathy
Severely compromised cardiopulmonary function or hemodynamic instability
Lack of a safe access route into the abscess
Uncooperative patient or inability to position the patient appropriately

basis; however there are several reports suggesting that abscesses ranging from ≤3 to 5 cm can be effectively treated with antibiotics alone [3, 4, 26–28, 38]. Risks of PCD include rigors, injury to adjacent organs, bleeding, bacteremia, worsening sepsis, and failure to resolve abscess [26, 36, 40]. PCD has also been shown to increase the length of hospital stay compared to antibiotics alone by nearly double [26]. For patients who are not high risk and don't have clinical signs of sepsis, initial treatment with antibiotics alone seems rational for abscesses ≤5 cm [3, 18, 26]. Antibiotics may have reduced uptake in some abscess cavities; so if fever, leukocytosis, abdominal pain/tenderness, and inability to tolerate oral intake fail to resolve within 48–72 hours, the patient should be reimaged and considered for PCD [26]. Patients who present with an abscess >5 cm, but are unsuitable for PCD due to any of the aforementioned contraindications, may be considered for antibiotic therapy alone on a case-by-case basis or proceed to surgery as necessary [3, 38].

Techniques for PCD have been well described since the 1980s, and approaches including anterior, transgluteal, transrectal, and transvaginal have been well described using CT and US guidance [28–30, 36, 41–45]. The most direct path is typically chosen as site of drainage unless there is an interposing structure such as bowel. These procedures should take place in a hospital setting where ancillary support such as anesthesia and surgical services are available [32]. Most procedures can be performed with IV sedation, and some using only local anesthetic [32, 40]. Periprocedural antibiotics in the form of second- or third-generation cephalosporins are recommended within 1 hour of the procedure start, with antibiotic coverage for at least 48 hours afterward [23]. If there is no clinical improvement after 72 hours of PCD, patients should be considered for reimaging to assess the need for additional drainage catheters, or modification/repositioning of existing drains [13].

The specifics of each procedure may vary with respect of imaging modality, trocar vs. Seldinger technique, and patient positioning, and these are usually based on the preference of the interventional radiologist. There are multiple types and sizes of drains available for drainage. Most drains are sized between 8 to 16 French depending on the operator with larger drains typically required for more viscous fluid collections. Once the drain is placed, abscess fluid is aspirated until no further return, and the drain is attached to either gravity drainage or to bulb suction. Samples of aspirated fluid should be sent for culture and sensitivities. Most IR references cite gravity drainage; however bulb suction is commonly seen in post-op surgical patients. There are no studies to determine if one is superior to the other.

Drain management should focus on monitoring of output and maintaining patency of the drain. Drains should be flushed about three times daily with 5–10 cc of normal saline, subtracting any flush volume from daily output totals [13, 31, 41]. If drains are not flushed regularly, output may cease misleading one to think that the abscess has resolved [40]. Continued high output from the drain suggests the presence of a fistula, which occurs in ~14% of cases. Small fistulas will usually resolve by leaving the drain in place; however a persistent fistula may require continued drainage and can be removed during surgical resection of the diseased bowel [9]. Feculent output is suspicious and should elicit surgical evaluation as this may indicate a large fistula or bowel perforation [13]. A large amount of blood seen in the drain could indicate puncture or erosion into a blood vessel; if this occurs, the tube should be clamped, and interventional radiology should be contacted immediately [40].

Drain removal criteria vary from institution to institution; however a few main principles should be met [6, 31, 36, 38, 41]. Most importantly, it is imperative to not remove the drain prematurely, or this could lead to re-accumulation of the abscess possibly requiring a second percutaneous drain or other invasive procedure [36]. First, the patient's clinical symptoms such as fever, leukocytosis, and abdominal pain should be resolved. When drain output drops to less than 10–20 cc/day, the tube should be flushed to ensure that it is not clogged. If the drain is patent, repeat imaging should be performed to ensure satisfactory drainage. Persistence of the abscess may indicate the presence of a fistula or viscous fluid that is inherently difficult to drain [31]. If this is the case, the

patient should be re-evaluated by the IR team to determine if there is need for drain modification or placement of a new drain. Drain modification entails injecting the drain with iodinated contrast under fluoroscopy in order to identify undrained areas or fistulous connections with the bowel, bladder, vagina, or skin [9]. Modifications such as drain upsizing, repositioning, or placing a catheter with additional side holes such as a biliary drain as an alternative [31]. For collections with thick fluid, serial injections of tPA into the cavity over a few days can be performed to promote drainage. This can also be done at the time of initial drainage if necessary [46]. Following any drain modification, the same process of flushing and monitoring output should take place. Once output ceases, and imaging does not reveal any further fluid, the drain can be safely removed.

Conclusion

Acute diverticulitis can present with a variety of symptoms and imaging findings. Treatment strategies can guide therapy based on the clinical presentation and whether the patient has uncomplicated or complicated disease. Percutaneous abscess drainage has become a frontline therapy for patients with abscess formation, the most common presentation of complicated disease. This minimally invasive procedure allows patients to recover from an acute infection and avoid a multistage surgical repair and associated operative morbidity.

References

1. Etzioni DA, Mack TM, Beart RW Jr, Kaiser AM. Diverticulitis in the United States: 1998–2005: changing patterns of disease and treatment. Ann Surg. 2009;249(2):210–7.
2. Stocchi L. Current indications and role of surgery in the management of sigmoid diverticulitis. World J Gastroenterol: WJG. 2010;16(7):804–17.
3. Sartelli M, Catena F, Ansaloni L, Coccolini F, Griffiths EA, Abu-Zidan FM, DiSaverio S, Ulrych J, Kluger Y, Ben-Ishay O, Moore FA, Ivatury RR, Coimbra R, Peitzman AB, Leppaniemi A, Fraga GP, Maier RV, Chiara O, Kashuk J, Sakakushev B, Weber DG, Latifi R, et al. WSES Guidelines for the management of acute left sided colonic diverticulitis in the emergency setting. World J Emerg Surg. 2016;11:37.
4. Feingold D, Steele SR, Lee S, Kaiser A, Boushey R, Buie WD, Rafferty JF. Practice parameters for the treatment of sigmoid diverticulitis. Dis Colon Rectum. 2014;57(3):284–94.
5. Destigter KK, Keating DP. Imaging update: acute colonic diverticulitis. Clin Colon Rectal Surg. 2009;22(3):147–55.
6. Garfinkle R, Kugler A, Pelsser V, Vasilevsky CA, Morin N, Gordon P, Feldman L, Boutros M. Diverticular abscess managed with long-term definitive nonoperative intent is safe. Dis Colon Rectum. 2016;59(7):648–55.
7. Lamb MN, Kaiser AM. Elective resection versus observation after nonoperative management of complicated diverticulitis with abscess: a systematic review and meta-analysis. Dis Colon Rectum. 2014;57(12):1430–40.
8. Elagili F, Stocchi L, Ozuner G, Dietz DW, Kiran RP. Outcomes of percutaneous drainage without surgery for patients with diverticular abscess. Dis Colon Rectum. 2014;57(3):331–6.
9. Onur MR, Akpinar E, Karaosmanoglu AD, Isayev C, Karcaaltincaba M. Diverticulitis: a comprehensive review with usual and unusual complications. Insights Imaging. 2017;8(1):19–27.
10. Siewert B, Tye G, Kruskal J, Sosna J, Opelka F, Raptopoulos V, Goldberg SN. Impact of CT-guided drainage in the treatment of diverticular abscesses: size matters. AJR Am J Roentgenol. 2006;186(3):680–6.
11. Ambrosetti P, Chautems R, Soravia C, Peiris-Waser N, Terrier F. Long-term outcome of mesocolic and pelvic diverticular abscesses of the left colon: a prospective study of 73 cases. Dis Colon Rectum. 2005;48(4):787–691.
12. Ricciardi R, Baxter NN, Read TE, Marcello PW, Hall J, Roberts PL. Is the decline in the surgical treatment for diverticulitis associated with an increase in complicated diverticulitis? Dis Colon Rectum. 2009;52(9):1558–63.
13. Stabile BE, Puccio E, van Sonnenberg E, Neff CC. Preoperative percutaneous drainage of diverticular abscesses. Am J Surg. 1990;159(1):99–104.
14. McNamara MM, Lalani T, Camacho MA, Carucci LR, Cash BD, Feig BW, Fowler KJ, Katz DS, Kim DH, Smith MP, Tulchinsky M, Yaghmai V, Yee J, Rosen MP. ACR Appropriateness Criteria®. Left lower quadrant pain-suspected diverticulitis. Revised 2014. Available at: https://acsearch.acr.org/docs/69356/Narrative/. American College of Radiology Accessed 4 Sept 2018.
15. Flor N, Maconi G, Cornalba G, Pickhardt PJ. The current role of radiologic and endoscopic imaging in the diagnosis and follow-up of colonic diverticular disease. AJR Am J Roentgenol. 2016;207(1):15–24.
16. Zaidi E, Daly B. CT and clinical features of acute diverticulitis in an urban U.S. population: rising fre-

quency in young, obese adults. AJR Am J Roentgenol. 2006;187(3):689–94.
17. Klarenbeek BR, de Korte N, van der Peet DL, Cuesta MA. Review of current classifications for diverticular disease and a translation into clinical practice. Int J Color Dis. 2012;27(2):207–14.
18. Kaiser AM, Jiang JK, Lake JP, Ault G, Artinyan A, Gonzalez-Ruiz C, Essani R, Beart RW Jr. The management of complicated diverticulitis and the role of computed tomography. Am J Gastroenterol. 2005;100(4):910–7.
19. Sallinen VJ, Leppäniemi AK, Mentula PJ. Staging of acute diverticulitis based on clinical, radiologic, and physiologic parameters. J Trauma Acute Care Surg. 2015;78(3):543–51.
20. Chabok A, Påhlman L, Hjern F, Haapaniemi S, Smedh K, AVOD Study Group. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. Br J Surg. 2012;99(4):532–9.
21. van Dijk ST, Daniels L, Ünlü Ç, de Korte N, van Dieren S, Stockmann HB, Vrouenraets BC, Consten EC, van der Hoeven JA, Eijsbouts QA, Faneyte IF, Bemelman WA, Dijkgraaf MG, Boermeester MA, Dutch Diverticular Disease (3D) Collaborative Study Group. Long-term effects of omitting antibiotics in uncomplicated acute diverticulitis. Am J Gastroenterol. 2018;113(7):1045–52.
22. Shabanzadeh DM, Wille-Jørgensen P. Antibiotics for uncomplicated diverticulitis. Cochrane Database Syst Rev. 2012;11:CD009092.
23. Venkatesan AM, Kundu S, Sacks D, Wallace MJ, Wojak JC, Rose SC, Clark TW, d'Othee BJ, Itkin M, Jones RS, Miller DL, Owens CA, Rajan DK, Stokes LS, Swan TL, Towbin RB, Cardella JF. Society of Interventional Radiology Standards of Practice Committee. Practice guidelines for adult antibiotic prophylaxis during vascular and interventional radiology procedures. J Vasc Interv Radiol. 2010;21(11):1611–30.
24. Wilkins T, Embry K, George R. Diagnosis and management of acute diverticulitis. Am Fam Physician. 2013;87(9):612–20.
25. Mazuski JE, Tessier JM, May AK, Sawyer RG, Nadler EP, Rosengart MR, Chang PK, O'Neill PJ, Mollen KP, Huston JM, Diaz JJ Jr, Prince JM. The Surgical Infection Society revised guidelines on the management of intra-abdominal infection. Surg Infect. 2017;18(1):1–76.
26. Kumar RR, Kim JT, Haukoos JS, Macias LH, Dixon MR, Stamos MJ, Konyalian VR. Factors affecting the successful management of intra-abdominal abscesses with antibiotics and the need for percutaneous drainage. Dis Colon Rectum. 2006;49(2):183–9.
27. Devaraj B, Liu W, Tatum J, Cologne K, Kaiser AM. Medically treated diverticular abscess associated with high risk of recurrence and disease complications. Dis Colon Rectum. 2016;59(3):208–15.
28. Park J, Charles HW. Intra-abdominal abscess drainage: interval to surgery. Semin Interv Radiol. 2012;29(4):311–3.
29. Neff CC, van Sonnenberg E, Casola G, Wittich GR, Hoyt DB, Halasz NA, Martini DJ. Diverticular abscesses: percutaneous drainage. Radiology. 1987;163(1):15–8.
30. Schechter S, Eisenstat TE, Oliver GC, Rubin RJ, Salvati EP. Computerized tomographic scan-guided drainage of intra-abdominal abscesses. Preoperative and postoperative modalities in colon and rectal surgery. Dis Colon Rectum. 1994;37(10):984–8.
31. Gee MS, Kim JY, Gervais DA, Hahn PF, Mueller PR. Management of abdominal and pelvic abscesses that persist despite satisfactory percutaneous drainage catheter placement. AJR Am J Roentgenol. 2010;194(3):815–20.
32. American College of Radiology. ACR–SPR practice parameter for specifications and performance of image-guided percutaneous drainage/aspiration of abscesses and fluid collections (PDAFC). 2018; Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/PDFAC.pdf?la=en. Accessed 4 Sept 2018.
33. Brandt D, Gervaz P, Durmishi Y, Platon A, Morel P, Poletti PA. Percutaneous CT scan-guided drainage vs. antibiotherapy alone for Hinchey II diverticulitis: a case-control study. Dis Colon Rectum. 2006;49(10):1533–8.
34. Gaertner WB, Willis DJ, Madoff RD, Rothenberger DA, Kwaan MR, Belzer GE, Melton GB. Percutaneous drainage of colonic diverticular abscess: is colon resection necessary? Dis Colon Rectum. 2013;56(5):622–6.
35. Sartelli M, Viale P, Koike K, Pea F, Tumietto F, van Goor H, Guercioni G, Nespoli A, Tranà C, Catena F, Ansaloni L, Leppaniemi A, Biffl W, Moore FA, Poggetti R, Pinna AD, Moore EE. WSES consensus conference: guidelines for first-line management of intra-abdominal infections. World J Emerg Surg. 2011;6:12.
36. Charles HW. Abscess drainage. Semin Interv Radiol. 2012;29(4):325–36.
37. Durmishi Y, Gervaz P, Brandt D, Bucher P, Platon A, Morel P, Poletti PA. Results from percutaneous drainage of Hinchey stage II diverticulitis guided by computed tomography scan. Surg Endosc. 2006;20(7):1129–33.
38. Elagili F, Stocchi L, Ozuner G, Kiran RP. Antibiotics alone instead of percutaneous drainage as initial treatment of large diverticular abscess. Tech Coloproctol. 2015;19(2):97–103.
39. Patel IJ, Davidson JC, Nikolic B, Salazar GM, Schwartzberg MS, Walker TG, Saad WA, Standards of Practice Committee, with Cardiovascular and Interventional Radiological Society of Europe (CIRSE) Endorsement. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Interv Radiol. 2012;23(6):727–36.
40. Lorenz J, Thomas JL. Complications of percutaneous fluid drainage. Semin Intervent Radiol. 2006;23(2):194–204.

41. Robert B, Chivot C, Rebibo L, Sabbagh C, Regimbeau JM, Yzet T. Percutaneous transgluteal drainage of pelvic abscesses in interventional radiology: a safe alternative to surgery. J Visc Surg. 2016;153(1):3–7.
42. Harisinghani MG, Gervais DA, Maher MM, Cho CH, Hahn PF, Varghese J, Mueller PR. Transgluteal approach for percutaneous drainage of deep pelvic abscesses: 154 cases. Radiology. 2003;228(3):701–5.
43. Mueller PR, Saini S, Wittenburg J, Simeone J, Hahn PF, Steiner E, Dawson SL, Butch RJ, Stark DD, Ottinger LW, et al. Sigmoid diverticular abscesses: percutaneous drainage as an adjunct to surgical resection in 24 cases. Radiology. 1987;164(2):321–5.
44. Bennett JD, Kozak RI, Taylor BM, Jory TA. Deep pelvic abscesses: transrectal drainage with radiologic guidance. Radiology. 1992;185(3):825–8.
45. vanSonnenberg E, D'Agostino HB, Casola G, Goodacre BW, Sanchez RB, Taylor B. US-guided transvaginal drainage of pelvic abscesses and fluid collections. Radiology. 1991;181(1):53–6.
46. Beland MD, Gervais DA, Levis DA, Hahn PF, Arellano RS, Mueller PR. Complex abdominal and pelvic abscesses: efficacy of adjunctive tissue-type plasminogen activator for drainage. Radiology. 2008;247(2):567–73.

Diverticulitis: Surgical Therapy

23

Dominic M. Forte and Andrew T. Schlussel

Introduction

The operative management of diverticulitis can broadly be categorized into emergent, urgent, and elective interventions. The surgeon should maintain an algorithmic approach to treatment, which should be guided based on clinical presentation and radiographic findings (Fig. 23.1). A cohort of patients may present with a significant amount of free air and remain clinically stable; however, others may succumb to overt sepsis with a more benign appearing radiograph. The discussion below should guide the surgical decision-making processes but the decision to operate, which procedure to perform, and what approach to utilize should be individualized to the patient.

Emergent and Urgent Interventions

Operative Indications

Emergent and urgent interventions are required for patients who present with generalized peritonitis, obstruction, and those who fail medical management [1]. Localized peritonitis or perforation in the absence of peritonitis does not demand surgery as this may respond to medical therapy in over 90% of patients [2, 3]. All efforts should be made to avoid performing a colectomy under emergent conditions due to the increased morbidity and mortality when compared to elective operations. Although, when indicated, interventions must be carried out in a timely fashion to avoid subsequent complications [4, 5]. In the case of an urgent operation, for instance, radiology-guided maneuvers may fail to adequately control the infectious source, and if the patient's condition worsens or even doesn't improve, then prompt surgical intervention should be considered.

Preoperative Care and Evaluation

It is imperative that intravenous fluid resuscitation and broad-spectrum antibiotics be initiated as early as possible to combat ongoing contamination. Beyond these initial resuscitative measures, minimal preoperative evaluation is needed in patients with generalized peritonitis or sepsis. Consideration may be given to the placement of a self-expanding metal stent (SEMS) in select patients presenting with distal obstruction. This is further discussed below.

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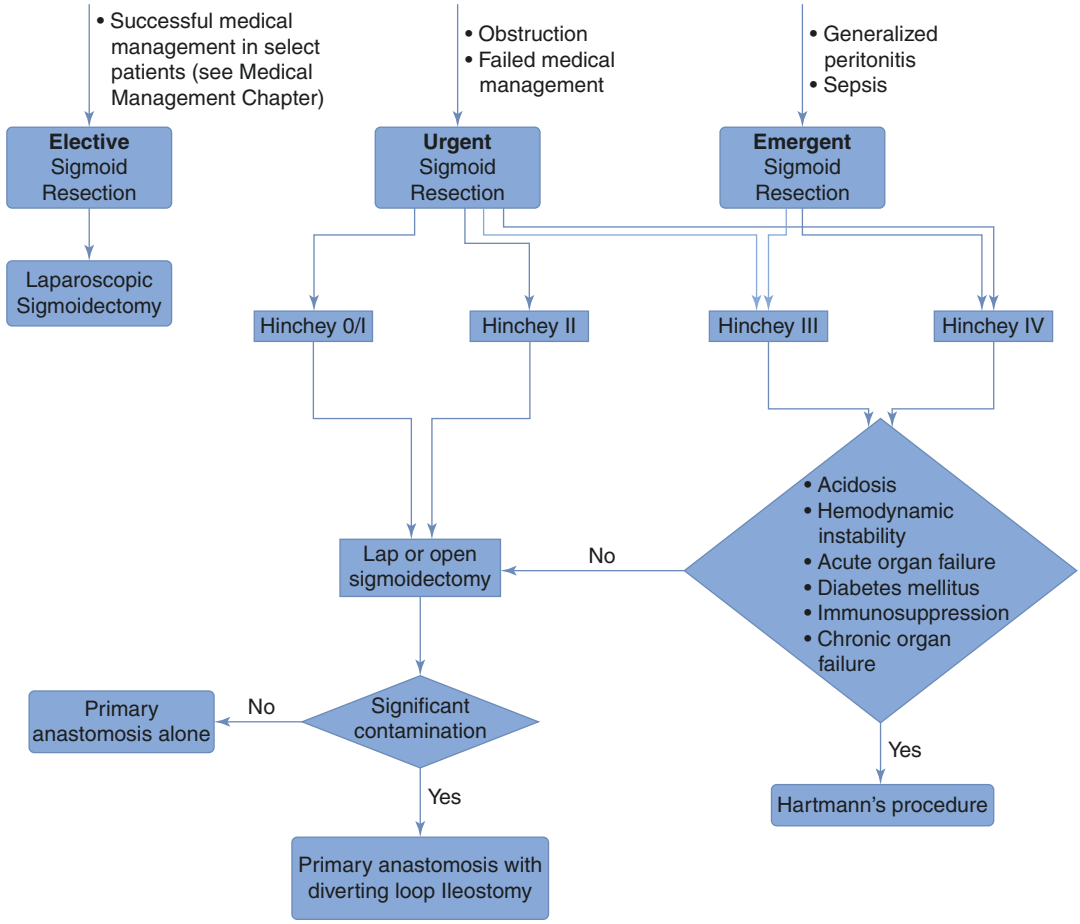

Fig. 23.1 Surgical management algorithm

Operative Decision-Making

The surgical options in the setting of acute diverticulitis include sigmoid colectomy with end colostomy (Hartmann's procedure), sigmoid colectomy with a primary anastomosis with or without a diverting loop ileostomy and laparoscopic peritoneal lavage [1]. These procedures can be performed through an open or minimally invasive approach based on surgeon experience. The decision to perform an anastomosis should be guided by the patient's clinical status, requirement of vasopressor therapy, and overall surgeon judgment. The environment of the abdomen upon initial entry should not mandate diversion; however, the surgeon must recognize that a primary anastomosis may require a significant increase in operative time due to additional left colon and possible splenic flexure mobilization [6, 7]. Clear communication with the anesthesia and the critical care team is essential as vasopressor use both intraoperatively and postoperatively greatly increase the risk of an anastomotic leak [odds ratio (OR) 3.25, $p = 0.02$] [8]. Although an end colostomy is a safe option, the surgeon must acknowledge the subsequent morbidity of reversing the colostomy in the future [9].

A pericolonic (Hinchey I) or pelvic (Hinchey II) abscess requiring operative management is best addressed with a one-stage procedure. In cases of significant pelvic contamination, the integrity of the proximal rectum must be carefully evaluated prior to creating an anastomosis. When a primary anastomosis is performed, a

protective loop ileostomy should be strongly considered. Factors favoring the creation of an end colostomy are summarized in Table 23.1; nevertheless, the approach should be individualized even in the setting of purulent (Hinchey III) or feculent (Hinchey IV) peritonitis [1].

When comparing sigmoid colectomy with primary anastomosis and end colostomy for acute diverticulitis, the short-term morbidity (67% vs. 75%) and mortality (13% vs. 9%) are similar. However, patients are less likely to undergo reversal of an end colostomy as compared to a loop ileostomy, due to an increased risk of postoperative adverse events, 50% versus 7.1%, respectively [9, 10]. As a result, 40–50% of patients who have undergone a Hartmann's procedure will never have intestinal continuity restored [10, 11]. A permanent colostomy may significantly affect a patient's quality of life, and this must be taken into consideration during the index operation [12, 13].

Table 23.1 Factors supporting creation of an end colostomy in emergency surgery for diverticulitis

Patient factors
Acidosis
Hypothermia
Hemodynamic instability
Acute organ failure
Diabetes mellitus
Immunosuppression
Chronic organ failure
Physician factors
Surgeon experience and comfort with colorectal anastomoses

An open or minimally invasive procedure may be utilized regardless of the operative indication [14]. As experience increases and technology improves, a trend towards the utilization of laparoscopy in both the emergent and elective setting has been observed nationwide. Laparoscopy is associated with a decreased morbidity, shorter length of stay, and a reduction in hospital costs, without an increased risk of disease recurrence [15, 16]. When utilizing a minimally invasive technique in the acute setting, the surgeon will be faced with intraoperative challenges. Anatomic dissection planes will be fused, and the degree of inflammation may affect the ability to identify key structures, increasing the risk for complications. A medial-to-lateral dissection allows the surgeon to create a plane underneath the inflammatory mass or abscess, often times facilitating early ureteral identification, and is perhaps a safer operation (Figs. 23.2 and 23.3). A surgeon's

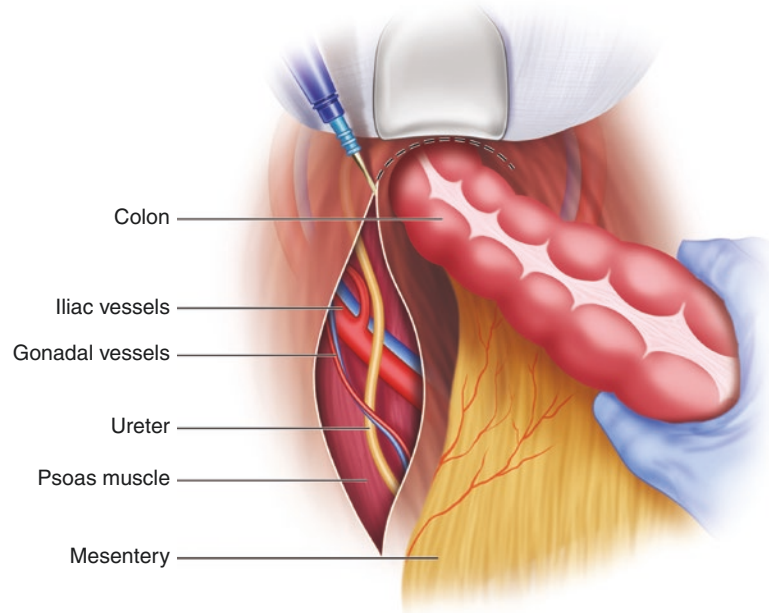

Fig. 23.2 The left ureter encountered in a lateral-to-medial approach

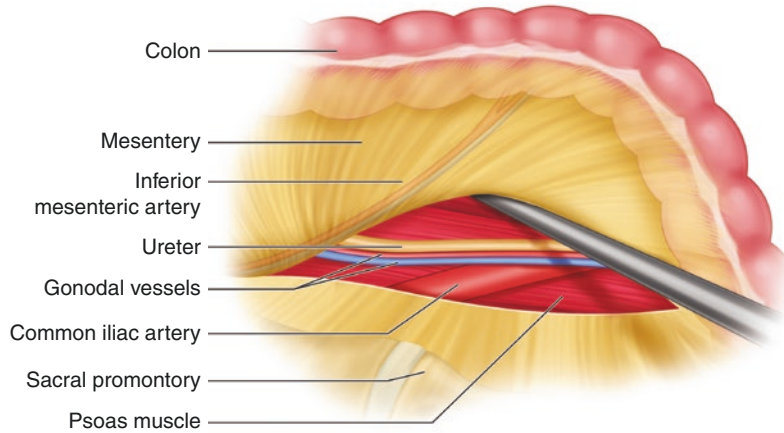

Fig. 23.3 The left ureter encountered in a medial-to-lateral approach

proficiency in laparoscopy and the degree of inflammation must be taken into consideration when determining the operative approach.

Regardless of the utilized technique, the tenants of diverticular surgery remain identical. The distal extent of resection should be the rectosigmoid junction, marked anatomically by splaying of the taenia coli [1]. When inflammation obscures the taenia, the rectosigmoid junction can be located just inferior to the sacral promontory. Division of the colon at the proximal rectum is paramount during this procedure, as performing a colosigmoid anastomosis is associated with a fourfold increase in the risk of recurrent diverticulitis [17, 18]. In addition, the development of a colocutaneous fistula has been associated with incomplete removal of all affected distal sigmoid colon [19].

Historically, the routine use of splenic flexure mobilization (SFM) was thought to be necessary in order to minimize complications and the development of recurrent disease [17]. Presently, there is no supporting literature on the effects of SFM and recurrence rates. Furthermore, this technique has been associated with an increased operative time and a greater risk of morbidity (OR 2.8, $p = 0.05$). Therefore, SFM should be performed in a selective fashion when required to create a tension-free anastomosis [7]. In addition, proximal resection should be performed of all thickened or diseased colon to ensure only healthy, supple tissue is incorporated in the anastomosis. The removal of all diverticulum is not necessary, and this has not been associated with a reduction in disease recurrence [20].

Operative Solutions and Adjuncts

Ensuring the colon is of adequate length for a tension-free anastomosis is a common challenge encountered in both the acute and elective setting. The initial maneuvers should include the complete medialization of the left colon from its retroperitoneal attachments and selective splenic flexure mobilization [7, 21]. Additional colon length may be gained through division of the inferior mesenteric artery at the level of the aorta or distal to the takeoff of the left colic pedicle, division of the inferior mesenteric vein at the inferior border of the pancreas, and mobilization of the superior rectum [22]. If significant difficulty persists in acute setting, consideration should be given to deferring formation of an anastomosis and creating an end colostomy.

The dense inflammation encountered during surgery for diverticulitis places the ureters at risk for injury. Emergent procedures greatly increase the risk of ureteral injury, with reported rates occurring at 0.25–0.28% of elective operations compared to 2.2% during emergent cases [23–25]. Common sites of injury include the pelvic brim, the origin of the inferior mesenteric artery, and low in the pelvis. The injury occurs through crushing, lacerating, or ligating the ureter. Avoidance of these injuries comes primarily

through adherence to meticulous surgical technique. Identification of the ureter prior to the division of the inferior mesenteric artery and superior hemorrhoidal artery is essential to avoid inadvertent division of ureter. If inflammation obscures anatomical planes, the ureter should be identified proximally, away from the pathology. Consideration should be given in these cases to utilization of an open technique or placement of ureteral stents. While preoperative placement of ureteral stents has not been shown to be effective at preventing ureteral injury, they may aid in early recognition and repair. This is meaningful as outcomes are superior when ureteral injuries are managed immediately [26]. The placement of ureteral stents carries the risk of ureteral perforation, urinary tract infections, hydronephrosis secondary to post-stent edema, as well as additional time under anesthesia and cost. In general, prudence argues toward placing stents when there is a significant risk of aberrant anatomy. Relative indications are summarized in Table 23.2 [1, 22]. If stents were not placed preoperatively and concern arises for an intraoperative ureteral injury, maneuvers to identify the injury include intraoperative stent placement, instillation of dilute methylene blue into the bladder, intravenous methylene blue, or instillation of dilute water-soluble contrast into the bladder with an on-table radiograph. If an injury is identified, an intraoperative urology consult should be obtained.

An additional concern in creating a primary anastomosis in the acute setting is the management of the unprepped colon and risk of anastomotic leak or surgical site infection. Although more recent data suggests preoperative mechanical bowel preparation with oral antibiotics reduces the risks of postoperative adverse events, this is not a feasible intervention in the emergent setting [27, 28]. Previously, the utilization of operative on-table lavage was implemented to clear out the colon prior to an anastomosis. It involves large volume irrigation of the distal colon with the objective of decreasing the stool burden. However, the role for a mechanical bowel prep alone in the elective setting is still debatable; therefore, the practice of on-table lavage has fallen out of favor. This maneuver is not mandatory and should only be performed based on the surgeon's preference [1, 29].

Table 23.2 Factors supporting the placement of ureteral stents

Patient factors
Obesity
History of abdominal/pelvic radiation
History of prior pelvic procedures
Findings on imaging
Abnormal anatomy on imaging
Hydronephrosis
Large phlegmon
Marked retroperitoneal inflammation

Laparoscopic Lavage

Laparoscopic lavage was first advocated in the early 2000s as a means of treating perforated diverticulitis. It involves an exploratory laparoscopy with high-volume irrigation without resection. Some authors discuss suture closure of the colonic perforation [30]. Initial reports demonstrated an association with a decrease in short-term morbidity and mortality when compared to emergent resection. Subsequent analysis has demonstrated many cases in this series to have been Hinchey I and II disease, and medical management alone may have been successful [1]. Recent randomized controlled trials (RCT) focusing on cases of Hinchey III disease demonstrated an increased requirement for additional procedures following laparoscopic lavage compared to resection, with no improvement in morbidity or mortality [31–33]. The SCANDIV RCT trial identified multiple cases of a missed perforated malignancy with the use of lavage [32]. Given the failure to establish a benefit in postoperative outcomes, in addition to the risk of a missed neoplastic process, laparoscopic lavage is not currently recommended [1].

Self-Expanding Metal Stents

Placement of a SEMS in the setting of a large bowel obstruction secondary to a diverticular

stricture may temporize the acute process and avoid an emergent operation for a bowel obstruction. The utilization of a SEMS for a benign stricture has been associated with initial technical success rates of 95–100%, with conversion of an urgent to an elective intervention in greater than 70% of cases. Notably, utilization of stents for benign disease, as compared to a malignant process, is associated with an increased risk of early complications to include perforation, migration, and re-obstruction [34, 35]. Accordingly, operative intervention should be considered in the first 1–2 weeks after placement of a SEMS provided the patient's clinical condition permits. There is no role for a SEMS in the setting of Hinchey III or IV diverticulitis.

Elective Procedures

Operative Indications

In the elective setting, the clinical complexity comes not necessarily from intraoperative challenges but rather the decision on whether one should operate. Previous paradigms sought to perform a prophylactic sigmoid colectomy in patients following two episodes of acute diverticulitis. This was predicated on the idea that each subsequent episode of diverticulitis increased the chances of developing complicated disease and requiring an emergent procedure [36]. In recent years there has been a significant shift in understanding the natural history of diverticulitis. Presently, the majority of diverticulitis can be managed nonoperatively and subsequent episodes typically are not more severe [36]. The risk of recurrence following successful medical treatment of diverticular disease is between 13% and 23%, and the risk of developing complicated diverticulitis is <6% [37–39]. In 2004, an economic based analysis demonstrated a decreased morbidity, mortality, and cost with delaying colectomy until after the fourth episode of diverticulitis [40]. Presently, it is recommended that the decision to proceed with elective sigmoid colectomy should be individualized and not based on the number of episodes. Patients should be engaged in a discussion on the frequency and severity of each episode, as well as their medical comorbidities and how this would influence their operative risk [4, 41–43].

Patient factors that should encourage the consideration of an early elective resection include collagen vascular disease (CVD), polycystic kidney disease (PKD), and chronic immunosuppression. These medical comorbidities are risk factors for developing subsequent severe episodes of diverticulitis [44–46]. Similarly, prior episodes of complicated diverticulitis are a relative indication for elective colectomy [1]. This is evidenced by retrospective studies demonstrating an increased rate of recurrence following successful medical management of an abscess >5 cm [47, 48]. Fistula formation or the development of an early diverticular stricture frequently requires resection for symptomatic relief [45]. Finally, young age was previously considered an indication for resection due to concerns for a more virulent disease process. However, these patients have subsequently been found to be at no greater risk of recurrence; therefore, age alone should not be used as a determining factor for elective resection [1, 49, 50].

Preoperative Evaluation

During the preoperative evaluation for an elective resection, the surgeon should ensure the correct diagnosis has been made. Neoplasia, inflammatory bowel disease (IBD), and irritable bowel syndrome can have similar radiographic appearances to diverticulitis, and these conditions must be excluded [51, 52]. Endoscopy remains the gold standard in evaluating mucosal pathology [51]. A paucity evidence exists to guide timing of colonoscopy following the resolution of acute diverticulitis, although 4–6 weeks is likely appropriate. A small RCT examined the feasibility and safety of colonoscopy at the conclusion of a patient's hospitalization for acute diverticulitis. These results demonstrated an improved compliance with no instance of perforation in the 45 patients who underwent early endoscopy. This

study excluded all patients with free perforation as well as those with pericolonic fluid or air [53].

Presently, there is no gold standard imaging modality to demonstrate a fistula secondary to diverticulitis, and operative resection may proceed even if the tract is not visualized. If there is clinical concern for a fistula in the context of prior diverticulitis (i.e., pneumaturia, fecaluria, or foul vaginal discharge), this is a sufficient indication to proceed with resection. A contrast enema or a CT scan with rectal contrast may be useful; however, exhaustive attempts at imaging to define the fistula can often be unfruitful and ultimately unlikely to change operative management [54, 55].

Operative Decision-Making

In the elective setting, the procedure of choice is a sigmoid colectomy. This can be performed utilizing an open and a laparoscopic approach, with or without robot-assistance. A minimally invasive technique is preferred provided the surgeon has sufficient experience [1]. Prospective and RCT data have demonstrated improved outcomes with laparoscopic surgery as opposed to an open approach when performed electively. Results have demonstrated a significant reduction in adverse events to include anastomotic leak, bleeding, and deep space infections. Additional benefits included a decreased length of stay and need for analgesia [56, 57]. The extent of resection should remain consistent regardless of the technology implemented.

Special Issues

Cecal Diverticulitis

Uncomplicated cecal diverticulitis typically responds to medical management. Complicated disease can be treated in a similar fashion as described above. Surgical options for cecal diverticulitis diagnosed at the time of laparoscopy include diverticulectomy, ileocecectomy, and right colectomy [58–60]. For cases in which there is minimal cecal inflammation at the time of laparoscopy, it is acceptable to perform an appendectomy alone [59]. Despite a paucity of data regarding diverticulectomy, some groups advocate for this technique if there is a single, readily identifiable diverticulum without significant inflammation at its base [61]. An ileocecectomy is also a reasonable approach if there is diagnostic uncertainty; however, Hinchey II–IV disease can be difficult to differentiate from a perforated carcinoma, and in these cases, a right colectomy is the preferred procedure [60, 61].

Conclusion

When feasible, an urgent or emergent operation for diverticulitis should be avoided. However, some patients presenting with peritonitis or sepsis require an intervention. Those who present with an obstruction from diverticular disease or who fail medical therapy, including radiology-guided drainage, should proceed with resection during their index hospitalization. Hinchey classification, degree of physiologic derangement, and hemodynamic stability during the procedure should dictate which operation is performed. In the elective setting, an individualized approach to determine the appropriate candidate for resection has become more popularized. Careful consideration should be made on a case-by-case basis to establish how resection will affect the patient's overall health and quality of life.

References

1. Feingold D, et al. Practice parameters for the treatment of sigmoid diverticulitis. Dis Colon Rectum. 2014;57(3):284–94.
2. Costi R, et al. Challenging a classic myth: pneumoperitoneum associated with acute diverticulitis is not an indication for open or laparoscopic emergency surgery in hemodynamically stable patients. A 10-year experience with a nonoperative treatment. Surg Endosc. 2012;26(7):2061–71.
3. Dharmarajan S, et al. The efficacy of nonoperative management of acute complicated diverticulitis. Dis Colon Rectum. 2011;54(6):663–71.

4. Zingg U, et al. Primary anastomosis vs Hartmann's procedure in patients undergoing emergency left colectomy for perforated diverticulitis. Color Dis. 2010;12(1):54–60.
5. Salem L, Flum DR. Primary anastomosis or Hartmann's procedure for patients with diverticular peritonitis? A systematic review. Dis Colon Rectum. 2004;47(11):1953–64.
6. Brennan DJ, et al. Routine mobilization of the splenic flexure is not necessary during anterior resection for rectal cancer. Dis Colon Rectum. 2007;50(3):302–7. discussion 307
7. Schlussel AT, et al. Location is everything: the role of splenic flexure mobilization during colon resection for diverticulitis. Int J Surg. 2017;40:124–9.
8. Zakrison T, et al. Perioperative vasopressors are associated with an increased risk of gastrointestinal anastomotic leakage. World J Surg. 2007;31(8):1627–34.
9. Oberkofler CE, et al. A multicenter randomized clinical trial of primary anastomosis or Hartmann's procedure for perforated left colonic diverticulitis with purulent or fecal peritonitis. Ann Surg. 2012;256(5):819–26; discussion 826–7.
10. van de Wall BJ, et al. Conventional and laparoscopic reversal of the Hartmann procedure: a review of literature. J Gastrointest Surg. 2010;14(4):743–52.
11. Vermeulen J, et al. Outcome after emergency surgery for acute perforated diverticulitis in 200 cases. Dig Surg. 2007;24(5):361–6.
12. Krouse R, et al. Quality of life outcomes in 599 cancer and non-cancer patients with colostomies. J Surg Res. 2007;138(1):79–87.
13. Vermeulen J, et al. Avoiding or reversing Hartmann's procedure provides improved quality of life after perforated diverticulitis. J Gastrointest Surg. 2010;14(4):651–7.
14. Jones OM, et al. Laparoscopic resection for diverticular disease: follow-up of 500 consecutive patients. Ann Surg. 2008;248(6):1092–7.
15. Masoomi H, et al. Trends in diverticulitis management in the United States from 2002 to 2007. Arch Surg. 2011;146(4):400–6.
16. Scheidbach H, et al. Laparoscopic approach to treatment of sigmoid diverticulitis: changes in the spectrum of indications and results of a prospective, multicenter study on 1,545 patients. Dis Colon Rectum. 2004;47(11):1883–8.
17. Thaler K, et al. Determinants of recurrence after sigmoid resection for uncomplicated diverticulitis. Dis Colon Rectum. 2003;46(3):385–8.
18. Benn PL, Wolff BG, Ilstrup DM. Level of anastomosis and recurrent colonic diverticulitis. Am J Surg. 1986;151(2):269–71.
19. Fazio VW, et al. Colocutaneous fistulas complicating diverticulitis. Dis Colon Rectum. 1987;30(2):89–94.
20. Dozois EJ. Operative treatment of recurrent or complicated diverticulitis. J Gastrointest Surg. 2008;12(8):1321–3.
21. Katory M, et al. A 6-year review of surgical morbidity and oncological outcome after high anterior resection for colorectal malignancy with and without splenic flexure mobilization. Color Dis. 2008;10(2):165–9.
22. Steele SR, et al. Complexities in colorectal surgery: decision-making and management. New York: Springer; 2014. xix, 632 pages.
23. Halabi WJ, et al. Ureteral injuries in colorectal surgery: an analysis of trends, outcomes, and risk factors over a 10-year period in the United States. Dis Colon Rectum. 2014;57(2):179–86.
24. Palaniappa NC, et al. Incidence of iatrogenic ureteral injury after laparoscopic colectomy. Arch Surg. 2012;147(3):267–71.
25. Dwivedi A, et al. Laparoscopic colectomy vs. open colectomy for sigmoid diverticular disease. Dis Colon Rectum. 2002;45(10):1309–14; discussion 1314–5.
26. Pokala N, et al. A randomized controlled trial comparing simultaneous intra-operative vs sequential prophylactic ureteric catheter insertion in re-operative and complicated colorectal surgery. Int J Color Dis. 2007;22(6):683–7.
27. Kim EK, et al. A statewide colectomy experience: the role of full bowel preparation in preventing surgical site infection. Ann Surg. 2014;259(2):310–4.
28. Scarborough JE, et al. Combined mechanical and oral antibiotic bowel preparation reduces incisional surgical site infection and anastomotic leak rates after elective colorectal resection: an analysis of colectomy-targeted ACS NSQIP. Ann Surg. 2015;262(2):331–7.
29. Guenaga KF, Matos D, Wille-Jorgensen P. Mechanical bowel preparation for elective colorectal surgery. Cochrane Database Syst Rev. 2011;(9):CD001544.
30. Jaffer U, Moin T. Perforated sigmoid diverticular disease: a management protocol. JSLS. 2008;12(2):188–93.
31. Vennix S, et al. Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial. Lancet. 2015;386(10000):1269–77.
32. Schultz JK, et al. Laparoscopic lavage vs primary resection for acute perforated diverticulitis: the SCANDIV randomized clinical trial. JAMA. 2015;314(13):1364–75.
33. Marshall JR, et al. Laparoscopic lavage in the management of Hinchey grade III diverticulitis: a systematic review. Ann Surg. 2017;265(4):670–6.
34. Small AJ, Young-Fadok TM, Baron TH. Expandable metal stent placement for benign colorectal obstruction: outcomes for 23 cases. Surg Endosc. 2008;22(2):454–62.
35. Keranen I, et al. Outcome of patients after endoluminal stent placement for benign colorectal obstruction. Scand J Gastroenterol. 2010;45(6):725–31.
36. Janes S, Meagher A, Frizelle FA. Elective surgery after acute diverticulitis. Br J Surg. 2005;92(2):133–42.
37. Hall JF, et al. Long-term follow-up after an initial episode of diverticulitis: what are the predictors of recurrence? Dis Colon Rectum. 2011;54(3):283–8.
38. Eglinton T, et al. Patterns of recurrence in patients with acute diverticulitis. Br J Surg. 2010;97(6):952–7.

39. Anaya DA, Flum DR. Risk of emergency colectomy and colostomy in patients with diverticular disease. Arch Surg. 2005;140(7):681–5.
40. Salem L, et al. The timing of elective colectomy in diverticulitis: a decision analysis. J Am Coll Surg. 2004;199(6):904–12.
41. Ambrosetti P, et al. Colorectal anastomotic stenosis after elective laparoscopic sigmoidectomy for diverticular disease: a prospective evaluation of 68 patients. Dis Colon Rectum. 2008;51(9):1345–9.
42. Kaser SA, et al. Timing of rectosigmoid resection for diverticular disease: the patient's view. Color Dis. 2012;14(3):e111–6.
43. Levack MM, et al. Sigmoidectomy syndrome? Patients' perspectives on the functional outcomes following surgery for diverticulitis. Dis Colon Rectum. 2012;55(1):10–7.
44. Lederman ED, et al. Diverticulitis and polycystic kidney disease. Am Surg. 2000;66(2):200–3.
45. Klarenbeek BR, et al. Indications for elective sigmoid resection in diverticular disease. Ann Surg. 2010;251(4):670–4.
46. Hwang SS, et al. Diverticulitis in transplant patients and patients on chronic corticosteroid therapy: a systematic review. Dis Colon Rectum. 2010;53(12):1699–707.
47. Gaertner WB, et al. Percutaneous drainage of colonic diverticular abscess: is colon resection necessary? Dis Colon Rectum. 2013;56(5):622–6.
48. Lamb MN, Kaiser AM. Elective resection versus observation after nonoperative management of complicated diverticulitis with abscess: a systematic review and meta-analysis. Dis Colon Rectum. 2014;57(12):1430–40.
49. Guzzo J, Hyman N. Diverticulitis in young patients: is resection after a single attack always warranted? Dis Colon Rectum. 2004;47(7):1187–90; discussion 1190–1.
50. Hjern F, et al. Outcome of younger patients with acute diverticulitis. Br J Surg. 2008;95(6):758–64.
51. Baker ME. Imaging and interventional techniques in acute left-sided diverticulitis. J Gastrointest Surg. 2008;12(8):1314–7.
52. Berman IR, et al. Late onset Crohn's disease in patients with colonic diverticulitis. Dis Colon Rectum. 1979;22(8):524–9.
53. Lahat A, et al. The feasibility and risk of early colonoscopy in acute diverticulitis: a prospective controlled study. Endoscopy. 2007;39(6):521–4.
54. Destigter KK, Keating DP. Imaging update: acute colonic diverticulitis. Clin Colon Rectal Surg. 2009;22(3):147–55.
55. Wen Y, et al. Evaluating surgical management and outcomes of colovaginal fistulas. Am J Surg. 2017;213(3):553–7.
56. Klarenbeek BR, et al. Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized control trial: short-term results of the Sigma Trial. Ann Surg. 2009;249(1):39–44.
57. Russ AJ, et al. Laparoscopy improves short-term outcomes after surgery for diverticular disease. Gastroenterology. 2010;138(7):2267–74, 2274 e1.
58. Park HC, Lee BH. Suspected uncomplicated cecal diverticulitis diagnosed by imaging: initial antibiotics vs laparoscopic treatment. World J Gastroenterol. 2010;16(38):4854–7.
59. Fang JF, et al. Aggressive resection is indicated for cecal diverticulitis. Am J Surg. 2003;185(2):135–40.
60. Schlussel AT, et al. Right-sided diverticulitis requiring colectomy: an evolving demographic? A review of surgical outcomes from the National Inpatient Sample Database. J Gastrointest Surg. 2016;20(11):1874–85.
61. Lane JS, et al. Surgical approach to cecal diverticulitis. J Am Coll Surg. 1999;188(6):629–34; discussion 634–5.

Part VIII

Bleeding and Hernias in Cirrhotic Patients

24

Coagulopathy in Cirrhotic Patients: Evaluation and Management

Richard Smith

Liver cirrhosis is a major source of morbidity and mortality worldwide. Liver cirrhosis is the 12th most common cause of death in the United States [49]. The incidence of cirrhosis continues to rise likely secondary to increasing rates of viral hepatitis and morbid obesity. From 2014 to 2015, cirrhosis deaths increased by 3.8% [69]. This trend has continued for the last decade and has resulted in increasing numbers of cirrhotic patients who will present for elective surgery and emergent surgery. Cirrhotic patients pose a challenge to surgeons based on liver dysfunction leading to increased complications and mortality. The two most common methods of determining risk in cirrhotic patients are the Child-Turcotte-Pugh (CTP) and the Model for End-Stage Liver Disease (MELD) scores [45, 77] (Table 24.1). A recent review of these scoring systems showed perioperative mortality of 2–10% for CTP A, 12–31% for CTP B, and 12–82% for CTP C patients with good correlation between CTP and MELD scores [41]. Both the CTP and MELD scores use the international normalized ratio (INR) to reflect the known hematologic derangements associated with liver dysfunction. Naturally there is a major concern for increased hemorrhage in the minds of surgeons operating on patients with cirrhosis.

There is a common misconception, though, within the surgical community that patients with chronic liver disease are "autoanticoagulated" [38]. The reality is that primary hemostasis and coagulation are preserved in most patients with cirrhosis [108]. To complicate matters further, the standard laboratory parameters (PT, aPTT, and INR) do not accurately reflect bleeding risk in cirrhotic patients. Portal hypertension appears to be the major risk factor for bleeding in cirrhotics. The relative balance between pro- and anticoagulation factors remains in cirrhotic patients, but the buffer (factors in quantities many times over physiologic need) is not present. Therefore, the increased risk for hemorrhage is seen in the most critically ill patients [29]. The reality is the hemostatic status of chronic liver disease is complicated. The hemostatic changes that occur in cirrhosis are a reflection of the interplay between decreases in both procoagulant and anticoagulant factors produced in the liver, increased production and decreased clearance of factors produced outside the liver, intravascular/systemic volume, and the clinical state of the patient [115]. This results in a somewhat tenuous but "rebalanced hemostasis" in most cirrhotic patients.

Rebalanced Hemostasis

Hemostasis can be broken down into three phases: primary, secondary, and tertiary. Primary hemostasis consists of platelet activation and formation of a platelet plug. Secondary hemostasis

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Table 24.1 Child-Turcotte-Pugh and MELD scores

	Points							
	1	2	3					
Encephalopathy	None	Grades 1–2 (acute)	Grades 3–4 (or chronic)	MELD =	$9.6 \times \log_e$	Serum	Creatinine	(mg/dL) +
Ascites	None	Mild to moderate (diuretic responsive)	Severe (refractory)		$3.8 \times \log_e$	Serum	Bilirubin	(mg/dL) +
Bilirubin (mg/dL)	<2	2–3	>3		$11.2 \times \log_e$	INR +	6.4	
Albumin (g/dL)	>3.5	2.8–3.5	<2.8					
INR	<1.7	1.7–2.3	>2.3					
Child-Turcotte-Pugh Class (add score for each parameter)								
Class A		5–6 points						
Class B		7–9 points						
Class C		10–15 points						

is activation of the coagulation cascade by tissue factor and platelet factors, resulting in thrombin activation and deposition of fibrin to stabilize the platelet plug. Tertiary hemostasis occurs with fibrinolysis of the clot mediated by tissue plasminogen activator and plasminogen [97]. Liver disease has complex effects on all three phases of hemostasis [51]. Bleeding time has been considered a measure of primary hemostasis. Bleeding time is prolonged in cirrhosis but does not appear to be of clinical significance [110]. Elevated bleeding time is not predictive of bleeding risk for liver biopsy or rate of bleeding from esophageal varices [6, 11]. Bleeding time has also been considered a measure of platelet function for their role in primary hemostasis.

The liver also has a direct role in platelet production via thrombopoietin, which stimulates megakaryocytes [60]. Platelets support hemostasis in two of the three phases of hemostasis. The first of these mechanisms is adhesion and forming aggregates adherent to damaged endothelial cells or to extracellular matrix structures exposed to flowing blood mediated by von Willebrand factor and fibrinogen [85]. The second is to provide suitable negatively charged phospholipid surfaces for formation of the enzymatic complexes needed for factor Xa and the formation of thrombin, which accelerates the formation of fibrin necessary to stabilize the clot [9].

A mild to moderate thrombocytopenia and a poorly defined change in platelet function are present in most patients with cirrhosis [78]. There is evidence in vitro that adhesion of platelets from patients with cirrhosis under flow conditions is normal, secondary to the increase of von Willebrand factor [58]. As shown previously, platelets support thrombin generation. The plasma of patients with cirrhosis shows a reduced endogenous thrombin potential when compared to controls. However, this can be corrected in the setting of thrombomodulin and normalization of the platelet count to 100,000/μl [101]. This suggests that platelet function in cirrhosis is intact and able to support adequate thrombin generation and that platelet numbers affect thrombin generation. This same study found, through analysis by linear regression, a rough estimate of the platelet numbers (56,000/μl) needed to support thrombin generation at the tenth percentile of the distribution of values recorded in the healthy control population [101]. This correlates well with the clinical data that showed an increase in bleeding complications for hepatitis C patients undergoing liver biopsy when the platelet count was <60,0000/μL [90]. However the standard practice of administering one adult equivalent unit of platelets prior to a procedure for patients with cirrhosis and thrombocytopenia has been shown to elevate platelet counts only marginally, with no or little effect on thrombin generation and thromboelastometry [104].

Sequestration of platelets from splenomegaly that develops in cirrhosis also complicates the interpretation of platelet function. A study of radiolabeled platelets in patients with splenomegaly demonstrated that up to 90% of radiolabeled PLTs underwent sequestration within minutes of transfusion. These radiolabeled PLTs redistributed to the peripheral circulation with injection of epinephrine [5]. It has been proposed that a similar redistribution of PLTs occurs after the endogenous release of epinephrine in response to bleeding in cirrhosis. In this situation, peripheral PLT counts would not represent the actual number of PLTs available at the time of a hemostatic challenge [117]. Response to platelet transfusions is also difficult to interpret when up to 90% of platelets transfused are rapidly sequestered [5].

The liver synthesizes the majority of coagulation factors (Fig. 24.1). As a result, all of the procoagulant factors decrease with the exception of factor VIII and von Willebrand factor (vWF) in cirrhosis. vWF appears to be increased through continuous low-grade activation of endothelial cells combined with decreased clearance by the liver. Factor VIII elevation may be due to compensatory production in other organs or increased level of the carrier protein vWF [115]. Levels of the endogenous anticoagulant factors, antithrombin, protein S, and protein C also decrease [59]. Levels of nitric oxide and prostacyclin increase. Levels of tissue plasminogen activator (tPA) and plasminogen activator inhibitor (PAI-1) reach a new equilibrium [115]. Tissue factor pathway

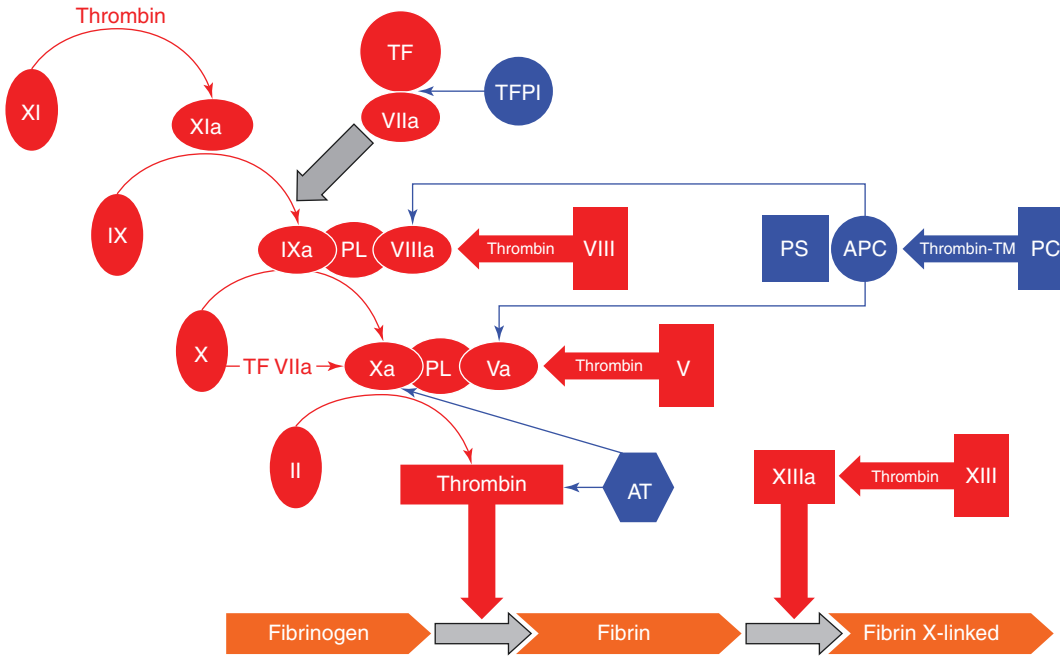

Fig. 24.1 Coagulation. Simplified representation of reactions leading to thrombin generation and inhibition. Roman numbers represent procoagulant (red) and anticoagulant factors (blue), respectively. APC activated protein C, AT antithrombin, PC protein C, PL negatively charged phospholipids on platelet membranes, PS protein S, TF tissue factor, TFPI tissue factor pathway inhibitor. (Reproduced from: Tripodi [106] with permission from Wolters Kluwer Health, Inc.)

inhibitor (TFPI) is synthesized by endothelial cells, and levels are normal or elevated in patients with chronic liver disease. TFPI downregulates the generation of thrombin. However, low levels of protein S, a cofactor, impair the TPFI anticoagulant pathway [76].

Similar to the clotting cascade, fibrinolysis (Fig. 24.2) appears to achieve a tenuous balance between pro- and antifibrinolytic pathways. In fibrinolysis under physiological conditions, plasminogen to plasmin conversion is regulated by profibrinolytic factors (tissue plasminogen activator [tPA], urokinase plasminogen activator, and activated factor XII). These effects are opposed by antifibrinolytic factors (tPA inhibitors [PAI-1], thrombin activatable fibrinolysis inhibitor [TAFI], and plasmin inhibitor. Derangements of this balance may result in hyperfibrinolysis or hypofibrinolysis [1]. Profibrinolytic changes in cirrhosis include increases in tissue plasminogen activator (tPA), plasmin activity, and a decrease in thrombin activatable fibrinolysis inhibitor (TAFI) and plasmin inhibitor. These changes are balanced by a decrease of plasminogen and an increase in plasminogen activator inhibitor (PAI-1) [24, 57] (Table 24.1). Some authors have described a hyperfibrinolytic state in cirrhosis [60]. Fibrinogen levels are often within the normal range in patients with stable cirrhosis, but decreased levels are found with advanced cirrhosis and in acute failure [17]. Dysfibrinogen or functionally aberrant fibrinogen has been shown in cirrhosis and is due to excessive sialic acid content [31]. Dysfibrinogenemia develops in 50–78% of patients with chronic liver disease. Regenerating hepatocytes synthesize an abnormal fibrinogen with increased sialic acid residues, which impairs polymerization of fibrin monomers [83, 106]. Based on the changes in both the pro- and antifibrinolytic actors, hyperfibrinolysis is likely to be overestimated. This overestimation is supported by a study that utilized thromboelastography (TEG) to show no evidence of fibrinolysis in 84 patients with

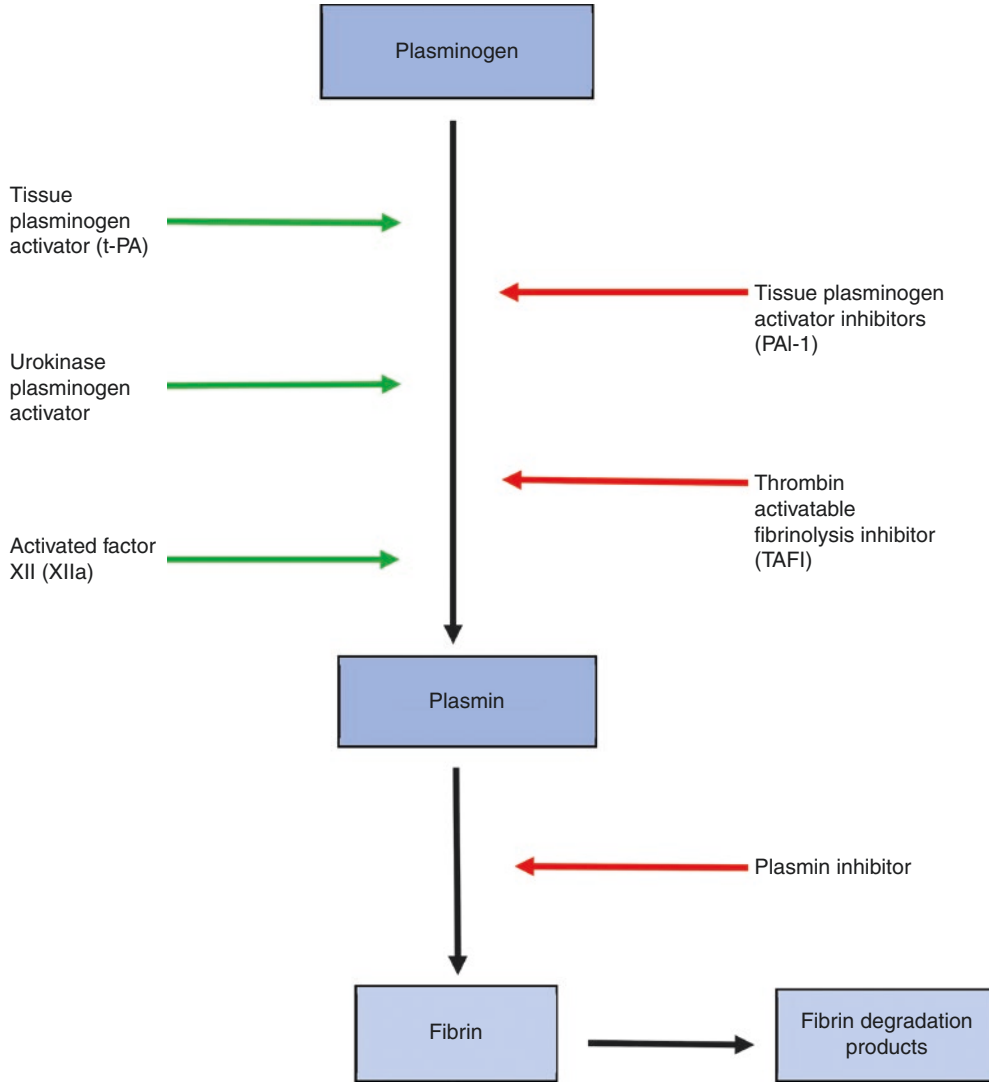

Fig. 24.2 Fibrinolysis

decompensated cirrhosis [72]. However, a true hyperfibrinolytic state may develop when a stressor overrides the fragile balance of pro- and antifibrinolytic factors present in patients with cirrhosis. Sepsis and release of endotoxin can set off a hyperfibrinolytic state through increased release of tPA [72].

Both procoagulant and anticoagulant drivers are lowered in cirrhosis, and compensatory mechanisms for hemostatic defects develop. Specifically, coagulation and fibrinolysis are in a rebalanced status because of a decline in both activators and inhibitors, and thrombocytopenia and platelet function dysfunction are compensated by elevated levels of VWF [115]. Despite the rebalancing of hemostatic factors, there are major alterations in the hemostatic pathways in most patients with liver disease. These include altered platelet and endothelial function, altered clotting factors, hyperfibrinolysis, dysfibrinogenemia, thrombocytopenia, and renal failure [17]. The elevated portal hypertension and splenomegaly, respectively, lead to alterations in hemodynamics and

increased platelet sequestration [115]. Despite a rebalanced hemostasis in patients with cirrhosis, this balance is less stable than in healthy patients because plasma levels of most factors are substantially reduced. This eliminates a natural buffer present in the healthy patient who has many times the necessary level for normal hemostasis (Fig. 24.3). This loss of buffer makes the hemostatic balance easily disturbed by complications of the disease including infections and renal failure leading to both bleeding and thrombotic events in these patients [60].

This "rebalanced hemostasis" of procoagulant and anticoagulant factors requires coagulation tests that can show the net result of these changes [21]. Basic labs (PT, aPTT, and platelets) fail to reflect the complex changes in the hemostatic profile of patients with liver disease. The platelet count does not take the elevated VWF levels or sequestration into account, and the PT and APTT are only sensitive for procoagulant factors and not the anticoagulant factors, tissue factor pathway inhibitor, or the role of the endothelium in hemostasis [60, 115].

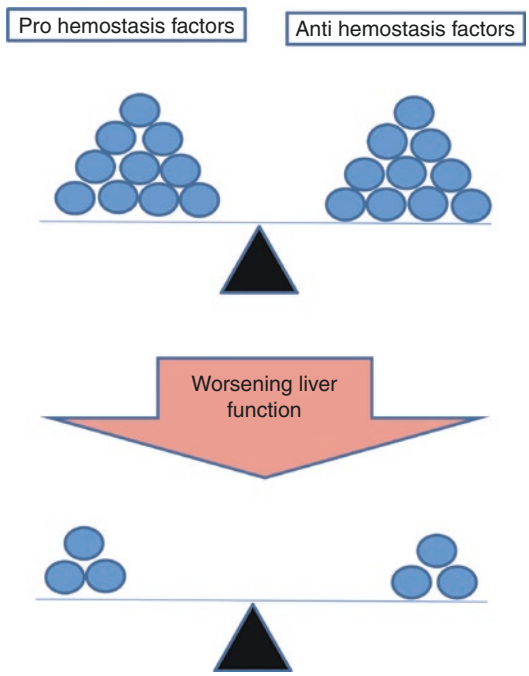

Fig. 24.3 Rebalanced hemostasis

Thrombin Generation Assay

A thrombin generation assay modified to include thrombomodulin is normal in patients with cirrhosis. Thrombomodulin is the main protein C activator operating in vivo but is not present in standard coagulation labs (PT, aPTT, INR) [100]. Therefore, patients with stable cirrhosis or patients undergoing liver transplantation (LT) can still generate thrombin at a normal to increased rate in the presence of a prolonged PT and APTT [59, 100].

Thromboelastometry/ Thromboelastography

Whole blood thromboelastography is another technique that may be helpful in the management of hemostasis in patients with liver disease [62, 98]. Whole blood viscoelastic tests evaluate the kinetics of coagulation, evaluating initial clot formation through final clot strength. As such they are a more comprehensive representation of the activity of procoagulants, natural anticoagulants, platelets, and the fibrinolytic pathway [83]. This overall assessment of hemostasis, including both plasmatic and cellular contributions, can be used to identify specific coagulopathies such as hyperfibrinolysis [88, 98]. There are two point-of-care devices (Thromboelastography (TEG), Haemonetics Corp., Braintree, MA, and Rotational Thromboelastometry (ROTEM), Tem International GmbH, Munich, Germany) available, and they have been routinely used to assess hemostasis and guide transfusion during liver transplantation [62, 88].

Five parameters are recorded in a standard TEG (Fig. 24.4). The reaction (R)-time (in minutes) represents the latency of clot formation from the beginning of the clotting reaction to the initial formation of fibrin and generally corresponds to the plasmatic component (INR and aPTT). The kinetic (K)-time (in minutes) describes the time required for the initial fibrin formation to reach a specific clot firmness. The alpha-angle (in degrees) reflects the rate of fibrin formation and cross-linking of platelets. The

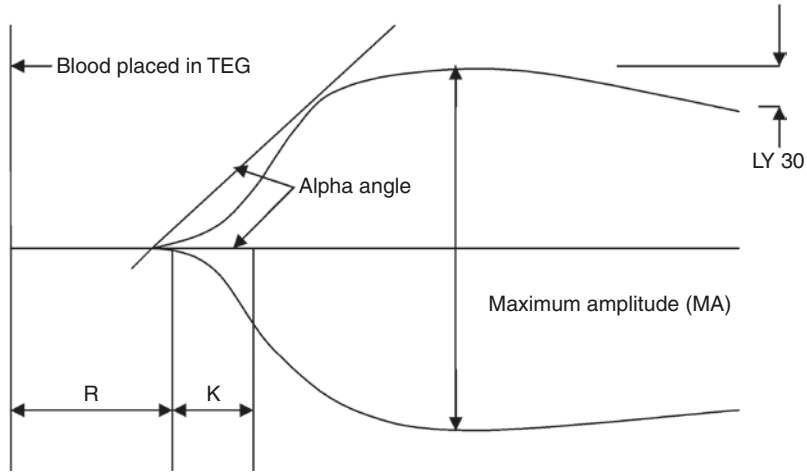

Fig. 24.4 Thromboelastography (TEG) tracing. (Reproduced from Chau et al. [20] with permission from BMJ Publishing Group Ltd.)

maximum amplitude (in mm) measures the maximum clot strength. The kinetic time, alpha-angle, and maximum amplitude are most dependent on platelet count/function and fibrinogen concentration. Finally, clot lysis at 30 minutes reflects clot dissolution and is a measure of fibrinolysis [98].

In stable cirrhosis, mean and median TEG parameters are generally within normal limits [98, 99]. However the maximum amplitude is decreased in proportion to the severity of thrombocytopenia. With greater degree of decompensation of cirrhosis (INR $\geq$1.5), the mean maximum amplitude of clot formation was below normal limits and correlated with a lower platelet count. The a-angle is also depressed in patients with decompensated cirrhosis and hypofibrinogenemia [98]. The findings from use of TEG in patients with cirrhosis support the observations made using thrombin generation assays, which showed that overall hemostasis is relatively well preserved [99, 100, 103, 107].

TEG has been shown to be superior to standard lab evaluation (INR, aPTT, or platelet count) for predicting esophageal varices rebleed rate. TEG parameters (r-time, k-time, and a-angle) on the day of variceal rebleeding showed significant differences when compared with the mean of the daily results in patients without rebleeding. In contrast, none of the standard laboratory tests of hemostasis differed between those who rebled and those who did not [19]. TEG-guided factor repletion has been shown to decrease red blood cell and plasma transfusion volumes [46, 61, 71, 88]. A small randomized trial that compared TEG versus standard lab testing (PT/INR) in patients undergoing orthotopic liver transplant (OLT) showed a significant decrease in FFP use in the TEG group compared to the standard lab test group but no differences in PRBCs administered and 3-year overall survival was seen between the two groups [113]. A follow-up study that used cutoffs 35% above baseline for transfusion of platelets and plasma did not result in increased bleeding or need for increased transfusion [114]. These studies suggest that TEG gives a more complete picture of the hemostatic picture in cirrhosis and the second study even suggests that the cirrhotic patient may even lean closer to thrombosis than bleeding. TEG monitoring during OLT to guide use of e-aminocaproic acid and aprotinin to treat hyperfibrinolysis has also been shown to decrease transfusion requirements [47, 75].

Infection and bleeding risk are tightly linked in cirrhosis. This is related to increased plasma concentrations of endothelium-derived endogenous heparinoids due to increased production and decreased hepatic clearance of these molecules [98]. TEG has also been useful in detecting infec-

tion in patients with cirrhosis. In a prospectively studied cohort of hospitalized decompensated cirrhotics, TEG parameters became more hypocoagulable in the patients who developed an infection compared to patients who did not develop an infection [72].

The appropriate "normal" range of TEG values in patients with cirrhosis has not been established. Some recent studies show a slower and less stable clot formation with a trend toward hypocoagulability [28, 53, 92]. Patients with cirrhosis may show a satisfactory coagulation balance without increased risk for bleeding, even if their TEG values are beyond the normal values for healthy patients [28]. The parameters for TEG correction during liver transplant have not been standardized, but authors have recommended two units of plasma for an R-time greater than 15 minutes, ten units of platelets for a maximum amplitude less than 40 mm, and six units of cryoprecipitate for an alpha-angle less than 40–45° [46, 75].

Unfortunately, to date, no studies have directly tested whether TEG, ROTEM, or other global tests such as thrombin generation testing are useful in predicting procedural bleeding risk in patients with liver disease [98]. In addition, the use of TEG- or ROTEM-guided transfusion in actively bleeding patients without liver disease was shown to reduce the amount of bleeding but has no clear effect on mortality [3]. The viscoelastic test values to trigger transfusion have not been validated, and large controlled clinical trials comparing different strategies and trigger values for transfusion of blood products are still needed [21].

Treatment Guidelines

Blood Products

The majority of clinical data for rebalanced hemostasis is the result of work done in OLT. It is common practice in some centers not to administer any blood products prior to or during the procedure unless active bleeding occurs [22, 42, 66, 79]. It would seem reasonable, and other authors have argued, to apply this to less complex procedures as well [115]. However, there are conflicting recommendations between societal guidelines. The American Association for the Study of Liver Diseases (AASLD) guidelines for liver biopsy carefully argue against prophylactic transfusion [84], whereas the Society of Interventional Radiology guidelines advise to correct an INR greater than 1.5 and a platelet count less than 50,000/μL [73].

Blood transfusion carries a number of significant risks. These include transfusion-related immunomodulation (TRIM); transfusion-associated circulatory overload; transfusion-associated acute lung injury (TRALI); hemolytic transfusion reactions; acute non-hemolytic transfusion reactions (febrile, allergic, or both in nature); transfusion-associated graft-versus-host disease; and transfusion-transmitted infection (bacterial, viral, and prion) [21]. The use of blood products during OLT has been shown to increase morbidity and mortality. Multiple studies have shown the intraoperative transfusion of red blood cells (RBCs) to be a major predictor of postoperative mortality [66, 80].

Because of the recognized risks of blood products, transfusion medicine has undergone a switch from product-specific to patient-specific care. Patient blood management (PBM) is defined as "the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in an effort to improve patient outcome" [91]. The three pillars of PBM consist of treating preoperative anemia, reducing perioperative blood loss, and optimizing anemia tolerance [95]. More generally this describes identifying anemic patients preoperatively and intervening prior to surgery, using recognized techniques for minimizing blood loss, and using evidence-based patient-specific restrictive transfusion targets. This has been shown to decrease in-hospital mortality, length of stay, myocardial infarction/stroke, and infectious complications while decreasing overall transfusions of blood and factor products [52]. These concepts can be applied to patients with cirrhosis.

There is data to support a restrictive blood transfusion approach. A RCT of 921 patients with GI bleeding showed that a "restrictive" transfusion strategy (initiating PRBC transfusion at a hemoglobin threshold of 7 g/dL and maintaining it at 7–9 g/dL) was associated with a significant decrease in mortality compared to a more traditional transfusion strategy (initiating PRBC transfusion at a hemoglobin threshold of 9 g/dL and maintaining it at 9–11 g/dL). Patients with cirrhosis represented 31% of these patients and were shown to have a significantly lower early rebleeding and mortality rates with the restrictive strategy [109].

Given the limitations of current laboratory testing, the best strategy is to treat only those cirrhotic patients who develop significant hemostatic bleeding. Hemostatic bleeding is characterized by persistent oozing/bleeding at multiple sites and from nonidentifiable sources. Another marker is delayed bleeding after adequate control of surgical bleeding. When hemostatic bleeding occurs, then the platelet count, PT, APTT, and fibrinogen level may be useful in guiding the transfusion of blood products. More comprehensive measurements of hemostasis such as thromboelastography (TEG or ROTEM) may be useful to assess the hemostatic status intraoperatively [115].

There is no evidence for administering prophylactic FFP based upon INR [62]. AASLD in recognition of the limitations of conventional coagulation tests (PT and international normalized ratio [INR]) discourages the use of arbitrary values for the basis of the transfusion of plasma [84]. Intraoperative plasma transfusions are associated with adverse outcomes in liver transplantation [8, 66]. In addition, volume introduced through plasma transfusions may increase bleeding risks by raising portosystemic pressures [117]. Therefore, mild to moderate INR (<2.5) elevation should not be corrected with FFP before invasive procedures with the exception of intracranial pressure monitor insertion [50, 117]. One author recommends, if the INR is more than 2.5, to give 10 mg of intravenous (IV) vitamin K and check fibrinogen levels. Plasma is reserved for unresponsiveness to the vitamin K or in the presence of active bleeding [117].

Hypofibrinogenemia has been shown to increase blood product requirements. The use of fibrinogen concentrates for significant bleeding if accompanied by low fibrinogen is warranted. Fibrinogen concentrates have been shown to improve coagulation, reduce perioperative bleeding, and significantly reduce transfusion [21]. A fibrinogen concentration above 2 g/L has been shown to be the minimum concentration in vitro at which clot formation normalizes [12]. A concentration of <1.5–2 g/L or signs of functional fibrinogen deficit on TEG or ROTEM ROTEM/TEG should be triggered for fibrinogen replacement [50]. Fibrinogen concentrates should be used over cryoprecipitate when available to reduce the risk of pathogen transmission and immune-mediated complications [21].

Euthermia, free ionized calcium, and the acid-base balance all play a role in coagulation [115]. Plasma and RBCs contain citrate, which leads to hypocalcemia. Free ionized calcium should therefore be measured regularly and corrected to at least 1 mmol/L to prevent disorders of hemostasis [93].

Platelets

Currently there are no universally accepted clinical practice guidelines for platelet transfusion in patients with cirrhosis undergoing invasive procedures [2]. Despite the lack of high-quality evidence, the American Association for the Study of the Liver Diseases (AASLD) suggests prophylactic transfusion of PLTs for a PLT less than 50,000/mL [84, 117]. The recommendation from an institution with a large experience in treating patients with cirrhosis is that they be transfused platelets for counts less than 30,000/μL if undergoing a major procedure. A single dose (equivalent to single-donor apheresis PLTs or five-pooled whole blood-derived PLTs) of intraprocedural PLTs is given. They recognize that the peripheral count is unlikely to increase significantly or be maintained for a meaningful amount of time [117]. This recommendation is based on a retrospective study evaluating thrombocytopenic patients with hematologic malignancies undergoing transjugular liver biopsy. There were no

bleeding complications in the entire cohort despite half the patients couldn't reach the goal of greater than 30,000/mL with multiple transfusions prior to the procedure [112].

Eltrombopag is an oral thrombopoietin-receptor agonist approved for use in patients with chronic immune thrombocytopenia. Eltrombopag was shown to increase platelet counts in patients with thrombocytopenia and hepatitis C [67]. This study was a placebo randomized control trial to assess ability to get patients onto retroviral therapy and was successful. A larger study was performed to examine if the drug could decrease the use of platelets for patients undergoing invasive procedures. This RCT did indeed show a significant increase in platelet counts and a decreased need for transfusion of platelets but an increased risk of mesenteric thrombosis. This result led the authors of the study to recommend against its use perioperatively until further studies can be done [2].

Preoperative Optimization

Iron deficiency anemia is often seen in cirrhosis [33]. The use of iron has been found beneficial in patients with iron deficiency anemia and is a correctible problem in cirrhotic patients preoperatively [26, 86]. Erythropoietin is produced in the kidney, stimulating erythrogenesis. Erythropoiesis begins within 3 d of administartion, and the equivalent of one unit of blood is produced in 7 d and five units within 28 d. This can be associated with functional iron deficiency, and iron supplementation is recommended for patients undergoing rEPO therapy [26, 106]. One center used rEPO 20,000 U subcutaneously twice a week or 40,000 U once a week preoperatively until the hematocrit reached 45% in Jehovah's Witness patients awaiting OLT.

Hemostatic balance in cirrhosis may be variable depending on the degree of liver dysfunction, underlying cause of liver disease, and current clinical state. The existence of *bacterial infection* has been shown to increase the risk of bleeding, mortality, and failure to control bleeding in patients with variceal bleeding [13, 35, 111]. Prophylactic administration of antibiotics to patients with cirrhosis is known to reduce mortality and improve hemostatic function in the setting of variceal bleed. The exact mechanism for this is unknown. Patients at risk for bacterial infections should receive prophylactic antibiotics to optimize hemostatic function. The adequate treatment of any infections before invasive procedures is also paramount [115, 117].

Renal insufficiency is associated with an increased risk of bleeding [43, 74]. The effects of kidney failure on hemostasis are complex and include the effect of uremia on platelet function [70]. The uremic effect on platelets is due to decreased platelet aggregation and adhesion. Dialysis can improve platelet function by removing uremic toxins and decrease risks of bleeding associated with volume overload [21, 117].

Fibrinogen levels can be decreased in cirrhotics. Patients undergoing OLT with low preoperative plasma fibrinogen ($\leq$2 g/L) have significantly higher rates of transfusion of RBCs than in the patients with fibrinogen values >2 g/L [25]. However, although preemptive administration of fibrinogen concentrate can increase plasma levels of fibrinogen to normal values and increase maximum clot firmness on TEG, it does not reduce the need for RBC transfusions in LT [87].

Control Portal Pressures

Portal hypertension is the main consequence of cirrhosis and is responsible for the majority of its complications. As such, it is the major cause of the increased risk of bleeding associated with cirrhosis. Portal pressure can be directly measured as the hepatic venous pressure gradient (HVPG). The HVPG has been shown to be more accurate than liver biopsy in predicting development of complications of cirrhosis [10]. Portal hypertension can be divided into mild PH (HVPG >5 but <10 mm Hg) and those with clinically significant portal hypertension (HVPG >10 mm Hg) [32]. Clinically significant PH is associated with an increased risk of varices, variceal hemorrhage ascites, encephalopathy,

postsurgical decompensation, and hepatocellular carcinoma (HCC) [16, 36, 81, 82].

Patients with cirrhosis and portal hypertension have a response to volume loading that can exacerbate bleeding. Volume loading leads to increased blood pooling in the splanchnic circulation, by a greater magnitude than in the central and arterial circulation [21]. The resultant increase in portal venous pressure from volume loading can lead to increased bleeding. Intraoperatively, an important strategy to prevent bleeding during invasive procedures is to maintain a low splanchnic and portal pressure. This is primarily achieved by using CVP as a surrogate for portal pressures and maintaining a low total circulating volume intraoperatively [94]. A variety of methods are used to maintain a low CVP including a restrictive infusion policy, forced diuresis, and preoperative phlebotomy [39, 64, 65, 115]. Maintaining a low CVP has been shown to considerably reduce perioperative blood loss during liver resection and liver transplant surgery [44, 94]. A major concern with the low CVP approach is to maintain sufficient tissue perfusion, especially of the kidneys. This can be accomplished through the use of vasoconstrictors [65]. In a randomized controlled trial by Feng et al., comparing the use of low and normal CVP during liver transplantation, a significant reduction of blood loss was achieved with no adverse effect on kidney function [30].

Antifibrinolytic Therapy

Antifibrinolytic therapy has been shown to decrease blood loss and need for transfusion [40]. Aprotinin has been shown to reduce blood loss and transfusion requirements [37]. Aprotinin is a bovine-derived serine protease inhibitor that leads indirectly to diminution of fibrinolysis [17]. However, it was withdrawn from the market due to safety concerns [50]. Antifibrinolytic agents, such as aminocaproic acid (EACA) and tranexamic acid (TA), are derivatives of lysine that inhibit plasmin. Lysine analogues, such as tranexamic acid, have been shown to have a lower risk of death when compared to aprotinin. Meta-analyses have shown both tranexamic acid and aprotinin to reduce RBC transfusion during OLT [68]. Tranexamic acid competitively inhibits the activation of plasminogen to plasmin. The usual dose of tranexamic acid is in 1–2 g increments. TEG/ROTEM can be used to guide further doses [21].

Recombinant Factor VIIa

Recombinant factor VIIa (rFVIIa) is a hemostatic agent approved for hemophilia. rFVIIa offers the theoretical advantage of augmentation of the physiological thrombin accumulation at the site of injury, enhanced activation of platelets, and avoids excessive volume [17]. rFVIIa binds to the surface of activated platelets and to tissue factor (TF) at sites of vascular injury activating factor X. Factor X augments the conversion of prothrombin to thrombin forming the hemostatic plug (Fig. 24.1). Unfortunately, randomized trials assessing the use of rFVIIa in upper GI and variceal bleeding failed to show improvement in blood use or mortality [14, 15]. The TF-independent clotting potential of rFVIIa has raised concern for unintended, off-target thrombosis [34]. Meta-analysis and systematic reviews of the use of rFVIIa in hepatic surgery (including transplantation) have failed to show a benefit in the number of blood transfusions yet showed, but they did show a significant increase in arterial thrombotic complications [20, 55, 116]. Despite these findings, based on its mechanism of action, it may still have a role as a rescue agent in severe hemorrhage when conventional blood component replacement is insufficient and the thromboembolic risk is outweighed by the risk of ongoing bleeding [17, 34, 54].

Desmopressin

Desmopressin (DDAVP, 1-deamino-8- D-arginine vasopressin) is an analogue of the antidiuretic hormone vasopressin, which increases endogenous secretion of vWF and FVIII. Surprisingly, in light of the already elevated levels of vWF and factor VIII in cirrhosis, the agent shortens bleeding time in cirrhotics. However, clinical trials in cirrhosis have been disappointing [17].

Prothrombin Complex Concentrate

Factor concentrates like a prothrombin complex concentrate (PCC) are pharmaceutical agents in lyophilized volume. As such they are highly concentrated, low volume, virally inactivated products that do not require thawing and can be rapidly administered [7]. The nonactivated vitamin K-dependent coagulation factors in PCC are 25 times more concentrated when compared with FFP [18]. The use of PCC may mitigate infectious risk, decrease volume, and decrease administration time associated with FFP [23]. The concern with these agents is their effectiveness and the risk for thromboembolic complications. Retrospective studies have been inconclusive in the decrease in blood product usage in the setting of liver transplant and limited in evaluation for thrombotic complications [23, 48]. A randomized controlled trial (the PROTON trial) studying prothrombin complex concentrate (PCCs) effect on RBC transfusion requirements in OLT is currently in progress [4].

Cryoprecipitate

There is no consensus regarding appropriate levels of fibrinogen necessary in nonbleeding or bleeding cirrhotic patients [117]. Hematologic defects have been seen in studies looking at massive hemorrhage when fibrinogen levels have decreased below 100 mg/dL [56]. Based on these studies that did not specifically look at cirrhotics, a fibrinogen level of 100 mg/dL as a minimum has been recommended for perioperative bleeding [63, 96]. Cryoprecipitate, which has a higher concentration of fibrinogen, should be used instead of FFP for replacement. This avoids the increased volume issues [117].

Conclusions

Under general conditions the patient with liver cirrhosis is in hemostatic balance and at risk for both bleeding and thrombotic events. Standard laboratory evaluations (platelet count, PT, and APTT) are poor predictors of bleeding risk. Furthermore, attempts to prophylactically correct abnormal values with platelet concentrates or plasma do not reduce bleeding. The use of blood products to correct abnormalities may actually exacerbate bleeding by increasing volume load. Treatment of coagulopathy should only be treated when experiencing active bleeding of hemostatic origin.

The strategy for preventing bleeding should be keeping CVP and total circulating volume low intraoperatively. Modifiable risk factors for bleeding in patients with cirrhosis such as infection and renal failure should be addressed preoperatively. Ideally procedures should be undertaken in facilities with experience in dealing with patients with cirrhosis such as transplant centers where physicians from all disciplines dealing with liver disease can provide a comprehensive treatment plan. The concept of rebalanced hemostasis in patients with liver disease and the above strategies have been implemented successfully in liver transplantation. Although it is clear that prophylactic correction of abnormal hemostatic parameters should be abandoned, specific data to support treatment schemes based on this new approach are scarce. Patients with cirrhosis are a heterogenous group and can present in a variety of clinical situations. Although these patients are better off as a group when treated as outlined, it is possible that a true coagulopathy does exist in an individual patient. Because of the lack of a clinically applicable coagulation test that reliably predicts the risk of bleeding, clinicians currently cannot identify individual patients with an increased bleeding risk, apart from the risk factors mentioned in this chapter. Further research is needed to accurately predict bleeding risk in patients with liver disease.

Bibliography

Works Cited

1. (SIMI), U. t. Hemostatic balance in patients with liver cirrhosis: report of a consensus conference. Dig Liver Dis. 2016;48(5):455–67.
2. Afdhal NH. Eltrombopag before procedures in patients with cirrhosis and thrombocytopenia. N Engl J Med. 2012;367(8):716–24.

3. Afshari AW. Thrombelastography (TEG) or thromboelastometry (ROTEM) to monitor haemotherapy versus usual care in patients with massive transfusion. Cochrane Database Syst Rev. 2011;3:CD007871.
4. Arshad F, Ickx B, et al. Prothrombin complex concentrate in the reduction of blood loss during orthotopic liver transplantation: PROTON-trial. BioMed Central Surg. 2013;13:22.
5. Aster R. Pooling of platelets in the spleen: role in the pathogenesis of "hypersplenic" thrombocytopenia. J Clin Investig. 1966a;45:645–57.
6. Basili SF. Bleeding time does not predict gastrointestinal bleeding in patients with cirrhosis. The CALC group. Coagulation abnormalities in liver cirrhosis. J Hepatol. 1996;24(5):574–80.
7. Behring C. Full prescribing information: Kcentra prothrombin complex concentrate (human) [cited 2014 Apr 10]. 2014. Retrieved from http://labeling.cslbehring.com/PI/US/Kcentra/EN/Kcentra-Prescribing-Information.pdf.
8. Benson AB, Burton JR, et al. Differential effects of plasma and red blood cell transfusions on acute lung injury and infection risk following liver transplantation. Liver Transplant. 2011;17:149–58.
9. Bevers EM. Platelet procoagulant activity: physiological significance and mechanisms of exposure. Blood Rev. 1991;5(3):146–54.
10. Blasco A, Forns X, et al. Hepatic venous pressure gradient identifies patients at risk of severe hepatitis C recurrence after liver transplantation. Hepatology. 2006;43(3):492–9.
11. Boberg KM. Is a prolonged bleeding time associated with an increased risk of hemorrhage after liver biopsy? Thromb Hemost. 1999;81(3):387–1.
12. Bolliger D, Szlam F, et al. Finding the optimal concentration range for fibrinogen replacement after severe haemodilution: an in vitro model. Br J Anesth. 2009;102(6):793–9.
13. Borzio MS. Bacterial infection in patients with advanced cirrhosis: a multicentre prospective study. Dig Liver Dis. 2001;33(1):41–8.
14. Bosch J, Thabut D, Bendtsen F, D'Amico G, Albillos A, Gonzalez Abraldes J, Fabricius S, Erhardtsen E, de Franchis R, Haemorrhage ES. Recombinant factor VIIa for upper gastrointestinal bleeding in patients with cirrhosis: a randomized, double-blind trial. Gastroenterology. 2004;127(4):1123–30.
15. Bosch J, Thabut D, Albillos A, Carbonell N, Spicak J, Massard J, D'amico G, Lebrec D, de Franchis R, Fabricius S, Cai Y, Hemorrhage IS. TitleRecombinant factor VIIa for variceal bleeding in patients with advanced cirrhosis: a randomized, controlled trial. Hepatology. 2008;47(5):1604–14.
16. Bruix JC-P. Surgical resection of hepatocellular carcinoma in cirrhotic patients: prognostic value of preoperative portal pressure. Gastroenterology. 1996;111(4):1018–22.
17. Caldwell SH. Coagulation disorders and hemostasis in liver disease: pathophysiology and critical assessment of current management. Hepatology. 2006;44(4):1039–46.
18. Cappabianca G, Mariscalco G. Safety and efficacy of prothrombin complex concentrate as first-line treatment in bleeding after cardiac surgery. Crit Care. 2016;20:5.
19. Chau TN, Chan YW, Patch D, Tokunaga S, Greenslade L, Burroughs AK. Thrombelastographic changes and early rebleeding in cirrhotic patients with variceal bleeding. Gut. 1998;43(2):267–71.
20. Chavez-Tapia NC, Alfaro-Lara R, Tellez-Avila F, et al. Prophylactic activated recombinant factor VII in liver resection and liver transplantation: systematic review and meta-analysis. PLoS One. 2011;6(7):e22581.
21. Clevenger B, Mallett SV. Transfusion and coagulation management in liver transplantation. World J Gastroenterol. 2014;20(20):6146–58.
22. Coelho GR. Single-center transfusion rate for 555 consecutive liver transplantations: impact of two eras. Transplant Proc. 2013;45(9):3305–9.
23. Colavecchia A, Cohen D, Harris J, Thomas J, Lindberg S, Leveque C, Salazar E. Impact of intraoperative factor concentrates on blood product transfusions during orthotopic liver transplantation. Transfusion Practice. 2017;57:3026–34.
24. Colucci MB. Deficiency of thrombin activatable fibrinolysis inhibitor in cirrhosis is associated with increased plasma fibrinolysis. Hepatology. 2003;38(1):230–7.
25. Costa MD. Low plasma fibrinogen levels and blood product transfusion in liver transplantation. Minerva Anestesiol. 2014;80(5):568–73.
26. Darwish A. Liver transplant in Jehovah's Witnesses patients. Curr Opin Organ Transplant. 2011;16(3):326–30.
27. de Boer MT. Minimizing blood loss in liver transplantation: Progress through research and evolution of techniques. Dig Surg. 2005;22(4):265–75.
28. De Pietri L, Bianchini M, Rompianesi G, Bertellini E, Begliomini B. Thromboelastographic reference ranges for a cirrhotic patient population undergoing liver transplantation. World J Surg. 2016;6(3):583–93.
29. Drolz AH. Coagulation parameters and major bleeding in critically ill patients with cirrhosis. Hepatology. 2016;64(2):556–68.
30. Feng ZY. Effects of low central venous pressure during preanhepatic phase on blood loss and liver and renal function in liver transplantation. World J Surg. 2010;34(8):1864–73.
31. Francis JL. Acquired dysfibrinogenaemia in liver disease. J Clin Pathol. 1982;35(6):667–72.
32. Garcia-Tsao G. Current management of the complications of cirrhosis and portal hypertension: variceal hemorrhage, ascites, and spontaneous bacterial peritonitis. Dig Dis. 2016;34(4):382–96.
33. Gkamprela ED. Iron deficiency anemia in chronic liver disease: etiopathogenesis, diagnosis and treatment. Ann Gastroenterol. 2017;30(4):405–13.

34. Goodnough LT. The judicious use of recombinant factor VIIa. Semin Thromb Hemost. 2016;42:125–32.
35. Goulis JA. Bacterial infection is independently associated with failure to control bleeding in cirrhotic patients with gastrointestinal hemorrhage. Hepatology. 1998;27(5):1207–12.
36. Groszmann RJ-T. Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. N Engl J Med. 2005;353(21):2254–61.
37. Gurusamy KS. Methods to decrease blood loss and transfusion requirements for liver transplantation. Cochrane Database Syst Rev. 2011;12:CD009052.
38. Ha NB. Anticoagulation in patients with cirrhosis: caught between a rock-liver and a hard place. Ann Pharmacother. 2016;50(5):402–9.
39. Hashimoto TK. Intraoperative blood salvage during liver resection: a randomized controlled trial. Ann Surg. 2007;245(5):686–91.
40. Henry DA. Anti-fibrinolytic use for minimizing perioperative allogeneic blood transfusion. Cochrane Database Syst Rev. 2011;(1):CD001886.
41. Im GY. Surgery in patients with portal hypertension: a preoperative checklist and strategies for attenuating risk. Clin Liver Dis. 2015;18(2):477–505.
42. Jabbour NG. Impact of a transfusion-free program on non-jehovah's witness patients undergoing liver transplantation. Arch Surg. 2006;141(9):913–7.
43. Jalal DI. Disorders of hemostasis associated with chronic kidney disease. Semin Thromb Hemost. 2010;36(1):34–40.
44. Jones RM. Central venous pressure and its effect on blood loss during liver resection. Br J Surg. 1998;85(8):1058–60.
45. Kamath PS. A model to predict survival in patients with end-stage liver disease. Hepatology. 2001;33(2):464–70.
46. Kang YG. Intraoperative changes in blood coagulation and thrombelastographic monitoring in liver transplantation. Anesth Analg. 1985;64(9):888–96.
47. Kang YL. Epsilon-aminocaproic acid for treatment of fibrinolysis during liver transplantation. Anesthesiology. 1987;66(6):766–73.
48. Kirchner C, Dirkmann D, et al. Coagulation management with factor concentrates in liver transplantation: a single-center experience. Transfusion. 2014;54:2760–8.
49. Kochanek KD. Mortality in the United States, 2016. NCHS Data Brief. 2017;293:1–8.
50. Kozek-Langenecker SA. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology: first update 2016. Eur J Anaesthesiol. 2017;34(6):332–95.
51. Kujovich JL. Coagulopathy in liver disease: a balancing act. Hematology Am Soc Hematol Educ Program. 2015;2015:243–9.
52. Leahy MF. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. Transfusion. 2017;57(6):1347–58.
53. Lentschener C, Flaujac C, Ibrahim F, Gouin-Thibault I, Bazin M, Sogni P, Samama C. Assessment of haemostasis in patients with cirrhosis: relevance of the ROTEM tests?: A prospective, cross-sectional study. Eur J Anesthesiol. 2016;33(2):126–33.
54. Levi MP. Efficacy and safety of recombinant factor VIIa for treatment of severe bleeding: a systematic review. Crit Care Med. 2005;33(4):883–90.
55. Levi ML. Safety of recombinant activated factor VII in randomized clinical trials. N Engl J Med. 2010;363(19):1791–800.
56. Levy JH, Goodnough LT. How I use fibrinogen replacement therapy in acquired bleeding. Blood. 2015;125:1387–93.
57. Lisman TL. Thrombin-activatable fibrinolysis inhibitor deficiency in cirrhosis is not associated with increased plasma fibrinolysis. Gastroenterology. 2001;121(1):131–9.
58. Lisman TB. Elevated levels of von willebrand factor in cirrhosis support platelet adhesion despite reduced functional capacity. Hepatology. 2006;52(3):53–61.
59. Lisman TB. Normal to increased thrombin generation in patients undergoing liver transplantation despite prolonged conventional coagulation tests. J Hepatol. 2010;52(3):355–61.
60. Lisman T, Porte RJ. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences. Blood. 2010;116(6):878–85.
61. Mallett SV. The intra-operative use of trasylol (aprotinin) in liver transplantation. Transpl Int. 1991;4(4):227–30.
62. Mallett SV. Clinical utility of viscoelastic tests of coagulation in patients with liver disease. Liver Int. 2013;33(7):961–74.
63. Management AS. Practice guidelines for perioperative blood management: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management*. Anesthesiology. 2015;122:241–75.
64. Massicotte LL. Effect of low central venous pressure and phlebotomy on blood product transfusion requirements during liver transplantations. Liver Transpl. 2006;12(1):117–23.
65. Massicotte LP. Effects of phlebotomy and phenylephrine infusion on portal venous pressure and systemic hemodynamics during liver transplantation. Transplantation. 2010;89(8):920–7.
66. Massicotte LD. Transfusion rate for 500 consecutive liver transplantations: experience of one liver transplantation center. Transplantation. 2012;93:1276–81.
67. McHutchison JG-T. Eltrombopag for thrombocytopenia in patients with cirrhosis associated with hepatitis C. N Engl J Med. 2007;357(22):2227–36.
68. Molenaar IQ. Efficacy and safety of antifibrinolytic drugs in liver transplantation: a systematic review and meta-analysis. Am J Transplant Off J Am Soc Transplant Am Soc Transplant Surg. 2007;7(1):185–94.
69. Murphy SL. Deaths: final data for 2015. National vital statistics reports: from the Centers for Disease

Control and Prevention, National Center for Health Statistics, National Vital Statistics System. Natl Vital Stat Rep. 2017;66(6):1–75.
70. Noris M, Remuzzi G. Uremic bleeding: closing the circle after 30 years of controversies? Blood. 1999;94(8):2569–74.
71. Owen CA. Hemostatic evaluation of patients undergoing liver transplantation. Mayo Clin Proc. 1987;62(9):761–72.
72. Papatheodoridis GV. Infection and hemostasis in decompensated cirrhosis: a prospective study using thrombelastography. Hepatology. 1999; 29(4):1085–90.
73. Patel IJ. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Intervent Radiol JVIR. 2012;23(6):727–36.
74. Pavord S, Myers B. Bleeding and thrombotic complications of kidney disease. Blood Rev. 2011;25(6):271–8.
75. Porte RJ. Systemic effects of tissue plasminogen activator-associated fibrinolysis and its relation to thrombin generation in orthotopic liver transplantation. Transplantation. 1989;47(6):978–84.
76. Potze WA. Decreased tissue factor pathway inhibitor (TFPI)-dependent anticoagulant capacity in patients with cirrhosis who have decreased protein S but normal TFPI plasma levels. Br J Hematol. 2013;162(6):819–26.
77. Pugh RN-L. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg. 1973; 60(8):646–9.
78. Qureshi KP. The use of thrombopoietin receptor agonists for correction of thrombocytopenia prior to elective procedures in chronic liver diseases: review of current evidence. Int J Hepatol. 2016;2016:1802932.
79. Ramos HC. Liver transplantation without the use of blood products. Arch Surg. 1995;129(5):528–32; discussion 532.
80. Rana AP. Blood transfusion requirement during liver transplantation is an important risk factor for mortality. J Am Coll Surg. 2013;216(5):902–7.
81. Ripoll CG-T. Hepatic venous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. Gastroenterology. 2007;133(2):481–8.
82. Ripoll CG-T. Hepatic venous pressure gradient predicts development of hepatocellular carcinoma independently of severity of cirrhosis. J Hepatol. 2009;50(5):923–8.
83. Roberts LN. Hemostasis and thrombosis in liver disease. Br J Haematol. 2010;148(4):507–21.
84. Rockey DC. Liver biopsy. Hepatology. 2009; 49(3):1017–44.
85. Ruggeri ZM. Von willebrand factor, platelets and endothelial cell interactions. J Thromb Haemost JTH. 2003;1(7):1335–42.
86. Sabate AD. Coagulopathy management in liver transplantation. Transplant Proc. 2012;44(6):1523–5.
87. Sabate AG. Impact of preemptive fibrinogen concentrate on transfusion requirements in liver transplantation: a multicenter, randomized, double-blind, placebo-controlled trial. Am J Transplant. 2016;16(8):2421–9.
88. Saner FH. Delicate balance of bleeding and thrombosis in end-stage liver disease and liver transplantation. Digestion. 2013;88(3):135–44.
89. Schwartz DH. Initial resuscitation and management of the hemodynamically unstable patient. In: Moore L, Todd S, editors. Common problems in acute care surgery. Cham: Springer; 2017. p. 3–15.
90. Seeff LB. Complication rate of percutaneous liver biopsies among persons with advanced chronic liver disease in the HALT-C trial. Clin Gastroenterol Hepatol. 2010;8(10):877–83.
91. Shander AH. Patient blood management–the new frontier. Best Pract Res Clin Anaesthesiol. 2013;27(1):5–10.
92. Shin K, Kim I, Lee H, Kim H, Chang C, Hong Y, Yoon K, Cho M. Thromboelastographic evaluation of coagulation in patients with liver disease. Ann Lab Med. 2017;37(3):204–12.
93. Sihler KC. Complications of massive transfusion. Chest. 2010;137(1):209–20.
94. Smyrniotis VK. The role of central venous pressure and type of vascular control in blood loss during major liver resections. Am J Surg. 2004;187(3):398–402.
95. Spahn DR. Patient blood management: the new standard. Transfusion. 2017;57(6):1325–7.
96. Stainsby D, MacLennan S. Guidelines on the management of massive blood loss. Br J Haematol. 2006;135:634–41.
97. Stine JG. Coagulopathy before and after liver transplantation: from the hepatic to the systemic circulatory systems. Clin Liver Dis. 2017;21(2):253–74.
98. Stravitz RT. Potential applications of thromboelastography in patients with acute and chronic liver disease. Gastroenterol Hepatol. 2012;8(8):513–20.
99. Thalheimer UT. A comparison of kaolin-activated versus nonkaolin-activated thromboelastography in native and citrated blood. Blood Coagul Fibrinolysis. 2008;19(6):495–501.
100. Tripodi AS. Evidence of normal thrombin generation in cirrhosis despite abnormal conventional coagulation tests. Hepatology. 2005;41(3):553–8.
101. Tripodi AP. Thrombin generation in patients with cirrhosis: the role of platelets. Hepatology. 2006;44(2):440–5.
102. Tripodi AP. An imbalance of pro- vs anti-coagulation factors in plasma from patients with cirrhosis. Gastroenterology. 2009;137(6):2105–11.
103. Tripodi AP. Detection of the imbalance of procoagulant versus anticoagulant factors in cirrhosis by a simple laboratory method. Hepatology. 2010;52(1):249–55.
104. Tripodi AP. Global hemostasis tests in patients with cirrhosis before and after prophylactic platelet transfusion. Liver Int. 2013;33(3):362–7.

105. Tripodi A. Hemostasis abnormalities in cirrhosis. Curr Opin Hematol. 2015;22(5):406–12.
106. Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. N Engl J Med. 2011;365(2):147–56.
107. Tripodi A, Chantarangkul V, Primignani M, Clerici M, Dell'era A, Aghemo A, et al. Thrombin generation in plasma from patients with cirrhosis supplemented with normal plasma: Considerations on the efficacy of treatment with fresh-frozen plasma. Intern Emerg Med. 2012;7(2):139–44.
108. Valla DC. The coagulation system in patients with end-stage liver disease. Liver Int. 2015;35(Supplement 1):139–44.
109. Villanueva CC-G. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013;368(1):11–21.
110. Violi FL. Bleeding time in patients with cirrhosis: relation with degree of liver failure and clotting abnormalities. C.A.L.C. Group. Coagulation abnormalities in cirrhosis study group. J Hepatol. 1994;20(4):531–6.
111. Vivas SR. Presence of bacterial infection in bleeding cirrhotic patients is independently associated with early mortality and failure to control bleeding. Dig Dis. 2001;46(12):2752–7.
112. Wallace MJ, Narvios A. Transjugular liver biopsy in patients with hematologic malignancy and severe thrombocytopenia. J Vasc Interv Radiol. 2003;14:323–7.
113. Wang SC. Thromboelastography-guided transfusion decreases intraoperative blood transfusion during orthotopic liver transplantation: randomized clinical trial. Transplant Proc. 2010;42(7):2590–3.
114. Wang SC. Use of higher thromboelastogram transfusion values is not associated with greater blood loss in liver transplant surgery. Liver Transplant. 2012;18(10):1254–8.
115. Weeder PD. Hemostasis in liver disease: implications of new concepts for perioperative management. Transfus Med Rev. 2014;28(3):107–13.
116. Yank VT. Systematic review: benefits and harms of in-hospital use of recombinant factor VIIa for off-label indications. Ann Intern Med. 2011;154(8):529–40.
117. Yates SG. How do we transfuse blood components in cirrhotic patients undergoing gastrointestinal procedures? Transfusion. 2016;56:791–8.
118. Zakeri N, Tsochatzis EA. Bleeding risk with invasive procedures in patients with cirrhosis and coagulopathy. Curr Gastroenterol Rep. 2017;19(9):45–017.

Gastrointestinal Bleeding as a Result of Portal Hypertension

25

Jonathan Marshall

Introduction

Before leaving Prague for Oregon Health and Sciences University (OHSU), it's unlikely Josef Rosch realized how profound an affect he would have on the treatment of portal hypertension and gastrointestinal (GI) hemorrhage in the twenty-first century. The concept of transjugular intrahepatic shunt (TIPS) found its origin from the serendipitous inadvertent access to the portal system during transhepatic cholangiography to evaluate biliary obstruction. TIPS was initially tested in canine models, and the first human TIPS was performed in the early 1980s by ballooning the parenchymal tract between the hepatic vein and portal (this technique was limited by early thrombosis). By the mid-1980s, self-expanding stents were deployed within the parenchymal tract, and by the late 1990s, the introduction of the Viatorr stent graft further refined tract patency.

TIPS was initially used to treat variceal hemorrhage; however, several additional indications continue to grow in popularity including the treatment of Budd-Chiari, hepatorenal syndrome, acute and chronic portal thrombus, and mesenteric venous thrombus. Additionally, the major complication rate for TIPS is approximately 1.4% with that rate dropping at institutions performing a greater volume of the procedure.

Indications for TIPS [1]

Secondary prophylaxis of variceal bleeding
Acute variceal bleeding
Portal hypertensive gastropathy
Recurrent acute variceal bleeding
Refractory ascites
Hepatorenal syndrome
Budd-Chiari
Hepatic veno-occlusive disease
Hepatic hydrothorax
Hepatopulmonary syndrome
Portal vein thrombosis

Contraindications for TIPS [1]

Absolute	Relative
Primary prevention of variceal bleeding	Hepatoma
CHF	Obstruction of all hepatic veins
Tricuspid regurgitation	Severe hepatic encephalopathy
Multiple hepatic cysts	Uncorrectable coagulopathy INR >5
Biliary obstruction	Severe thrombocytopenia
Severe pulmonary HTN	MELD > 18, total bilirubin > 3

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Technique

Conceptually, a TIPS is created by placing a stent graft in the parenchymal tract between the right hepatic vein and the undivided right portal vein. This is possible due to the anatomic orientation of the right portal vein anterior to the right hepatic vein. At the author's institution, elective TIPS are performed under general anesthesia. In cases of hemodynamically unstable variceal hemorrhage, these patients typically are intubated and paralyzed making a technically challenging procedure more manageable and allowing the proceduralist to focus on the procedure itself.

Not uncommonly and due to the nature of chronic liver disease, patients have suboptimal coagulation laboratory parameters. In the author's institution, an INR of 1.7 or less and a platelet count of >50, 000 are acceptable starting points especially given the limited effectiveness of FFP transfusions above this level [2]. Beyond these parameters, each patient should be managed on a case by case basis with attention to the acuity of the patient's condition and the risk reward associated with performing the procedure and transfusing the applicable blood products (Fig. 25.1).

Through a right or left internal jugular approach, the right hepatic vein is catheterized. Pressures are measured within the right atrium and right hepatic vein. Right atrial pressures of >20 mmHg and a mean pulmonary artery pressure of greater than or equal to 45 mmHg would be considered a contraindication as a result of increased preload as a result of TIPS venous return [3]. An occlusion balloon is advanced into the right hepatic vein, and CO_2 portovenography is performed. The occlusion balloon assisted injected allows the reflux of CO_2 through the hepatic sinusoids into the portal venules creating a blue print for access. A long metal cannula is advanced into the right hepatic vein through which a smaller less traumatic needle is advanced to gain access. Using the portovenogram as a frame of reference, a puncture is made with the Colapinto needle under fluoroscopic guidance. A syringe is attached to the back of the needle and the needle is slowly withdrawn. The return of blood signals intraluminal tip location within the portal vein. The location of the needle tip is confirmed with the injection of contrast material. Once placement within the portal vein is confirmed, stiff wire access into

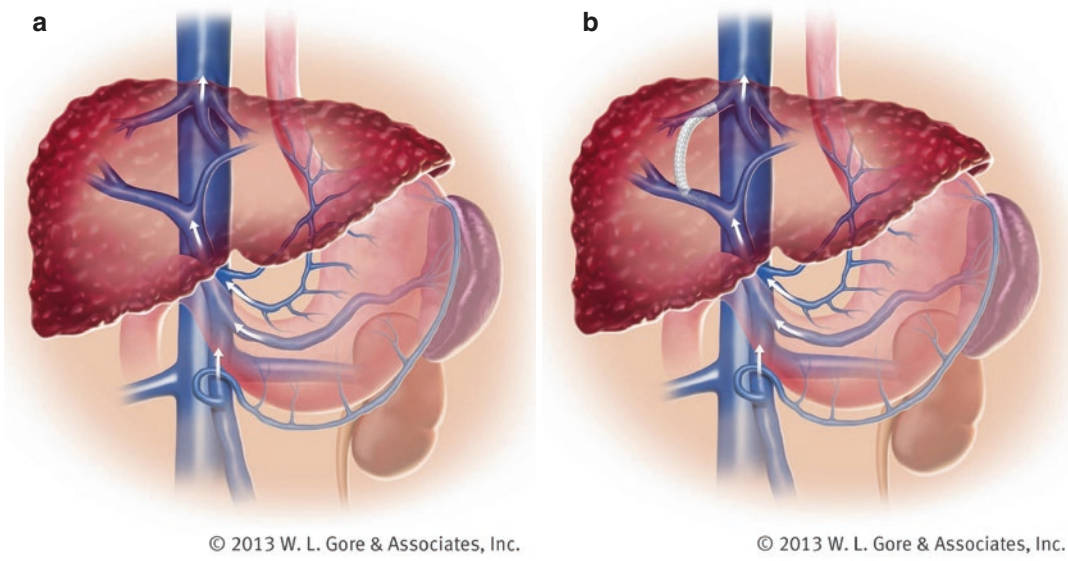

Fig. 25.1 (**a**) Diagram showing the anatomy of the systemic and portal venous systems prior to TIPS placement. (**b**) Stent deployment within the parenchymal tract creating a shunt bypass from the portal venous system into the systemic circulation. (Images courtesy of Gore USA)

the mesenteric portal system or splenic vein is obtained. The portosystemic gradient (PSG) is the measure of the difference in pressure between the portal and systemic systems. Portal hypertension is defined as being >6 mmHg [4]. The post TIPS target PSG is approximately 12 mmHg which can usually be managed with a 10 mm stent ballooned to 8 mm [5].

Cirrhotic livers tend to be stiff and fibrotic making catheter exchanges difficult. In this case, sequential balloon dilation is performed to facilitate vascular sheath placement in the main portal vein. Once sheath access to the main portal vein is obtained, portal pressures and gradients are measured, and the stent graft is deployed into the parenchymal tract (Figs. 25.2, 25.3, and 25.4).

Traditionally, bare metal stents in the form of the Boston Scientific Wallstent can be used; however, there is evidence to suggest better patency with the Gore Viatorr Endoprosthesis. The Viatorr stent has a covered component, which is deployed in the parenchymal tract to avoid bile leakage and stent occlusion, and a bare metal component which maintains flow through the portal system and averts "jailing" of the portal branches and liver infarction (Figs. 25.5, 25.6, and 25.7).

Multiple meta-analyses have demonstrated the improved benefit of TIPS vs. endoscopy in the prevention of variceal rebleeding. The rate of rebleeding in the TIPS group measured 19% vs. 44% in the endoscopy group [6].

Alternative Techniques

While the TIPS procedure has an up to 97% technical success rate in experienced hands, the orientation of the liver, right portal vein, and right hepatic vein as a result of cirrhosis and ascites can make TIPS challenging. Thrombus within the hepatic or portal veins can further complicate the procedure. A "reverse TIPS" can be performed by using an ultrasound-guided percutaneous puncture through the portal vein into the hepatic vein. A wire is then snared from a neck access, and TIPS stent graft deployment can be performed in a conventional manner.

Intravenous ultrasound (IVUS) can be used in the creation of a DIPS (direct intracaval portosystemic shunt). IVUS can guide needle puncture from the intrahepatic IVC into the portal vein. Primary patency following DIPS was measured at 100% with a follow-up range of 2 days to 30 months (mean 256 days) [7]. IVUS can also assist in portal access using conventional access from the right hepatic vein.

In the past, portal vein thrombus (either acute or chronic) was considered a contraindication to

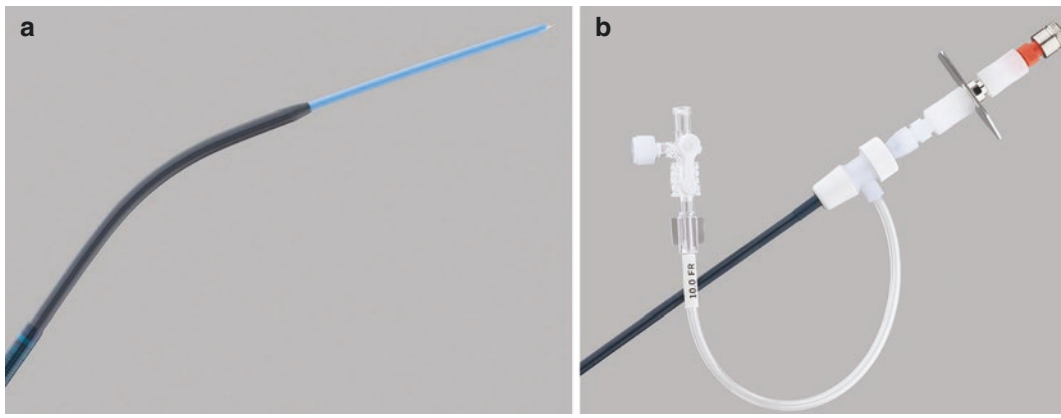

Fig. 25.2 (**a**) The Colapinto needle from the Rosch-Uchida Transjugular Liver Access Set (RUPS) from Cook Medical USA used for transjugular liver access for both diagnostic and interventional purposes. Note the curved end of the needle and smaller diameter in the event that multiple attempts at access are necessary. (**b**) Directional hub on the RUPS access sheath used to direct the needle anteriorly in the event that access is from the right hepatic vein or posteriorly if access is from the middle hepatic vein. (Images courtesy of Cook Medical USA)

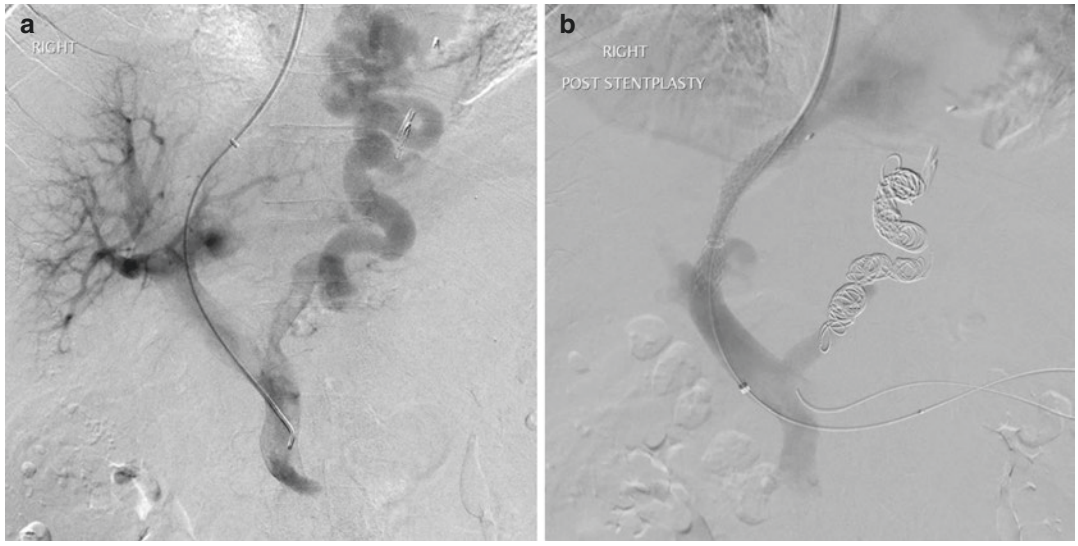

Fig. 25.3 (**a**) Demonstrates transhepatic portal access and a large gastroesophageal varix. Endoscopically placed clips are also noted; however, the varix remains widely patent. (**b**) Image following the complete endovascular coil embolization of the varix and placement of the Viatorr stent

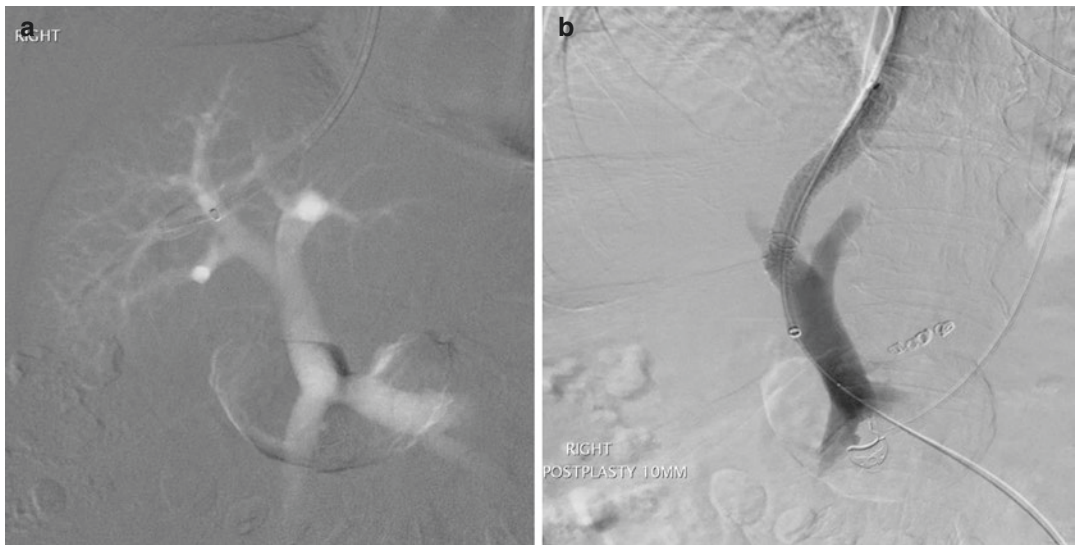

Fig. 25.4 (**a**) TIPS balloon-occluded CO_2 portovenogram is performed from the right hepatic vein with a Fogarty balloon and gentle CO_2 injection. A clear target of the "undivided right portal vein" is shown. (**b**) Same patient following TIPS placement and variceal embolization

TIPS. In the case of chronic portal vein thrombus, crossing a fibrotic cap can be difficult using hydrophilic wires and steerable catheters. Approaching the occlusion from a percutaneous access to the splenic vein can facilitate portal vein recanalization and TIPS creation by snaring the splenic access from the neck.

Acute mesenteric ischemia and infarction have mortality rates ranging from 15 to 50%. 5–15% of all cases of mesenteric ischemia are

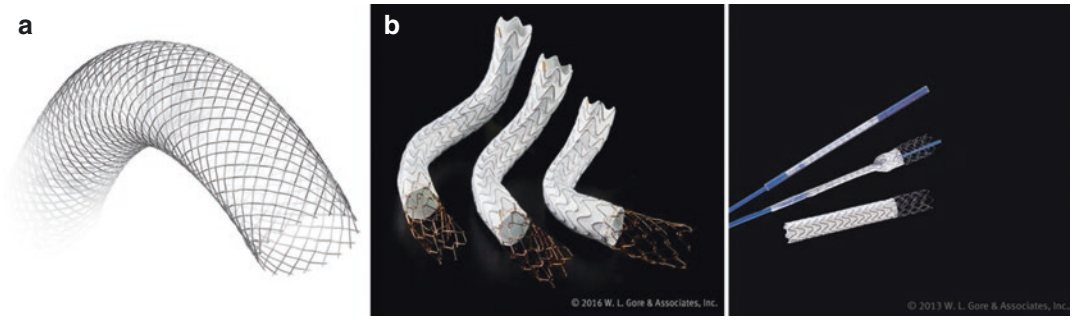

Fig. 25.5 (**a**) (above) The bare metal Boston Scientific Wallstent. (Images courtesy Boston Scientific USA). (**b**) (below) Various lengths of the Gore Viatorr with both a covered endoprosthesis and bare metal component and the deployment catheter. (Images courtesy of Gore USA)

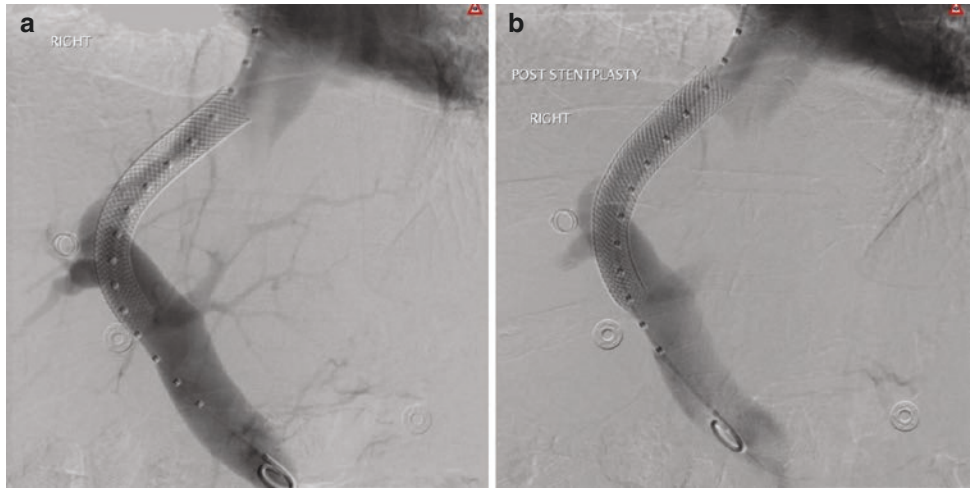

Fig. 25.6 (**a**) A 56-year-old male with alcoholic cirrhosis and refractory ascites. When the patient initially had his TIPS placed, his ascites resolved; however 6 months later, he again developed ascites which prompted a Doppler ultrasound demonstrating elevated velocities within the TIPS. Venography performed (left) demonstrates severe narrowing of the parenchymal component of the stent. The stenosis did not respond to simple balloon angioplasty. (**b**) Venographic images following the deployment of a Viabahn-covered stent within the parenchymal tract and complete resolution of the stenosis and revision of the TIPS

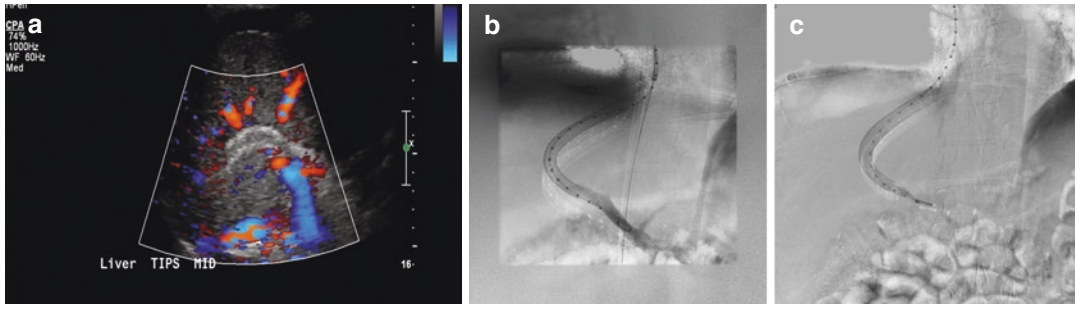

Fig. 25.7 (**a**) Color Doppler ultrasound of the TIPS postoperative day 1 without evidence of intrinsic flow within the TIPS. (**b**) Pigtail venography shows contrast refluxing into the portal vein as a result of complete thrombosis. (**c**) A Viabahn-covered stent was deployed within the parenchymal tract and contrast is seen flowing freely into the right atrium

the result of mesenteric vein thrombosis [8–11]. In the setting of portal mesenteric thrombus with continued risk of infarction and concomitant clinical decline despite systemic anticoagulation, transjugular intrahepatic portosystemic access can be used to thrombolyse the portal mesenteric system with TIPS deployment the following day. This technique can be associated with complication rates as high as 60%, but in many cases bowel resection can be avoided [12].

Esophageal Variceal Hemorrhage

The most lethal consequence of portal hypertension is esophageal variceal hemorrhage with the mortality rate within the first 2 years of the initial bleed ranging between 24% and 49% [13–18]. TIPS is considerably more successful than endoscopic therapy at preventing rebleeding (19% rebleeding in the TIPS group vs. 47% in the endoscopic therapy group). In the past, there was a belief that TIPS alone was sufficient for the treatment of acute variceal hemorrhage. Embolization at the time of TIPS has been shown to significantly reduce the rate of rebleeding versus TIPS alone (freedom from rebleed at 4 years 81% vs. 53%, respectively) [19]. A study performed by Pagan et al. challenged the use of TIPS as rescue therapy in patients with advanced liver disease and acute variceal hemorrhage. Child-Pugh B and C patients with active bleeding were randomized to vasoactive drugs with endoscopic therapy and rescue TIPS if necessary or early TIPS within 72 hours. The early TIPS groups had significantly fewer rebleeds, fewer deaths, and no difference in adverse events. Conversely, 57% of the patients in the control group that underwent rescue TIPS died [20]. It deserves mentioning that TIPS has comparable rates of encephalopathy when compared with surgical shunts.

TIPS and Hepatic Encephalopathy

While poorly understood, the postulated pathway upon which post TIPS encephalopathy develops is believed to be related to an increase in the systemic intestinally nitrogenous compounds that lack detoxification as a result of the shunt and a decrease in portal perfusion of the liver [21–25]. Following TIPS, the incidence of encephalopathy can increase as a result of increased dietary protein, other GI bleeding, sepsis, electrolyte abnormalities, or psychoactive drugs. Encephalopathy can be treated conservatively with high-fiber/protein-restricted diets (0.5 mg of protein per kilogram), with antibiotics like metronidazole or neomycin, or with zinc supplementation [26].

Hepatic encephalopathy is recognized as a complication in patients following TIPS and can occur 5–35% of the time [27]. In the majority of cases, post TIPS encephalopathy is controlled with the combination of rifaximin and lactulose. 3–7% of the time, post TIPS hepatic encephalopathy is refractory to medical and diet management and requires additional interventional management to reduce flow through the shunt [21]. Several techniques have been described for TIPS reduction including using a suture-constrained stent, deploying a stent or embolic material beside a second stent within a stent with external compression to narrow the lumen diameter, or complete embolization of a TIPS using an occlusion balloon or vascular plug or detachable coil. Gore USA has developed a controlled expansion Viatorr to control the diameter of the TIPS in a more sequential fashion. Typically, the Viatorr legacy endoprosthesis can reach its fully expanded diameter within 6 weeks despite the balloon-dilated diameter selected. The Viatorr with controlled expansion expands less than an additional 0.25 mm from its desired diameter following implantation.

Failed endoscopic therapy in the treatment of bleeding gastroesophageal varices with concomitant uncontrolled encephalopathy, severe liver failure, or technically unfeasible TIPS creation creates a complicated clinical scenario. Some studies suggest these patients can be treated with percutaneous transhepatic variceal embolization (PVTE) with partial splenic embolization (PSE) [28]. The embolization of esophageal varices without portal decompression with TIPS leads to an increase in portal pressures and as a result an increase in rebleeding rates and encephalopathy. In patients with cirrhosis and portal hypertension, a range of

60–70% of portal flow comes from the splenic vein [29]. Selective splenic infarction of 50–75% with splenic artery embolization leads to an overall decrease in portal hypertension, lower rebleeding rates, and fewer cases of encephalopathy [28].

Gastric and Parastomal Varices

Stomal or parastomal varices are associated with ileostomies and colostomies and often occur in patients with portal hypertension. Stomal variceal bleeding are uncommon, can be lethal, but in many cases can be controlled with manual compression. Manual compression is successful in focal bleeds but less helpful in diffuse high volume oozing, which occurs with those caused by portal hypertension. Endoscopy is typically only required when the culprit bleeding vein is not visible on the surface. As a result of the cirrhotic change within the liver, hepatofugal flow results in the afferent feeder from a branch of the superior mesenteric vein and the efferent branch typically draining into abdominal wall systemic venous branches that eventually drain into systemic iliofemoral branches [30].

Surgical or endoscopic therapies for bleeding stomal varices are uncommon. TIPS can be worthwhile in the treatment of bleeding stomal varices but in the long run can have a rebleed rate of 21–37% [31–33]. Coil embolization can be performed but should never involve submucosal veins since erosion can occur and delay healing. The most worthwhile techniques to control bleeding stomal varices involve the use of transvenous sclerosant obliteration using percutaneous access to portal branches within the liver, retrograde access through the systemic venous system, or using direct puncture of the varices with ultrasound guidance.

Gastric varices occur in 20–30% of patients with portal hypertension and typically have more lethal consequences as a result of higher blood volumes and flow rates with bleeding incidence as high as 25% [34, 35]. In addition, gastric varices tend to bleed at lower portosystemic gradients.

Historically it was believed that following the diagnosis of bleeding gastric varices by endoscopy, gastric varices could be decompressed with the creation of a TIPS. However, it has been shown that in 90% of cases, gastric varices are initially controlled with TIPS with rebleeding rates ranging between 13% and 53% [36, 37]. Several theories exist concerning why TIPS can be unsuccessful at treating isolated gastric varices. Importantly, Saad et al. demonstrated 0% rebleeding rates at 24 months with combined therapy using TIPS and retrograde obliteration [38]. The first published paper on balloon retrograde total obliteration (BRTO) was by Olson et al. in 1984 [39]. BRTO is performed via an internal jugular or femoral vein puncture and catheterization of the left renal vein and subsequently access to the gastrorenal shunt. A balloon is inflated at the base of the shunt to avoid reflux into the systemic venous circulation. Initially ethanolamine oleate was used, but it can cause hemolysis, hemoglobinuria, and renal tubular injury. More commonly in the United States, 3% sodium tetradecyl sulfate (Sotradecol, Angiodynamics) or polidocanol (Asclera, Merz) foam is deployed. Absolute alcohol or cyanoacrylate can also be used. BRTO requires leaving the occlusion balloon inflated for 4–24 hours to allow sclerosant dwell time. Additional described techniques include percutaneous transhepatic obliteration (PTO) also termed balloon-occluded antegrade total obliteration (BATO), coil-assisted retrograde total obliteration (CARTO), and plug-assisted retrograde total obliteration (PARTO). Occasionally, procedures can be combined using BATO technique from the portal side and BRTO from the systemic side. The goal for all of these procedures is to achieve stasis within the varices without the embolic agent entering the portal or systemic circulation.

The technical success rate of percutaneous variceal obliteration ranges from 79% to 100% [40–54]. The effectiveness of controlling active gastric variceal bleeding ranges between 91% and 100% [40, 44]. Gastric variceal obliteration has a tendency to aggravate non-gastric varices by increasing portal pressures with esophageal variceal aggravation rates at 3 years ranging from 45% to 91% [42, 48, 50, 55]. The gastric rebleed rate after successful BRTO ranges from 3.2% to

8.7%, while the global variceal rebleed rates were 19–31% [40, 43, 56].

Gastric variceal obliteration can result in resolution of encephalopathy and preservation of liver function but at the same time can aggravate global varices and ascites [44, 50, 51, 57, 58]. Overall, gastric variceal obliteration is effective, safe, and gaining popularity as a tool in the treatment of gastrointestinal bleeds as a result of portal hypertension (Figs. 25.8 and 25.9).

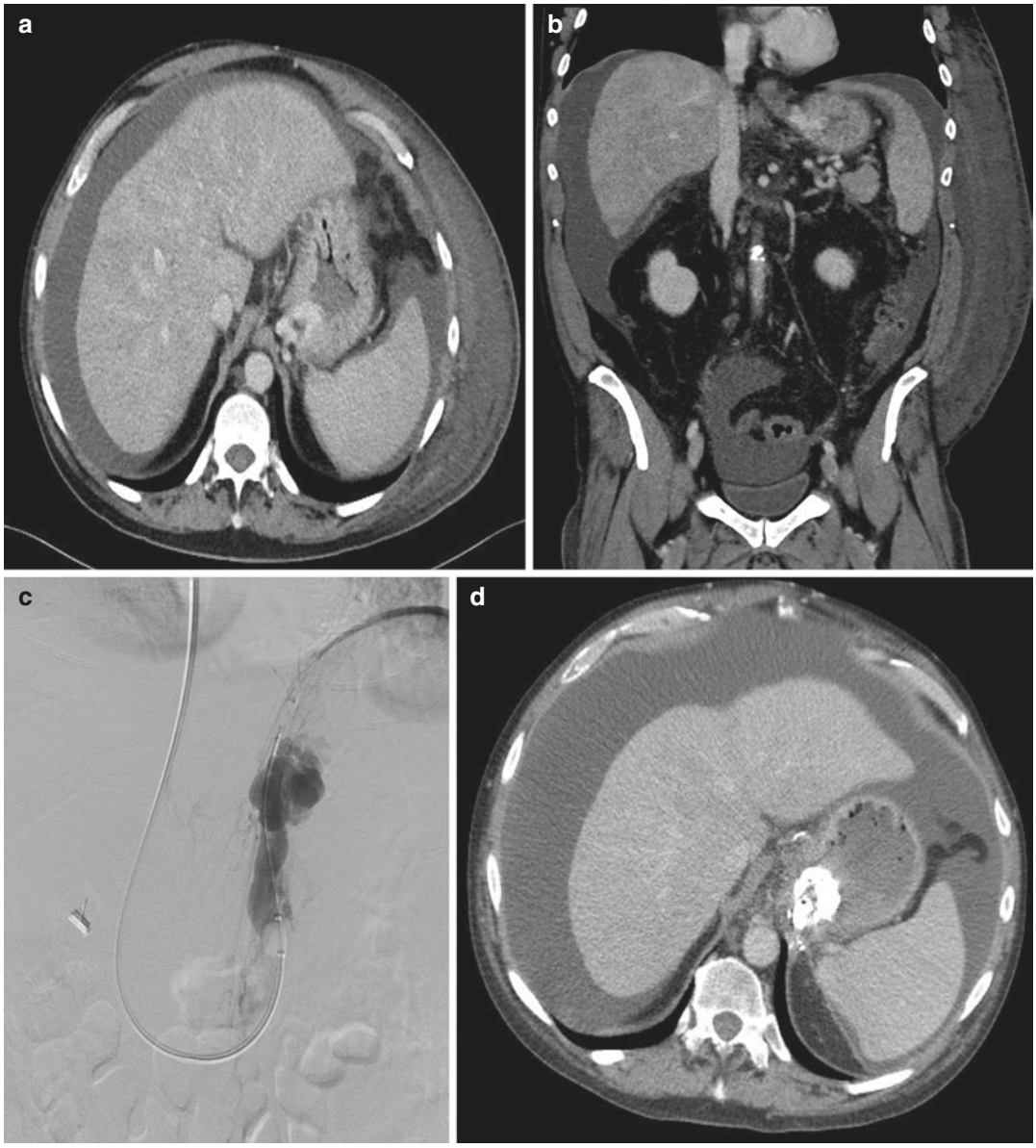

Fig. 25.8 (**a**, **b**) Axial and coronal CT scans of the abdomen demonstrate large gastric varices protruding into the lumen of the stomach in a 59-year-old male with a GI bleed that could not be controlled endoscopically. (**c**) Access to the gastric varix from a right internal jugular vein puncture and catheterization of the varix through the left renal vein. An occlusion balloon is inflated following the injection of Lipiodol and 3% Sotradecol to keep the sclerosing agent form entering the systemic system. (**d**) CT images following BRTO demonstrate complete occlusion of the varices. The patient was discharged from the hospital 3 days later

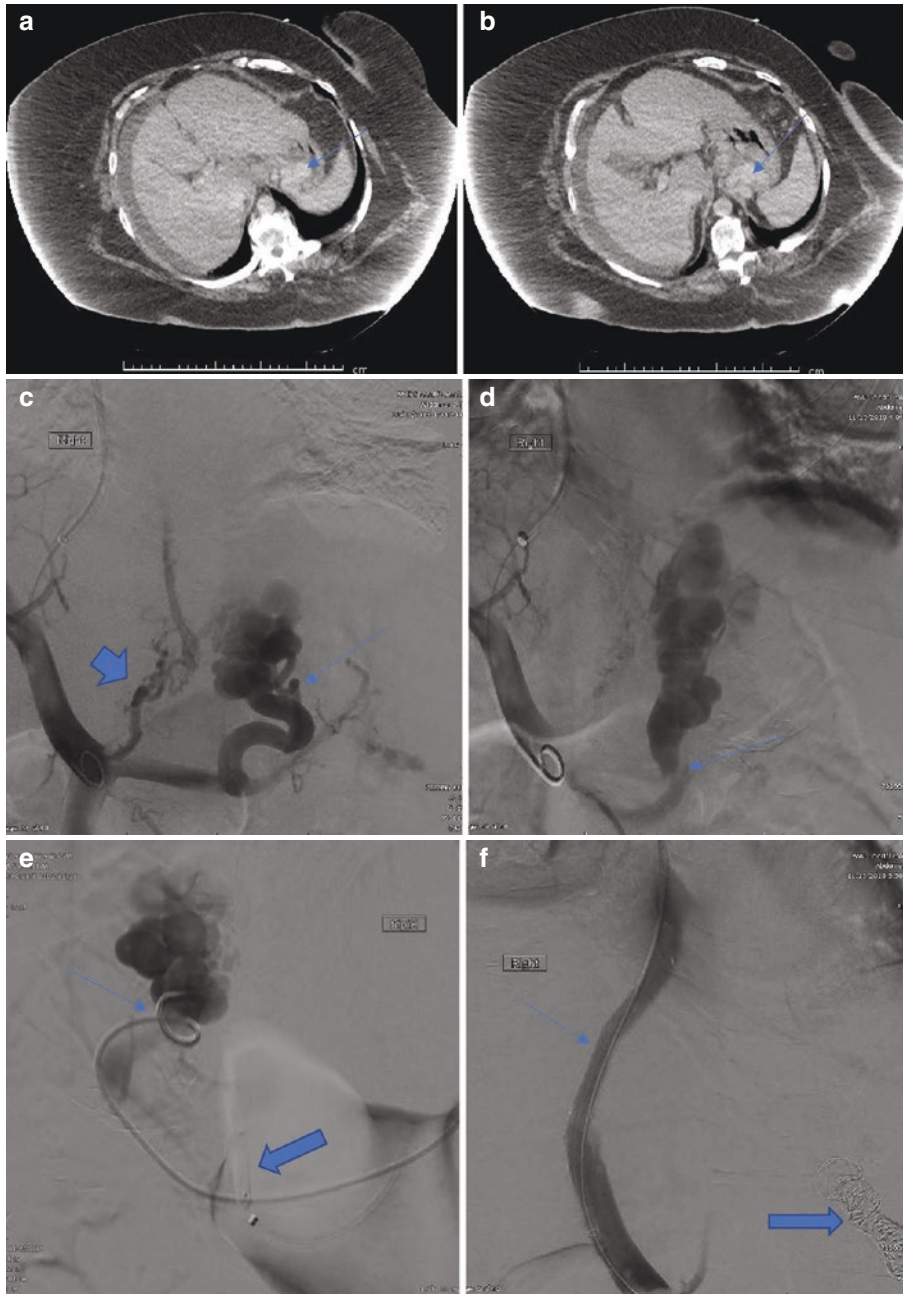

Fig. 25.9 (**a**, **b**) Demonstrate large varices (blue arrows) within the stomach with a patent splenic vein in a patient with a history of an upper GI bleed and NASH. (**c**) Angiographic images demonstrate the gastric varix (small blue arrow) filling from the splenic vein following transhepatic portal access and an esophageal varix (large blue arrow) and in (**d**) emptying of the varix into the systemic venous supply through the left renal vein on delayed images (blue arrow). (**e**) A second right internal jugular vein access was obtained, and an occlusion balloon (large blue arrow) was placed in the systemic side of the gastric varix with a catheter placed in the portal side of the varix for embolization. (**f**) Completion images demonstrating a patent TIPS (small blue arrow) with a combination of coils and 3% Sotradecol within the varix (large blue arrow). The occlusion balloon has been removed, and the esophageal varix is no longer identified. The patient was moved from the ICU to a general medical floor the next day

Conclusion

TIPS continues to be an important tool in the management of the complications of portal hypertension and specifically potentially lethal GI bleeds. New techniques including DIPS, BRTO, PTO, and CARTO are also important in patients with gastric varices which tend to bleed more or complicated hepatobiliary anatomy. TIPS continues to demonstrate low procedural complication rates, low rebleeding rates, low rates of unmanageable encephalopathy, and excellent patency rates. A majority of patients at the author's institution still receive TIPS despite endoscopic control of esophageal varices in the acute phase given the almost 50% rate of endoscopic rebleeding and the survival benefit of performing TIPS in this patient population.

Gastric varices as a result of liver disease also represent a complicated disease process. While controversial, the treatment of gastric varices in many cases requires both TIPS and BRTO. Most GI bleed patients with portal hypertension are complicated, unstable patients that require a multidisciplinary, team approach to optimize survival outcomes. Interventional radiology remains an important component of the team that should be implemented as early as possible in the management of these patients. In the situation where TIPS is not available at the hospital, endoscopy can be used to temporarily stabilize the bleeding to allow transfer to an institution where TIPS is more commonly performed.

References

1. Copelan A, Kapoor B, Sands M. Transjugular intrahepatic portosystemic shunt: indications, contraindications, and patient work-up. Semin Intervent Radiol. 2014;31:235–42.
2. Holland LL, Brooks JP. Toward Rational Fresh Frozen Plasma Transfusion: The effect of plasma transfusion on coagulation test results. American Journal of Clinical Pathology. 2006;126:133–39.
3. Gaba R. Transjugular intrahepatic portosystemic shunt creation with embolization or obliteration for variceal bleeding. Tech Vasc Interventional Rad. 2016;19:21–35.
4. Berzigotti A, Seijo S, Reverter E, Bosch J. Assessing portal hypertension in liver diseases. Expert Rev Gastroenterol Hepatol. 2013;7(2):141–55.
5. Garcia-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE, Glickman M. Portal pressure, presence of gastroesophageal varices and variceal bleeding. Hepatology. 1985;5(3):419–24.
6. Zheng M, Chen Y, Bai J, et al. Transjugular intrahepatic portosystemic shunt versus endoscopic therapy in the secondary prophylaxis of variceal rebleeding in cirrhotic patients: meta-analysis update. J Clin Gastroenterol. 2008;42(5):507–16.
7. Petersen BD, Clark WI. Direct intracaval portosystemic shunts. Tech Vasc Interv Radiol. 2008;4:230–4.
8. Alam H, Kim D, Provido H, Kirkpatrick J. Portal vein thrombosis in the adult: surgical implications in an era of dynamic imaging. Am Surg. 1997;63:681–4.
9. Valla D, Condat B. Portal vein thrombosis in adults: pathophysiology, pathogenesis and management. J Hepatol. 2000;32:865–71.
10. Condat B, Pessione F, Hillaire S, et al. Current outcome of portal vein thrombosis in adults: risk and benefit of anticoagulant therapy. Gastroenterology. 2001;120:490–7.
11. Janssen HLA. Changing perspectives in portal vein thrombosis. Scand J Gastroenterol. 2000; 232(suppl):69–73.
12. Hollingshead M, et al. Transcatheter thrombolytic therapy for acute mesenteric and portal vein thrombosis. J Vasc Interv Radiol. 2005;16(5):651–61.
13. Pascal JP, Cales P, Multicentre Study Group. Propranolol in the prevention of first upper gastrointestinal tract haemorrhage in patients with cirrhosis of the liver and oesophageal varices. N Engl J Med. 1987;317:856–61.
14. Ideo I, Bellati G, Fesce E, Grimoldi D. Nadolol can prevent the first gastrointestinal bleeding in cirrhotics: a prospective randomised study. Hepatology. 1988;8:6–9.
15. Lebrec D, Poynard T, Capron JP, Hillon P, Geoffrey P, Roulot D, Chaput JC, et al. Nadolol for prophylaxis of gastrointestinal bleeding in patients with cirrhosis. A randomised trial. J Hepatol. 1988;7:118–25.
16. Italian Multicentre Project for Propranolol in the Prevention of Bleeding. Propranolol prevents first gastrointestinal bleed in non-ascitic cirrhotic patients. Final report of a multicentre randomised trial. J Hepatol. 1989;9:75–83.
17. Conn HO, Grace ND, Bosch J, Groszmann RJ, Rodes J, Wright SC, Matloff DS, et al. Propranolol in the prevention of the first haemorrhage from oesophagogastric varices. A multicenter randomised clinical trial. Hepatology. 1991;13:902–12.
18. D'Amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: a meta analytical review. Hepatology. 1995;22:332–53.
19. Tesdal IK, Filser T, Weiss C, Holm E, Dueber C, Jaschke W. Transjugular intrahepatic portosystemic

shunts: adjunctive embolotherapy of gastroesophageal collateral vessels in the prevention of variceal rebleeding. Radiology. 2005;236(1):360–7.
20. García-Pagán JC, Caca K, Bureau C, Early TIPS (Transjugular Intrahepatic Portosystemic Shunt) Cooperative Study Group, et al. Early use of TIPS in patients with cirrhosis and variceal bleeding. N Engl J Med. 2010;362(25):2370–9.
21. Forauer AR, McLean GK. Transjugular intrahepatic portosystemic shunt constraining stent for the treatment of refractory postprocedural encephalopathy: a simple design utilizing a Palmaz stent and Wallstent. J Vasc Interv Radiol. 1998;9:443–6.
22. Pomier-Layrargues G. TIPS and hepatic encephalopathy. Semin Liver Dis. 1996;16:315–20.
23. Sanyal AJ, Freedman AM, Shiffman ML, Purdum PP, Luketic VA, Cheatham AK. Portosystemic encephalopathy after transjugular intrahepatic portosystemic shunt: results of a prospective controlled study. Hepatology. 1994;20:46–55.
24. Garcia N Jr, Sanyal AJ. Medical management of complications secondary to portal hypertension. In: Patel NH, Haskal ZJ, Kerlan Jr RK, editors. SCVIR syllabus volume XI: portal hypertension—diagnosis and interventions. 2nd ed. Fairfax: Society of Cardiovascular and Interventional Radiology; 2001. p. 47–62.
25. Madoff D, Wallace JM, Kamran A, Saxon RR. TIPS-related hepatic encephalopathy: management options with novel endovascular techniques. Radiographics. 2004;24:21–37.
26. Van der Rijt CC, Schalm SW, Schat H, et al. Overt hepatic encephalopathy precipitated by zinc deficiency. Gastroenterology. 1991;100:1114–8.
27. Zuckerman DA, Darcy MD, Bocchini TP, Hildebolt CF. Encephalopathy after transjugular intrahepatic portosystemic shunting: analysis of incidence and potential risk factors. AJR Am J Roentgenol. 1997;169:1727–31.
28. Duan XH, et al. Comparison of Percutaneous Transhepatic Variceal Embolization (PTVE) followed by partial splenic embolization versus ptve alone for the treatment of acute esophagogastric variceal massive hemorrhage. J Vasc Intervent Radiol. 2014;25(12):1858–65.
29. Xu RY, Liu B, Lin N. Therapeutic effects of endoscopic variceal ligation combined with partial splenic embolization for portal hypertension. World J Gastroenterol. 2004;10:1072–4.
30. Saad WE, Lippert A, Saad NE. Ectopic varices: anatomical classification, hemodynamic classification, and hemodynamic-based management. Tech Vasc Interv Radiol. 2013;16(2):108–25.
31. Kocher N, Tripathy D, McAvoy NC, et al. Bleeding ectopic varices in cirrhosis: the role of transjugular intra-hepatic portosystemic stent shunts. Aliment Pharmacol Ther. 2008;28:294–303.
32. Hashimoto N, Akhoshi T, Yoshida D, et al. The efficacy of balloon-occluded retrograde transvenous obliteration on small intestinal variceal bleeding. Surgery. 2010;148:145–50.
33. Vidal V, Joly L, Perreault P, et al. Usefulness of transjugular intrahepatic portosystemic shunt in the management of bleeding ectopic varices in cirrhotic patients. Cardiovasc Intervent Radiol. 2006;29:216–9.
34. Watanabe K, Kimura K, Matsutani S, Ohto M, Okuda K. Portal hemodynamics in patients with gastric varices. Gastroenterol. 1988;95:434–40.
35. Sarin SK, Lahori D, Saxena SP, Murthy NS, Makwana UK. Prevalence, classification, and natural history of gastric varices: a long-term follow up study in 568 portal hypertension patients. Hepatology. 1992;16:1343–9.
36. Saad WE, Darcy MD. Transjugular intrahepatic portosystemic shunt (TIPS) versus balloon-occluded retrograde transvenous obliteration (BRTO) for the management of gastric varices. Semin Intervent Radiol. 2011;28:339–49.
37. Saad WE. Vascular anatomy and the morphologic and hemodynamic classifications of gastric varices and spontaneous portosystemic shunts relevant to the BRTO procedure. Tech Vasc Interv Radiol. 2013;16:60–100.
38. Saad WE, Wagner CC, Lippert A, et al. Protective value of TIPS against the development of hydrothorax/ascites and upper gastrointestinal bleeding after balloon-occluded retrograde transvenous obliteration (BRTO). Am J Gastroenterol. 2013;108:1612–9.
39. Olson E, Yune HY, Klatte EC. Transrenal-vein reflux ethanol sclerosis of gastroesophageal varices. AJR Am J Roentgenol. 1984;143(3):627–8.
40. Kitamoto M, Imamura M, Kamada K, et al. Balloon-occluded retrograde transvenous obliteration of gastric fundal varices with hemorrhage. AJR Am J Roentgenol. 2002;178(5):1167–74.
41. Ninoi T, Nakamura K, Kaminou T, et al. TIPS versus transcatheter sclerotherapy for gastric varices. AJR Am J Roentgenol. 2004;183(2):369–76.
42. Ninoi T, Nishida N, Kaminou T, et al. Balloon-occluded retrograde transvenous obliteration of gastric varices with gastrorenal shunt: long-term follow-up in 78 patients. AJR Am J Roentgenol. 2005;184(4):1340–6.
43. Akahoshi T, Hashizume M, Tomikawa M, et al. Long-term results of balloon-occluded retrograde transvenous obliteration for gastric variceal bleeding and risky gastric varices: a 10-year experience. J Gastroenterol Hepatol. 2008;23(11):1702–9.
44. Fukuda T, Hirota S, Sugimura K. Long-term results of balloonoccluded retrograde transvenous obliteration for the treatment of gastric varices and hepatic encephalopathy. J Vasc Interv Radiol. 2001;12(3):327–36.
45. Sonomura T, Sato M, Kishi K, et al. Balloon-occluded retrograde transvenous obliteration for gastric varices: a feasibility study. Cardiovasc Intervent Radiol. 1998;21(1):27–30.
46. Kiyosue H, Matsumoto S, Onishi R, et al. Balloon-occluded retrograde transvenous obliteration (B-RTO) for gastric varices: therapeutic results and problems

[in Japanese]. Nippon Igaku Hoshasen Gakkai Zasshi. 1999;59(1):12–9.
47. Koito K, Namieno T, Nagakawa T, Morita K. Balloon-occluded retrograde transvenous obliteration for gastric varices with gastrorenal or gastrocaval collaterals. AJR Am J Roentgenol. 1996;167(5):1317–20.
48. Chikamori F, Kuniyoshi N, Kawashima T, Takase Y. Gastric varices with gastrorenal shunt: combined therapy using transjugular retrograde obliteration and partial splenic embolization. AJR Am J Roentgenol. 2008;191(2):555–9.
49. Kumamoto M, Toyonaga A, Inoue H, et al. Long-term results of balloon-occluded retrograde transvenous obliteration for gastric fundal varices: hepatic deterioration links to portosystemic shunt syndrome. J Gastroenterol Hepatol. 2010;25(6):1129–35.
50. Chikamori F, Kuniyoshi N, Shibuya S, Takase Y. Eight years of experience with transjugular retrograde obliteration for gastric varices with gastrorenal shunts. Surgery. 2001;129(4):414–20.
51. Hirota S, Matsumoto S, Tomita M, Sako M, Kono M. Retrograde transvenous obliteration of gastric varices. Radiology. 1999;211(2):349–56.
52. Shimoda R, Horiuchi K, Hagiwara S, et al. Short-term complications of retrograde transvenous obliteration of gastric varices in patients with portal hypertension: effects of obliteration of major portosystemic shunts. Abdom Imaging. 2005;30(3):306–13.
53. Takuma Y, Nouso K, Makino Y, Saito S, Shiratori Y. Prophylactic balloon-occluded retrograde transvenous obliteration for gastric varices in compensated cirrhosis. Clin Gastroenterol Hepatol. 2005;3(12):1245–52.
54. Arai H, Abe T, Takagi H, Mori M. Efficacy of balloon-occluded retrograde transvenous obliteration, percutaneous transhepatic obliteration and combined techniques for the management of gastric fundal varices. World J Gastroenterol. 2006;12(24):3866–73.
55. Arai H, Abe T, Shimoda R, Takagi H, Yamada T, Mori M. Emergency balloon-occluded retrograde transvenous obliteration for gastric varices. J Gastroenterol. 2005;40(10):964–71.
56. Cho SK, Shin SW, Lee IH, et al. Balloon-occluded retrograde transvenous obliteration of gastric varices: outcomes and complications in 49 patients. AJR Am J Roentgenol. 2007;189(6):W365–72.
57. Chikamori F, Kuniyoshi N, Shibuya S, Takase Y. Transjugular retrograde obliteration for chronic portosystemic encephalopathy. Abdom Imaging. 2000;25(6):567–71.
58. Park KS, Kim YH, Choi JS, et al. Therapeutic efficacy of balloon-occluded retrograde transvenous obliteration in patients with gastric variceal bleeding [in Korean]. Korean J Gastroenterol. 2006;47(5):370–8.

26

Bleeding Cirrhotic Patients: Endoscopic Therapy

John H. Holden and Umer A. Bhatti

Overview

Gastrointestinal (GI) hemorrhage is a serious medical condition commonly encountered in patients with cirrhosis. The etiology of bleeding is often grouped into causes proximal to the ligament of Treitz (upper GI bleed) or beyond it (lower GI bleed). Patients with cirrhosis are significantly more likely to present with upper GI bleed, which carries a higher risk of mortality [1]. Gastrointestinal hemorrhage in cirrhosis is often driven by portal hypertension, though it may arise from other causes [2, 3]. The goal of therapy is to prevent and correct shock by providing resuscitative and supportive measures alongside medical, interventional radiologic, and endoscopic therapies to prevent further bleeding and complications of bleeding. Medical team members must be able to recognize and treat a variety of presentations of gastrointestinal hemorrhage in the cirrhotic patient. This chapter will provide an overview of general principles of evaluation and treatment, with a focus on the endoscopic management of upper GI bleeding, particularly bleeding due to portal hypertension.

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Initial Approach

Assessment

Cirrhotic patients who present with suspected or overt bleeding should immediately be assessed for hemodynamic stability and need for resuscitation (Fig. 26.1). Most will need to be admitted for close hemodynamic monitoring and should be considered at high risk for decompensation. Patients with hemodynamic instability, active bleeding, or altered mental status should be cared for in an intensive care unit [4]. Reliable intravenous (IV) access, preferably with at least two large-bore (18 g or greater) IV cannulas, should be established. Alternatively, central venous access may be used. Patients should be made NPO. Close attention should be paid to the airway due to a high risk of aspiration. In patients with active hematemesis or altered mental status, elective intubation may be appropriate to reduce the risk of aspiration and facilitate endoscopy [5, 6]. Nasogastric tube placement and lavage may be considered, but is controversial. Although the presence of bright red blood can confirm the

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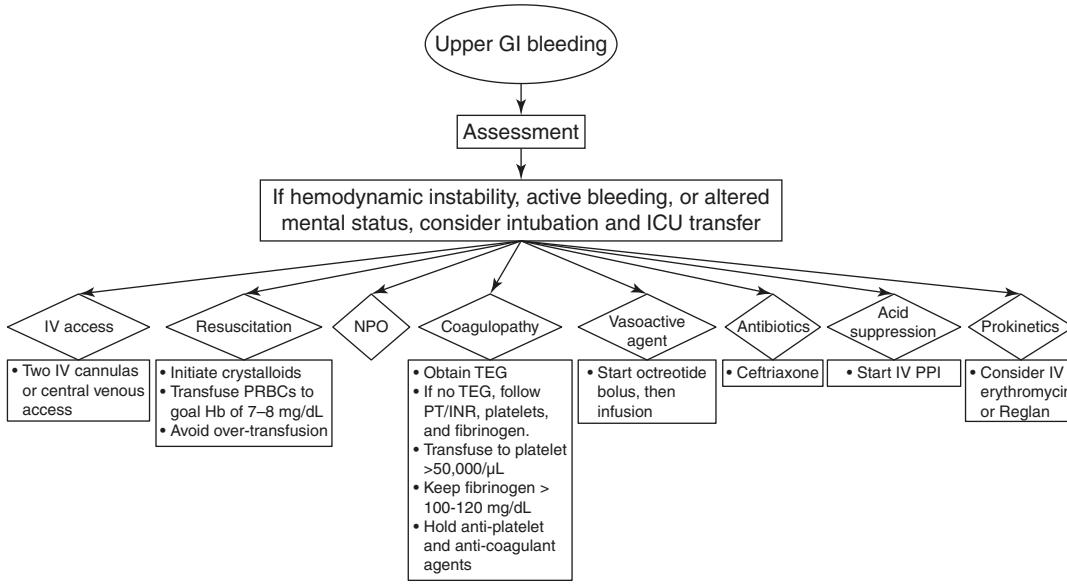

Fig. 26.1 Initial approach to suspected upper GI bleed in the cirrhotic patient

presence of an active upper GI bleed, a false-negative lavage can be seen in 15% of patients [7].

Fluid Resuscitation

Fluid resuscitation with crystalloids should be initiated with a goal of hemodynamic stability. Transfusion with packed red cells should be considered on an individual basis. Over-resuscitation and over-transfusion should be avoided as this may increase portal hypertension and worsen bleeding [2, 6]. A transfusion goal of 7–8 mg/dL is appropriate for most cirrhotic patients, though a higher threshold may be appropriate in patients with active cardiac or neurovascular disease [5, 6, 8].

Correction of Coagulopathy

The management of coagulopathy in the bleeding cirrhotic patient is critical to achieving hemostasis and patient stabilization. Patients with liver disease often demonstrate abnormalities of clotting parameters such as PT/INR and platelet count. However, diminished liver function may lead to both anticoagulant and procoagulant effects. Traditional measures of coagulation, particularly INR, often fail to capture a patient's bleeding risk [9]. Thromboelastography (TEG), when available, provides more reliable information and may be used to guide the transfusion of clotting factors and platelets [10]. Absent TEG, traditional parameters (PT/INR, platelet count, and fibrinogen) should be followed. Reflexive correction of an elevated INR with FFP or vitamin K should be avoided and should be administered on an individual basis [2, 11].

Patients with cirrhosis typically develop clinically significant thrombocytopenia due to hypersplenism, decreased thrombopoietin production, and immune-mediated factors [9]. The correlation between platelet number and bleeding risk is often poor [12]. As a result, reflex correction with platelet infusions should be avoided. However, a transfusion goal of 50,000/μL is appropriate in those with evidence of bleeding [9]. DDaVP should be considered in patients with evidence of uremia or severe renal disease.

Low fibrinogen levels and fibrinolysis are common in cirrhosis. Transfusion of cryoprecipitate either empirically or to maintain a fibrinogen level above 100–150 mg/dL should be initiated [9].

Attempts should be made to identify and mitigate the effects of antiplatelet and anticoagulant medications and to evaluate for other causes of coagulopathy such as renal dysfunction or infection. Consideration for advanced therapies, such as factor replacement, platelet growth factors, tranexamic acid, and aminocaproic acid may be considered in cases of severe or refractory bleeding in consultation with a hematologist.

Vasoactive Agents

Vasoactive agents should be initiated on presentation (prior to endoscopy) in all patients with suspected portal hypertensive-related hemorrhage. Vasoactive agents—octreotide, somatostatin, terlipressin, and vasopressin—reduce bleeding through the reduction of portal blood flow. Use of these agents improves control of hemorrhage and leads to lower patient morbidity and mortality [13, 14]. Once initiated, these therapies should be continued for 3–5 days following identification of a portal hypertensive bleeding source [6]. Local access dictates the choice of agent. Octreotide is the most commonly used agent in the United States [6].

Antibiotics

Up to 65% of patients with variceal bleeding develop bacterial infections [15, 16], including spontaneous bacterial peritonitis. Initiation of a prophylactic antibiotic has been shown to reduce mortality, rebleeding risk, and the development of infection in patients with cirrhosis and should be administered on presentation [15, 17–19]. Ceftriaxone is the preferred agent in the United States and is typically given for 7 days [6].

Acid Suppression

Acid suppressing therapy should be initiated in any patient suspected to have an upper GI bleed. The empiric use of IV proton pump inhibitors has been shown to decrease the need for therapeutic intervention at the time of upper endoscopy [20]. In patients with ulcer-related bleeding, PPI use also plays an important role in decreasing the risk of rebleeding and need for blood transfusions [21]. In patients with variceal bleeding, short-term PPI use has been shown to decrease the size of post-banding ulcers [22].

Prokinetics

A prokinetic agent such as erythromycin or metoclopramide may be used just prior to endoscopy to improve gastric visualization [23]. These agents should be reserved for situations where there is a high likelihood of impaired visualization (e.g., ongoing bleeding).

Etiology of Bleeding

Upper GI Bleed

Upper GI bleeding should be suspected in patients who present with hematemesis, melena, or—in the case of very brisk bleeds—hematochezia. In patients with cirrhosis, bleeding related to portal hypertension—from esophageal varices, gastric varices, or portal hypertensive gastropathy (PHG)—comprises the majority of upper GI bleeding. Bleeding may also occur from etiologies similar to those seen in the general population (Table 26.1). Variceal bleeding represents a medical emergency and has been associated with a 6-week mortality risk up to 20% [25]. Timely and effective resuscitation, medical intervention, and early endoscopic therapy have been shown to reduce this risk [26].

Lower GI Bleed

Lower GI bleeding should be suspected in patients with hematochezia or melena (following a negative upper endoscopy). Colonic and lower gastrointestinal bleeding comprise 15–20% of cases of bleeding in patients with cirrhosis [24]. Common etiologies of lower GI

Table 26.1 Common causes of GI bleeding in cirrhotic patients

Upper GI bleeding	80–85%
Esophageal varices	
Gastric varices	
Portal hypertensive gastropathy	
Peptic ulcer disease	
Esophagitis	
Mallory-Weiss tear	
Erosive gastropathy	
GAVE	
Other	
Lower GI bleeding	15–20%
Hemorrhoids	
Diverticulosis	
Arteriovenous malformations	
Ischemic/infection colitis	
Malignancy	
Rectal varices	
Portal colopathy	
Other	

Data from Chait [24] and Kalafateli et al. [3]

bleeding in cirrhotic patients include those seen frequently in the general population (Table 26.1). Management of these conditions is similar to that of patients without cirrhosis. Other etiologies, such as colorectal varices and portal colopathy, may also lead to bleeding.

Endoscopic Therapy

Variceal Bleeding

Endoscopy plays an essential role in the diagnosis and therapy of variceal bleeding. Following resuscitation and initial medical management, upper endoscopy should be performed urgently (within 12 hours of presentation) in cirrhotic patients suspected to have an upper GI bleed [2, 5, 6]. Variceal bleeding is diagnosed when one of the following is seen on endoscopy: active bleeding from a varix, signs of recent bleeding from a varix such as a "white nipple," or varices—accompanied by blood in the stomach—and no other identified bleeding source [27]. The treatment of variceal bleeding is largely dictated by the location of the varices found.

Esophageal Varices

Endoscopic variceal ligation (EVL), in which elastic bands are placed on varices (Figs. 26.2 and 26.3), is the preferred treatment for esophageal variceal bleeding. In the past, endoscopic sclerotherapy, in which a sclerosing agent[1] is injected

[1]Sclerosing agents include sodium tetradecyl sulfate,

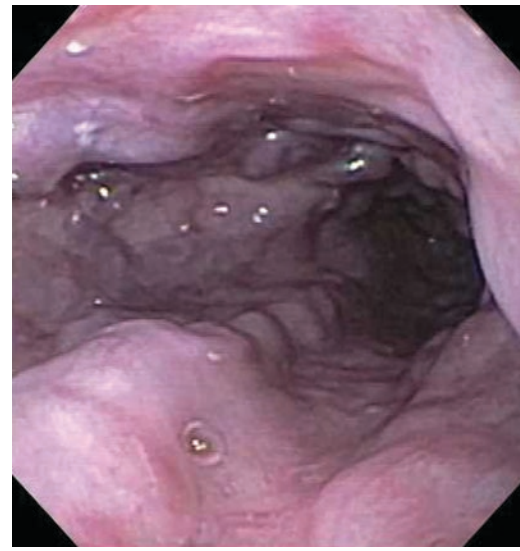

Fig. 26.2 Esophageal varices

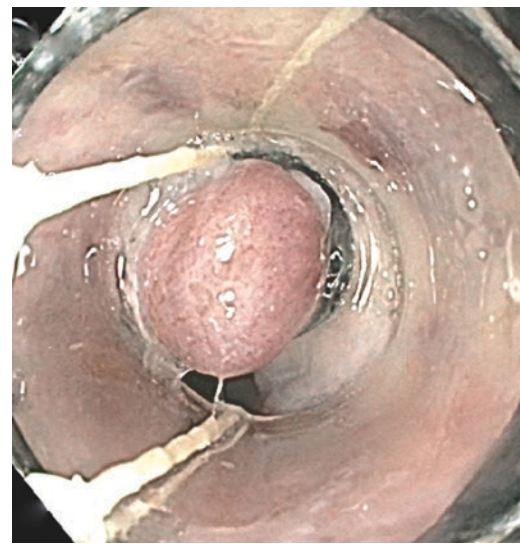

Fig. 26.3 Esophageal variceal ligation

into esophageal varices, was used to control bleeding. EVL is now preferred and has been shown to be effective, with lower rates of rebleeding, fewer complications, and lower mortality [28]. Following successful EVL, treatment with a nonselective beta-blocker should be considered to further reduce rebleeding risk [29]. After the initial EVL procedure, repeat EVL should be performed at 1- to 4-week intervals until variceal eradication is achieved. Routine endoscopic surveillance should follow at 3–6 months and at 6–12 months thereafter [2]. Early TIPS (within 72 hours of bleeding) may be considered in lieu of beta-blocker and serial banding in highly selected patients [30, 31].

Refractory Esophageal Variceal Bleeding

Medical and endoscopic therapy fails to achieve hemostasis in 10–20% of patients with variceal bleeding [2, 32]. In this setting, temporizing measures must be employed to prevent further decompensation and hemorrhagic shock while more definitive therapeutic modalities are considered. In the unstable patient, intubation (if not already done) and variceal tamponade should be considered.

Balloon tamponade, using a Minnesota or Sengstaken-Blakemore tube, is effective for the temporary control of refractory esophageal bleeding [33]. Due to the risk of esophageal injury, balloon tamponade should not exceed 24 hours [2, 5, 6]. Alternatively, limited data supports the use of self-expandable metal stents (SEMS) for esophageal variceal tamponade, with high rates of bleeding control [34, 35].

After successful stabilization of the patient, repeat endoscopy or transjugular intrahepatic portosystemic shunting (TIPS) should be performed (Fig. 26.4). TIPS therapy, using covered or uncovered endovascular stents, allows decompression of the portal system and is effective in the management of refractory variceal bleeding. Failure of repeat endoscopic therapy should prompt evaluation for TIPS placement [2, 5, 6]. Surgical portosystemic shunts are rarely used in the post-TIPS era and carry a high mortality risk [36].

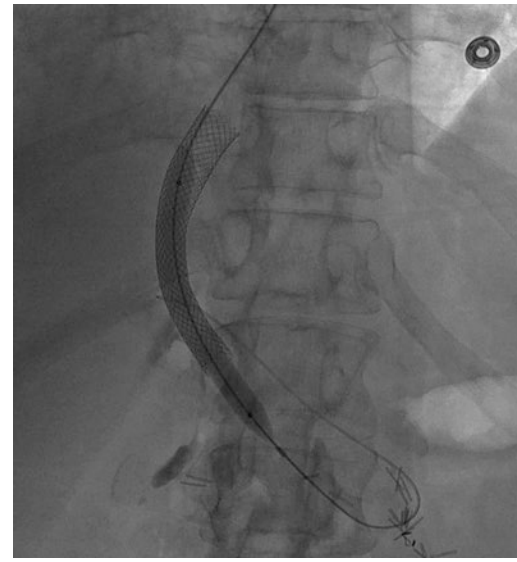

Fig. 26.4 TIPS

Gastric Varices

Endoscopic therapy for gastric varices (Fig. 26.5) is guided by the location of the varices within the stomach. Gastroesophageal varices (GOV) show continuity with esophageal varices and are further classified as GOV1 (which continue along the lesser curvature) or GOV2 (which extend into the gastric fundus). Isolated gastric varices (IGV) in the gastric fundus are termed IGV1, while those in other sites are termed IGV2 [37] (Fig. 26.6). Due to treatment complexity, therapy for gastric varices is best performed in a center with special endoscopic and radiologic expertise.

For bleeding gastric varices, gastric variceal obturation (GVO) with cyanoacrylate injection[2]

sodium morrhuate, polidocanol, ethanolamine oleate, and ethanol.

[2]Cyanoacrylate injection is not FDA approved, but is available at many tertiary centers in the United States. Injection may be performed with a standard upper endoscope or using endoscopic ultrasound.

(Figs. 26.7 and 26.8) should be considered first-line endoscopic therapy. For GOV1, GVO has shown decreased rebleeding rates when compared with EVL [38, 39]. EVL should only be used with small gastric varices (where the varix can be fully suctioned into the EVL device). Endoscopic sclerotherapy should be considered second-line endoscopic therapy for gastric varices [40]. TIPS is highly effective in the treatment of bleeding gastric varices [41]. For acute bleeding, endoscopic therapy (such as GVO) is often attempted first, with TIPS reserved for patients who fail medical and endoscopic therapy. Balloon-occluded retrograde transve-

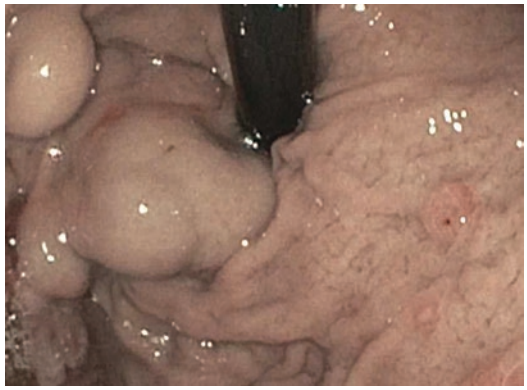

Fig. 26.5 Classification of gastric varices

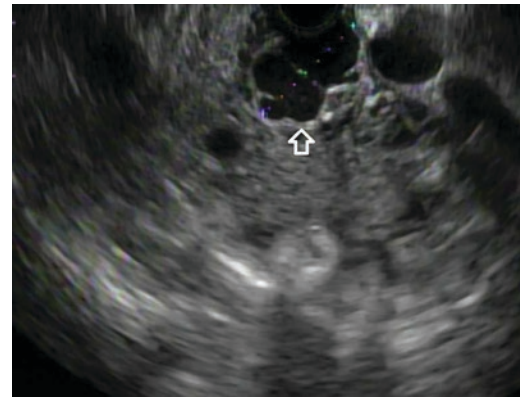

Fig. 26.7 Gastric varices on endoscopic ultrasound

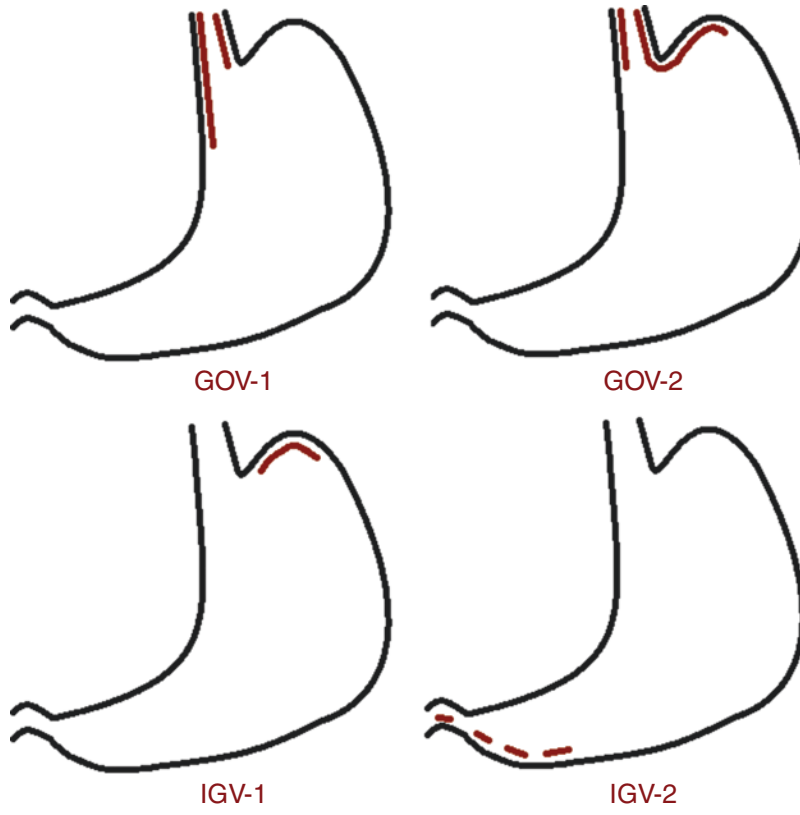

Fig. 26.6 Gastric varices

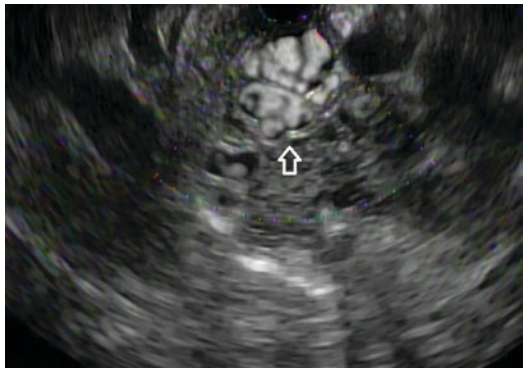

Fig. 26.8 Gastric varices following injection of cyanoacrylate

nous obliteration (BRTO) has also been used for bleeding gastric varices [42], but has not been compared to endoscopic intervention or TIPS in high-quality studies. All patients with IGV1 should be evaluated for the presence of splenic vein thrombus, as patients with IGV1 due to splenic thrombosis may benefit from surgical management, including splenectomy.

Following initial endoscopic intervention, patients with GOV1 should be treated with GVO or EVL and considered for a nonselective beta-blocker to reduce rebleeding risk [2]. After bleeding from GOV2 or IGV1, GVO or TIPS should be considered [43, 44].

Ectopic Varices

Bleeding from ectopic varices—varices in the small bowel, colon, or at stoma sites—is rare. Diagnosis and localization can be challenging. If lesions are endoscopically accessible, EVL (particularly in duodenal bleeding), sclerotherapy, endoscopic ultrasound-guided coil placement, and cyanoacrylate injections can be attempted. TIPS and BRTO may also be considered [2, 6, 45].

Portal Hypertensive Gastropathy

Portal hypertensive gastropathy occurs frequently in patients with portal hypertension and may lead

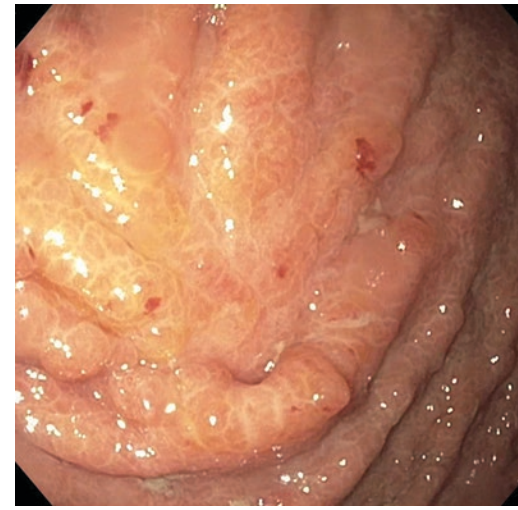

Fig. 26.9 Portal hypertensive gastropathy

to significant bleeding. Endoscopically, PHG is characterized by a mosaic-like or "snakeskin" appearance (Fig. 26.9) and is typically found in the gastric body and fundus. PHG may cause acute or chronic bleeding. Management of acute bleeding should center on medical therapies, such as vasoactive agents, to reduce portal hypertension [46]. Typically, endoscopic therapy does not play a therapeutic role. Once bleeding is controlled, a nonselective beta-blocker should be considered [47]. Patients with recurrent bleeding should be considered for TIPS to decompress the portal system [48].

Peptic Ulcer Disease

Peptic ulcer disease (PUD) is the most common cause of non-portal hypertensive-related bleeding in patients with cirrhosis (Fig. 26.10). The incidence of PUD and rebleeding from PUD is higher in cirrhotic patients than the general population [49], though management is similar. All patients should be started on IV PPI therapy empirically and undergo endoscopic evaluation as well evaluation and treatment of *Helicobacter pylori*. Combination endoscopic therapy with epinephrine injection and either thermal ablation or hemoclip

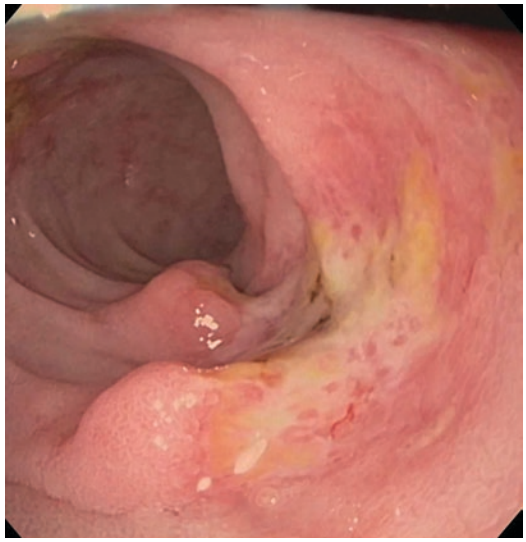

Fig. 26.10 Duodenal ulcer

placement is indicated if high-risk features, such as active bleeding or a visible vessel, are noted [50]. In patients with these high-risk features, IV PPI should be continued for 72 hours [50]. Otherwise, de-escalation to an oral PPI is appropriate [51]. Repeat upper endoscopy (in 8–12 weeks) should be considered in patients with gastric ulcers to rule out malignancy [52].

Gastric Antral Vascular Ectasia

Gastric antral vascular ectasia (GAVE) is more commonly found in cirrhotics than in the general population [53] and may lead to acute or chronic GI bleeding. Endoscopically, GAVE is characterized by the appearance of erythematous streaks of ectatic vessels, typically located in the gastric antrum (Fig. 26.11). When these streaks are linear, they give a "watermelon stomach" appearance. GAVE and PHG often appear similar, though GAVE may be differentiated by its location and the absence of the characteristic mosaic background of PHG. Endoscopic treatment with argon plasma coagulation is considered first-line therapy [54–56].

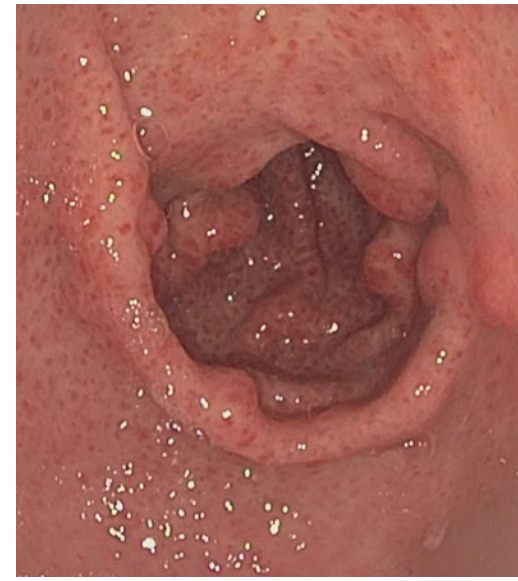

Fig. 26.11 Gastric antral vascular ectasias

References

1. North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. N Engl J Med. 1988;319:983–9.
2. Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology. 2017;65:310–35.
3. Kalafateli M, Triantos CK, Nikolopoulou V, Burroughs A. Non-variceal gastrointestinal bleeding in patients with liver cirrhosis: a review. Dig Dis Sci. 2012;57:2743–54.
4. Hwang JH, Sergill AK, Chandrasekhara V, et al. The role of endoscopy in the management of variceal hemorrhage. Gastrointest Endosc. 2014;80(2):221–7.
5. Cardenas A, Mendez-Bocanegra A. Report of the Baveno VI consensus workshop. Ann Hepatol. 2016;15:289–90.
6. Hwang JH, Fisher DA, Ben-Menachem T, et al. The role of endoscopy in the manangement of acute non-variceal upper GI bleeding. Gastrointest Endosc. 2012;75:1132–68.
7. Aljebreen AM, Fallone CA, Barkun AN. Nasogastric aspirate predicts high-risk endoscopic lesions in patients with acute upper-GI bleeding. Gastrointest Endosc. 2004;59:172–8.

8. Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013;368:11–21.
9. Northup PG, Caldwell SH. Coagulation in liver disease: a guide for the clinician. Clin Gastroenterol Hepatol. 2013;11:1064–74.
10. De Pietri L, Bianchini M, Montalti R, et al. Thrombelastography-guided blood product use before invasive procedures in cirrhosis with severe coagulopathy: a randomized, controlled trial. Hepatology. 2016;63:566–73.
11. Haas T, Fries D, Tanaka KA, Asmis L, Curry NS, Schochl H. Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: is there any evidence? Br J Anaesth. 2015;114:217–24.
12. Basili S, Raparelli V, Napoleone L, et al. Platelet count does not predict bleeding in cirrhotic patients: results from the PRO-LIVER study. Am J Gastroenterol. 2018;113:368–75.
13. Seo YS, Park SY, Kim MY, et al. Lack of difference among terlipressin, somatostatin, and octreotide in the control of acute gastroesophageal variceal hemorrhage. Hepatology. 2014;60:954–63.
14. Wells M, Chande N, Adams P, et al. Meta-analysis: vasoactive medications for the management of acute variceal bleeds. Aliment Pharmacol Ther. 2012;35:1267–78.
15. Bernard B, Grange JD, Khac EN, Amiot X, Opolon P, Poynard T. Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: a meta-analysis. Hepatology. 1999;29:1655–61.
16. Borzio M, Salerno F, Piantoni L, Cazzaniga M, Angeli P, Bissoli F, Boccia S, Colloredo-Mels G, Corigliano P, Fornaciari G, et al. Bacterial infection in patients with advanced cirrhosis: a multicentre prospective study. Dig Liver Dis. 2001;33:41–8.
17. Chavez-Tapia NC, Barrientos-Gutierrez T, Tellez-Avila F, et al. Meta-analysis: antibiotic prophylaxis for cirrhotic patients with upper gastrointestinal bleeding - an updated Cochrane review. Aliment Pharmacol Ther. 2011;34:509–18.
18. Chavez-Tapia NC, Barrientos-Gutierrez T, Tellez-Avila FI, Soares-Weiser K, Uribe M. Antibiotic prophylaxis for cirrhotic patients with upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2010;9:CD002907.
19. Soares-Weiser K, Brezis M, Tur-Kaspa R, Leibovici L. Antibiotic prophylaxis for cirrhotic patients with gastrointestinal bleeding. Cochrane Database Syst Rev. 2002;(2):CD002907.
20. Sreedharan A, Martin J, Leontiadis GI, et al. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2010;(7):CD005415.
21. Leontiadis GI, Sharma VK, Howden CW. Proton pump inhibitor therapy for peptic ulcer bleeding: Cochrane collaboration meta-analysis of randomized controlled trials. Mayo Clin Proc. 2007;82:286–96.
22. Shaheen NJ, Stuart E, Schmitz SM, et al. Pantoprazole reduces the size of postbanding ulcers after variceal band ligation: a randomized, controlled trial. Hepatology. 2005;41:588–94.
23. Barkun AN, Bardou M, Martel M, Gralnek IM, Sung JJ. Prokinetics in acute upper GI bleeding: a meta-analysis. Gastrointest Endosc. 2010;72:1138–45.
24. Chait MM. Lower gastrointestinal bleeding in patients with cirrhosis. Arch Dig Disord. 2017;1(1):14–21.
25. D'Amico G, de Franchis R, Cooperative Study Group. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology. 2003;38:599–612.
26. Carbonell N, Pauwels A, Serfaty L, Fourdan O, Levy VG, Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. Hepatology. 2004;40:652–9.
27. Garcia-Tsao G, Lim JK, Members of Veterans Affairs Hepatitis CRCP. Management and treatment of patients with cirrhosis and portal hypertension: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program. Am J Gastroenterol. 2009;104:1802–29.
28. Lo GH, Lai KH, Cheng JS, et al. A prospective, randomized trial of sclerotherapy versus ligation in the management of bleeding esophageal varices. Hepatology. 1995;22:466–71.
29. Puente A, Hernandez-Gea V, Graupera I, Roque M, Colomo A, Poca M, et al. Drugs plus ligation to prevent rebleeding in cirrhosis: an updated systematic review. Liver Int. 2014;34:823–33.
30. Garcia-Pagan JC, Caca K, Bureau C, et al. Early use of TIPS in patients with cirrhosis and variceal bleeding. N Engl J Med. 2010;362:2370–9.
31. Rudler M, Cluzel P, Corvec TL, et al. Early-TIPSS placement prevents rebleeding in high-risk patients with variceal bleeding, without improving survival. Aliment Pharmacol Ther. 2014;40:1074–80.
32. Augustin S, Altamirano J, Gonzalez A, et al. Effectiveness of combined pharmacologic and ligation therapy in high-risk patients with acute esophageal variceal bleeding. Am J Gastroenterol. 2011;106:1787–95.
33. Avgerinos A, Armonis A. Balloon tamponade technique and efficacy in variceal haemorrhage. Scand J Gastroenterol Suppl. 1994;207:11–6.
34. Escorsell A, Pavel O, Cardenas A, et al. Esophageal balloon tamponade versus esophageal stent in controlling acute refractory variceal bleeding: a multicenter randomized, controlled trial. Hepatology. 2016;63:1957–67.

35. Hubmann R, Bodlaj G, Czompo M, et al. The use of self-expanding metal stents to treat acute esophageal variceal bleeding. Endoscopy. 2006;38:896–901.
36. Gur I, Diggs BS, Orloff SL. Surgical portosystemic shunts in the era of TIPS and liver transplantation are still relevant. HPB (Oxford). 2013;16(5):481–93.
37. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology. 1992;16:1343–9.
38. Rios Castellanos E, Seron P, Gisbert JP, Bonfill Cosp X. Endoscopic injection of cyanoacrylate glue versus other endoscopic procedures for acute bleeding gastric varices in people with portal hypertension. Cochrane Database Syst Rev. 2015;12(5):CD010180.
39. El Amin H, Abdel Baky L, Sayez Z, et al. A randomized trial of endoscopic variceal ligation versus cyanoacralate injection for treatment of bleeding junctional varices. Trop Gastroenterol. 2010;31(4):279–84.
40. Sarin SK, Jain AK, Jain M, et al. A randomized controlled trial of cyanoacrylate versus alcohol injection in patients with isolated fundic varices. Am J Gastroenterol. 2002;97:1010–5.
41. Procaccini NJ, Al-Osaimi AM, Northup P, Argo C, Caldwell SH. Endoscopic cyanoacrylate versus transjugular intrahepatic portosystemic shunt for gastric variceal bleeding: a single-center U.S. analysis. Gastrointest Endosc. 2009;70:881–7.
42. Saad WE. Balloon-occluded retrograde transvenous obliteration of gastric varices: concept, basic techniques, and outcomes. Semin Interv Radiol. 2012;29:118–28.
43. Mishra SR, Chander SB, Kumar A, Sarin SK. Endoscopic cyanoacrylate injection versus beta-blocker for secondary prophylaxis of gastric variceal bleed: a randomised controlled trial. Gut. 2010;59:729–35.
44. Lo GH, Liang HL, Chen WC, Chen MH, Lai KH, Hsu PI, et al. A prospective, randomized controlled trial of transjugular intrahepatic portosystemic shunt versus cyanoacrylate injection in the prevention of gastric variceal rebleeding. Endoscopy. 2007;39:679–85.
45. Norton ID, Andrews JC, Kamath PS. Management of ectopic varices. Hepatology. 1998;28:1154–8.
46. Zhou Y, Qiao L, Wu J, Hu H, Xu C. Comparison of the efficacy of octreotide, vasopressin, and omeprazole in the control of acute bleeding in patients with portal hypertensive gastropathy: a controlled study. J Gastroenterol Hepatol. 2002;17:973–9.
47. Perez-Ayuso RM, Pique JM, Bosch J, et al. Propranolol in prevention of recurrent bleeding from severe portal hypertensive gastropathy in cirrhosis. Lancet. 1991;337:1431–4.
48. Kamath PS, Lacerda M, Ahlquist DA, McKusick MA, Andrews JC, Nagorney DA. Gastric mucosal responses to intrahepatic portosystemic shunting in patients with cirrhosis. Gastroenterology. 2000;118:905–11.
49. Hsu Y-C, et al. Long-term risk of recurrent peptic ulcer bleeding in patients with liver cirrhosis: a 10-year nationwide cohort study. Hepatology. 2012;56(2):698–705.
50. Laine L, McQuaid KR. Endoscopic therapy for bleeding ulcers: an evidence-based approach based on meta-analyses of randomized controlled trials. Clin Gastroenterol Hepatol. 2009;7:33–47.
51. Javid G, Zargar SA, U-Saif R, et al. Comparison of p.o. or i.v. proton pump inhibitors on 72-h intragastri c pH in bleeding peptic ulcer. J Gastroenterol Hepatol. 2009;24:1236–43.
52. Pruitt RE, Truss CD. Endoscopy, gastric ulcer, and gastric cancer. Follow-up endoscopy for all gastric ulcers? Dig Dis Sci. 1993;38:284–8.
53. Smith E, Tekola B, Patrie J, Cornella S, Caldwell S. Clinical characterization of gastric antral vascular ectasia: a potential manifestation of the metabolic syndrome. Am J Med. 2016;129(12):1329–e19.
54. Cho S, Zanati S, Yong E, et al. Endoscopic cryotherapy for the management of gastric antral vascular ectasia. Gastrointest Endosc. 2008;68:895–902.
55. Dulai GS, Jensen DM, Kovacs TO, Gralnek IM, Jutabha R. Endoscopic treatment outcomes in watermelon stomach patients with and without portal hypertension. Endoscopy. 2004;36:68–72.
56. Herrera S, Bordas JM, Llach J, et al. The beneficial effects of argon plasma coagulation in the management of different types of gastric vascular ectasia lesions in patients admitted for GI hemorrhage. Gastrointest Endosc. 2008;68:440–6.

27 Hernia Repair in Patients with Cirrhosis

Richard Smith

Hernia repair is one of the most common procedures performed worldwide. The most common scenarios of a nonrecurrent umbilical or inguinal hernia are associated with a relatively low risk and are straightforward procedures. However, these procedures have been associated with significant morbidity and mortality in patients with cirrhosis. del Olmo et al. compared 135 cirrhotic patients with 86 non-cirrhotic patients undergoing non-hepatic general surgery and found a 16.3% perioperative mortality in patients with cirrhosis compared with 3.5% in patients without cirrhosis [14]. The literature on patients with cirrhosis undergoing hernia repair shows a wide range for morbidity and mortality rates. The variability is a result of the heterogeneity of this patient population. These factors include the type of procedure, whether it was elective or emergent, and the degree of liver dysfunction.

There are two major ways that liver dysfunction is categorized (Table 27.1). The Child-Turcotte-Pugh (CTP) score was formulated empirically in 1964 as a predictive formula for patients with liver disease undergoing portosystemic surgery; however, it also has proven to be a useful tool in estimating the risks for both hepatic and non-hepatic surgery [17]. A criticism of the CTP score is the reliance on the subjective assessment of ascites and encephalopathy. The subjective nature was particularly problematic for organ allocation in transplant. Therefore, in 1999, Model for End-Stage Liver Disease (MELD) score was developed. The MELD score was initially designed by physicians at the Mayo Clinic for patients undergoing transjugular intrahepatic portosystemic shunting (TIPS), a procedure intended as a short-term bridge to liver transplantation. The MELD score is calculated from a validated predictive equation based on the patient's serum bilirubin level, creatinine level, and international normalized ratio for prothrombin time [18]. Good correlation has been shown between MELD and CTP scores for a variety of procedures [17]. Mortality following open abdominal operations ranges from 10% in patients with Child-Pugh classification A cirrhosis to 82% in patients with Child-Pugh classification C [36].

Hernia patients with cirrhosis and ascites usually have significant symptoms because ascites enters into the hernia sac both in the standing position and when recumbent. The hernia is then enlarged and often painful and can inhibit ambulation. If the ascites is significant, it can force the patient to stay in bed. Unfortunately, the majority of studies on hernia in patients with cirrhosis consist of a low number of nonuniform patients and thus make it hard to make specific recommendations [46]. Despite the fact that cirrhotic patients can pose a formidable challenge for the surgeon, we do know that abdominal wall hernias

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Table 27.1 Child-Turcotte-Pugh and MELD scores

	Points							
	1	2	3					
Encephalopathy	None	Grades 1–2 (acute)	Grades 3–4 (or chronic)	MELD =	$9.6 \times \log_e$	Serum	Creatinine	(mg/dL) +
Ascites	None	Mild to moderate (diuretic responsive)	Severe (refractory)		$3.8 \times \log_e$	Serum	Bilirubin	(mg/dL) +
Bilirubin (mg/dL)	<2	2–3	>3		$11.2 \times \log_e$	INR +	6.4	
Albumin (g/dL)	>3.5	2.8–3.5	<2.8					
INR	<1.7	1.7–2.3	>2.3					
Child-Turcotte-Pugh Class (add score for each parameter)								
Class A		5–6 points						
Class B		7–9 points						
Class C		10–15 points						

have a major impact on the quality of life in patients with cirrhosis [41]. We will examine the available studies on site of the hernia, degree of liver dysfunction, and specific techniques of repair to make recommendations.

Umbilical Hernia

An umbilical herniorrhaphy in low-risk patients without underlying medical disease is a simple procedure with very low morbidity and mortality. Although umbilical herniorrhaphy may be a simple procedure, in patients with liver cirrhosis, it can be associated with high morbidity and mortality [52]. Cirrhotic patients with umbilical hernias have an increased likelihood of complications following herniorrhaphy, such as wound complications combined with leakage of ascites, impending liver failure, or recurrence of the umbilical hernia. Patients with liver cirrhosis who undergo surgery with general anesthesia are expected to have a high morbidity and mortality rate that progressively increases in relation to the severity of preoperative liver dysfunction [14, 17]. Therefore, surgeons often choose not to perform surgery on cirrhotic patients with umbilical hernia in spite of the simplicity of the procedure.

The incidence of umbilical hernia in end-stage liver disease is up to 20% and in patients with significant ascites as high as 40% [5, 7]. The etiology of umbilical hernias in cirrhosis is often multifactorial. There is an attenuation of abdominal wall fascia and musculature secondary to compromised nutrition and the increased intra-abdominal pressure associated with ascites [4, 5]. In the setting of portal hypertension, recannulation of the umbilical vein may restore the pre-existing, supra-umbilical fascial defect [48].

The concern for umbilical hernia in the setting of ascites is that if left untreated, the hernia will continue to grow in size; increased pressure then leads to necrosis of the overlying skin, skin breakdown, ascitic leak, and the potential for bacterial peritonitis [7]. However, historically, hernia repair in cirrhotic patients is fraught with wound complications such as persistent ascitic leak through the incision, wound and mesh infection, and a high rate of hernia recurrences [5, 16, 27, 32, 33, 36]. Umbilical hernias in patients with liver cirrhosis and ascites also have a high rate of incarceration. Therefore, non-operative management is not without significant risk of needing emergent surgery [37]. So while conservative management avoids initial operative risk, this approach has a high risk of resulting in an emergent operative intervention for the patient secondary to incarcerated or strangulated hernias [16, 21].

Incarceration appears to be a higher risk following removal of large amounts of ascites, such as large-volume paracentesis after transjugular intrahepatic portosystemic shunt (TIPS) or liver transplantation. Both of these procedures result in an acute decrease in the diameter of the fascial defect. When this occurs, abdominal contents inside the hernia sac can become incarcerated [54].

Patients with a patent umbilical vein and severe liver failure represent a special case. The repair of an umbilical hernia necessitates ligation of a reopened umbilical vein. This reopened umbilical vein can be an important outflow for the portal circulation in patients with severe portal hypertension. If the vein is ligated during umbilical hernia, this can lead to acute portal vein thrombosis and subsequent acute failure of the liver necessitating emergency liver transplantation [15]. Pescovitz et al. noted that interruption of the periumbilical collaterals at the time of herniorrhaphy does on occasion lead to variceal bleeds; the overall risk is very small and not correlated with the preoperative presence of varices [44]. Rarely, massively dilated veins entering the spermatic cord can be confused for an inguinal hernia. The use of preoperative Doppler ultrasound has been advocated in patients with cirrhosis and suspected inguinal hernias [25].

Optimizing the patients with liver cirrhosis before elective umbilical hernia repair is crucial to minimizing postoperative complications and reducing recurrence. Such optimization includes low salt intake, free water restriction, and use of diuretics, such as furosemide and spironolactone. Large-volume paracentesis and intravenous infusion of salt-poor albumin can help to control ascites. Careful consideration of the patient's suitability for liver transplant should also be given prior to

surgery [11]. Umbilical hernia repair simultaneously with liver transplantation appears to be the optimal setting for repair in patients with severe cirrhosis. However, due to organ shortages, wait time for transplantation can be excessive, exposing patients on the waiting list to a greater risk of developing complications of the hernia and necessitating an emergency operation [15].

More recent studies have reported improved outcomes and have recommended elective or early umbilical herniorrhaphies in patients with liver cirrhosis [7, 21, 38]. Unfortunately, selection of the patient, the optimal timing to surgery, and the method of repair are not well studied and remain controversial. There are no high-quality, prospective studies addressing this issue.

Marsman et al. retrospectively studied 34 patients with cirrhosis, ascites, and a symptomatic umbilical hernia. Seventeen underwent elective repair, four had repairs at time of orthotopic liver transplantation (OLT), and thirteen were followed with non-operative management. Age, sex, and MELD score distribution did not differ significantly between both groups. In the elective repair group, there were no perioperative deaths, and wound complications occurred in 18%. The majority (94%) had primary repair which was associated with a relatively high recurrence rate of 25%. Ten of thirteen (77%) of the non-operatively managed patients had a complication. Six of these patients required an emergency operation with a 40% complication rate and a 20% mortality rate [37]. Based on these results, the authors advocated elective repair based on the high complication and mortality rate of the patients requiring emergency procedures.

Choi et al. examined 44 patients with cirrhosis and umbilical hernia. 31 patients underwent umbilical hernia repair. Of the patients who underwent repair, 9 patients had emergent and 22 had elective repairs. Nine were CTP class C and 22 were CTP class B. Morbidity was 42% and mortality was 6.5% for the patients who underwent repair. There were four (13%) cases of postoperatively recurrent umbilical hernias due to poor ascites control. Patients undergoing elective hernia repairs required fewer combined resection and shorter operative times and postoperative hospital stay and developed less postoperative complications than patients requiring emergency hernia repairs. However, in contrast to the previous study, there was no difference in mortality. Based on this the authors concluded that elective umbilical herniorrhaphies should be considered in patients with relatively well-preserved liver function [11]. The well-preserved comment is based on the MELD and CTP scores of the non-operative group which were significantly higher. Their overall outcomes were not examined.

The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database was used to identify patients with ascites or varices who underwent umbilical hernia repair. 390 patients were identified and compared to the other 22,952 patients who underwent umbilical hernia repair and did not have evidence of portal hypertension. Patients with evidence of portal hypertension were more likely to have comorbidities, higher American Society of Anesthesiologists (ASA) class, and higher mean model for end-stage liver disease (MELD) (13 vs 8). In addition, the patients in the study group were more likely than those in the control group to require emergency surgery for umbilical hernia (37.7% vs 4.9%). The overall morbidity and mortality rates after umbilical hernia repair for the patients with portal hypertension were 13.1% and 5.1%, respectively. This was significantly higher than the control group with a 3.9% morbidity and 0.1% mortality rate, respectively. In patients with portal hypertension, emergency umbilical hernia repair was associated with higher morbidity than the elective surgery (20.8% vs 8.3%) but not significantly higher mortality (7.4% vs 3.7%). This finding suggests that the detrimental effects of cirrhosis override the increased risks associated with emergency surgery on postoperative mortality. On logistic regression analysis, age older than 65 years, MELD score greater than 15, preoperative sepsis, and albumin level less than 3.0 g/dL significantly increased mortality risk. Specifically, mortality with a MELD of 15 or less was 1.3% and 11.1% over 15 [10].

Saleh et al. again examined the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) for adults

with ascites who underwent umbilical hernia repair, this time in order to create a model for predicting mortality. A total of 688 patients were identified. The overall 30-day postoperative mortality was 6%. Although emergency repairs were associated with a significant increase in mortality (9% vs 5%) on univariate analysis, it did not hold up on multivariant analysis. Multivariable logistic regression to predict 30-day mortality found only MELD score, albumin, WBC, and platelet count (less than 150×10^9/L) to be significant predictors of mortality. A mean MELD score of 19.3 was found in the non-survivors compared to 13.9 in the survivors. Mortality begins to increase at a MELD score of 12 rising to a mortality of greater than 20% at a MELD of 30. The authors developed a nomogram using MELD and albumin levels compared at platelet levels less than and greater than 150,000 and for WBC less than 10 and greater than 10 to predict postoperative mortality (Table 27.2). This data can be used to estimate postoperative risk of mortality in patients with ascites undergoing umbilical hernia repair.

Finally, a unique presentation of cirrhotic patients with ascites is spontaneous umbilical rupture and attendant infection [20, 32]. Postoperative morbidity is about 70% and mortality is 6–20% after urgent surgical repair in these patients. Mortality with supportive care is between 60% and 80% [9, 31, 53]. Current published series concur that the exact timing of the operation is not of concern. What is most important is resuscitation and optimization. This includes intravenous fluids, prophylactic antibiotics, and local measures, such as nonocclusive dressings [9, 16, 53]. Other authors have recommended that patients with spontaneous umbilical rupture undergo preoperative TIPS prior to semi-elective primary herniorrhaphy [16].

Slakey et al. suggested the insertion of temporary peritoneal dialysis catheter at the end of umbilical herniorrhaphy in cirrhotic patients to control ascites postoperatively. This technique was effective in eight patients with moderate to massive ascites in controlling ascites without infectious complications, and it allowed management as an outpatient [49]. However, a larger study looking at the use of peritoneal dialysis catheters for refractory ascites showed a 10% risk of bacterial peritonitis and significant mortality associated with infection [29]. Given this, postoperative drains are generally not recommended.

Inguinal Hernia

In contrast to umbilical hernia, the incidence of inguinal hernia is not markedly increased with ascites. In addition, incarceration and strangulation are uncommon with inguinal hernia in cirrhosis [36, 40]. In addition, the increased risk of recurrence for umbilical herniorrhaphy in the setting of ascites does not seem to occur to the same degree with inguinal herniorrhaphy [5, 27]. Again, the available data on hernia repair is limited to a few retrospective studies.

Hurst et al. reported on 18 patients with inguinal hernia and ascites secondary to cirrhosis. Patients underwent diuretics, large-volume paracentesis, and peritoneovenous shunting for the control of ascites. A total of 13 of the 18 patients underwent repair of their hernias. Three of the 18 patients presented with incarceration but only 1 needed urgent surgery. No patients requiring peritoneovenous shunting underwent hernia repair. Mesh was used in only 1 of the 11 patients. The 30-day morbidity was 36%, but all were minor complications and no perioperative deaths were seen. The long-term survival was 75% at 2 years and there was an 8% recurrence rate. There were no complications or death noted in the group that did not undergo repair. Based on a limited survival and a low rate of complications in the observed group, the author recommended an expectant approach to the management of groin hernias in patients with ascites if there are little or no symptoms. Conversely, in the symptomatic patient, repair can be performed safely in selected patients [27].

One of the larger studies is a retrospective study of 129 patient with cirrhosis and inguinal hernia operated on by a single surgeon. All patients underwent a standard McVay hernia repair with relaxing incisions. Eighty-one patients had ascites. The overall complication rate was 10.9% and 12.3% in the patients with ascites. The postoperative mortality rate was

Table 27.2 Nomogram to predict postoperative mortality for patients with cirrhosis undergoing umbilical hernia repair

MELD score												
	6	9	12	15	18	21	24	27	30	33	36	
WBC < 10.0	Mortality											Albumin (9/dL)
Platelet >150	0.2	0.4	0.6	0.9	1.4	2.2	3.4	5.1	7.8	11.6	17.0	**4.0**
	0.4	0.5	0.9	1.3	2.0	3.1	4.8	7.3	10.9	16.0	22.9	**3.5**
	0.5	0.8	1.3	2.0	3.1	4.7	7.2	10.8	15.8	22.7	31.4	**3.0**
	0.9	1.4	2.1	3.3	5.0	7.7	11.4	16.7	23.9	32.8	43.2	**2.5**
	1.7	2.6	3.9	6.0	9.0	13.4	19.4	27.3	36.9	47.7	58.7	**2.0**
	3.6	5.5	8.4	12.5	18.2	25.7	35.0	45.6	56.7	67.1	76.0	**1.5**
Platelet <150	1.0	1.6	2.5	3.8	5.8	8.7	12.9	18.8	26.5	36.0	46.7	**4.0**
	1.5	2.3	3.5	5.4	8.2	12.2	17.7	25.1	34.4	44.9	56.0	**3.5**
	2.3	3.5	5.3	8.1	12.0	17.6	24.9	34.1	44.6	55.7	66.2	**3.0**
	3.7	5.7	8.6	12.7	18.5	26.2	35.6	46.3	57.3	67.6	76.5	**2.5**
	6.7	10.1	14.9	21.4	29.8	39.8	50.8	61.6	71.5	79.6	85.9	**2.0**
	13.9	20.0	28.1	37.8	48.7	59.6	69.7	78.2	84.8	89.7	93.1	**1.5**
WBC > 10	Mortality											
Platelet >150	1.1	1.6	2.5	3.9	5.9	8.9	13.2	19.2	27.0	36.6	47.3	**4.0**
	1.5	2.4	3.6	5.5	8.3	12.4	18.1	25.6	34.9	45.6	56.6	**3.5**
	2.3	3.6	5.5	8.3	12.3	17.9	25.4	34.7	45.3	56.3	66.7	**3.0**
	3.8	5.8	8.8	13.0	18.9	26.7	36.2	46.9	57.9	68.2	77.0	**2.5**
	6.9	10.3	15.2	21.9	30.3	4D.4	51.4	62.2	72.0	80.0	86.2	**2.0**
	14.2	20.5	28.6	38.5	49.3	603	70.3	78.6	85.2	89.9	93.3	**1.5**
Platelet <150	4.4	6.6	10.0	14.7	21.2	29.5	39.4	50.4	61.3	71.1	79.3	**4.0**
	6.2	9.3	13.8	20.0	28.0	37.8	48.6	59.6	69.7	78.2	84.8	**3.5**
	9.2	13.7	19.8	27.8	37.5	48.3	59.3	69.4	78.0	84.6	89.6	**3.0**
	14.5	20.9	29.1	39.1	50.0	60.9	70.8	79.1	85.5	90.2	93.5	**2.5**
	24.0	33.0	43.4	54.5	65.1	74.4	81.9	87.5	91.7	94.5	96.4	**2.0**
	41.4	52.4	63.2	72.8	80.6	86.6	91.0	94.0	96.1	97.5	98.4	**1.5**

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2.5% for the entire group. The recurrence rate at a median follow-up of 22.9 months was 2.3%. The author also compared his results to 651 patients without cirrhosis who underwent the same repair over the same time period. There were no differences in recurrence or complications between the two groups [40].

Another retrospective study reported the outcome of 22 patients with cirrhosis and symptomatic inguinal hernia operated on by single surgeon under local anesthetic. All patients had ascites but no patient had refractory ascites. Minor complications occurred in 13.6%, with no major complications and no 30-day mortalities [26].

Patients with inguinal hernia and cirrhosis were identified in the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database. 18,360 patients for which a MELD score could be calculated were identified. 14,354 patients had an open repair and 4006 had a laparoscopic repair. Both laparoscopic and open repairs were performed even in patients with high MELD scores (15–40). Patients who underwent open repair were more likely to have comorbidities, higher MELD scores, and a higher incidence of preoperative infections and were more likely to be emergent cases. Overall there was no difference in complications, death, or length of stay between open and laparoscopic repair. Most importantly complications and mortality were very low compared to the similar series for umbilical hernias. Complications were 2.67% for open repair vs

2.35% for lap repair and mortality rates of 0.27% vs 0.12%, respectively [42].

Ascites

In cirrhotic patients with ascites, up to 10% are refractory to standard medical therapy [43, 51]. Two-year mortality for patients with refractory ascites without operative intervention is reported to be about 50% [47]. Refractory ascites increases the rate of wound complications and recurrence of the hernia. Management options currently include large-volume paracentesis, liver transplant (LT), and TIPS [5]. Transjugular intrahepatic portosystemic shunt (TIPS) is an endovascular method for the formation of an artificial channel between the portal and hepatic vein to decrease portal venous pressure [3, 19, 45, 47]. Peritoneovenous shunting (PVS) has shown to lower hernia recurrence rate when used in the setting of refractory ascites and umbilical hernia [5, 33]. Unfortunately, however, PVS is associated with high complication (40–60%) and mortality (50%) rates and has largely been abandoned [35]. Surgical portosystemic shunts have also been proven effective in controlling refractory ascites but are also associated with high mortality rate (10%), high incidence of associated encephalopathy (50%) and effect potential subsequent liver transplantation and so are also not ideal [5, 35].

Chatzizacharias et al. examined 11 consecutive patients with advanced hepatic cirrhosis and refractory ascites. Ten of eleven were managed with diuretics and large-volume paracentesis. The one patient with spontaneous rupture was managed with TIPS. Complications occurred in 25% of the patients, but there were no perioperative deaths. The recurrence rate at a median follow-up of 8 months was 8.3%. The authors made the following recommendations: intravenous fluid management using a combination of crystalloids and human albumin solution to account for the loss of ascitic fluid and primary closure with sutures. They argued against the use of mesh based on a presumed increased risk of infection and potential serious and life-threatening complications. (This is certainly not a universal opinion.) They went on to comment that the use of absorbable meshes, like Vicryl® or biologic mesh, could be utilized in the rare cases with an inability for primary closure due to a large abdominal wall defect [9].

Eker et al. looked prospectively at 30 consecutive patients with umbilical hernia and ascites treated under a protocol electively. This included preoperative diuretics, nutritional support, and intravenous albumin to increase the patient's serum albumin to greater than 3 g/dL. There was no 30-day mortality and the major morbidity rate was 7%. The long-term death rate at a median of 10 months' follow-up was 7%. The authors concluded that "elective umbilical hernia repair is a safe approach and seems preferable over conservative treatment in selected cirrhotic patients." They again recommended this be done in specialized centers [15].

More recently, TIPS in the preoperative setting in patients without severe hepatic or renal insufficiency confers improved perioperative and longer-term results. Several multicenter, randomized controlled trials have demonstrated TIPS to be superior to large-volume paracentesis in patients with refractory ascites [3, 19, 45, 47]. TIPS effectively controls ascites in 80–90% of patients, with a 1-year mortality rate of less than 5% and a shunt occlusion rate of approximately 20% [3, 19, 45, 47].

In a study of 21 patients with umbilical hernia and advanced cirrhosis with refractory ascites, 6 underwent semi-emergent repair and 15 underwent emergent repair. All 6 of the semi-urgent patients underwent preoperative TIPS. None of the patients who underwent an emergent procedure received preoperative TIPS. The overall morbidity rate for the 21 patients was 71% and the mortality rate was 5%. After multivariate analysis, spontaneous umbilical rupture was the only factor to correlate independently with adverse outcome with an associated odds ratio (OR) of 25.0. The wound complication rate was 17% in patients who underwent preoperative TIPS compared to 27% in patients that did not undergo TIPS (P = NS). Additionally, they looked at the use of a closed-suction drain in the patients who had not undergone preoperative TIPS, and

the rate of wound complication was 40% in patients treated with versus 20% if no drain was used ($P = 0.4$). Follow-up at a mean of 36 months for patients with advanced cirrhosis demonstrated a long-term 20% mortality rate. Patients with spontaneous rupture of the umbilical hernia had a decreased, 36-month, transplant-free survival as compared to those with incarcerated hernia (50% vs 86%). The authors felt that preoperative TIPS placement for patients undergoing semi-elective hernia repair may decrease wound complications, without influencing short- or long-term mortality. Placement of a closed-suction drain did not appear to control or decrease postoperative ascites-related wound complications [53].

Ventral Hernia

Studies on ventral hernia repair are again limited to retrospective studies with heterogeneity within and between studies. In a recent study, Licari et al. retrospectively reviewed 27 patients with cirrhosis undergoing incisional hernia repair. All repairs were done with inlay mesh technique. Ten of the 27 repairs were done emergently. The overall mortality rate was 18.5%, but four of the five mortalities were in emergently repaired hernia. The complication rate was also higher in the emergent patients. Overall recurrence rate was 11% [34].

The University Health System Consortium (UHC), an alliance comprised of 129 academic medical centers, performed a retrospective review of 32,033 inpatient ventral hernia repairs performed between 1999 and 2004. They compared 30,836 non-cirrhotics and 1197 cirrhotic patients who underwent ventral/umbilical herniorrhaphy. As expected cirrhotics had more ICU admissions than non-cirrhotics (15.9% vs 6%; $P < 0.0001$). Length of stay (5.4 vs 3.7 days), morbidity (16.5% vs 13.8%; $P = 0.008$), and mortality (2.5% vs 0.2%; $P < 0.0001$) were all higher in cirrhotics. One of the major differences between the two groups that may have accounted for some of the differences was that cirrhotics underwent emergent surgery more commonly than non-cirrhotics (58.9% vs 29.5%). When this was factored out, elective surgery morbidity in cirrhotics was no different from non-cirrhotics (15.6% vs 13.5%; $P = 0.18$). There was a non-statistically significant increase in surgical mortality in cirrhotics overall (0.6% vs 0.1%; $P = 0.06$). The increase in mortality for cirrhotics became significant when emergency surgery was examined (3.8% vs 0.5%; $P < 0.0001$). The data was gathered from a discharge database and did not include same-day, short-stay, or ambulatory surgical cases. Mortality and complication information was limited to in hospital events, which may not accurately reflect 30-day mortality typically reported in other series. The authors also comment that these results are reflective of specialized centers and may not reflect outcomes in all settings [7].

Mesh

Use of synthetic mesh has been shown to reduce the recurrence rate in a randomized trial of patients without cirrhosis undergoing umbilical hernia repair [1]. However, in patients with cirrhosis, there is a concern for impaired mesh ingrowth and wound infection in the presence of ascites [11]. The use of non-absorbable mesh in complicated hernias in non-cirrhotic patients is associated with minimal wound-related morbidity and a low incidence of hernia recurrence [8, 30].

When comparing primary repair and mesh repair of primary ventral and umbilical hernia repairs, there is an increased risk of postoperative local complications following mesh repair but a reduced rate of recurrence in comparison to suture repair [2, 39, 50]. There are three methods for placement of mesh: onlay (anterior to the aponeurosis and the defect), sublay/retrorectus (between the rectus muscle and posterior rectus sheath), and inlay/intraperitoneal (inside the peritoneum). Controversy continues regarding the best site of mesh placement [13, 23]. The risks and types of complications are related to the space in which the mesh is placed [12, 24]. In the onlay technique, wound complications (seroma, hematoma, ascites

drainage, and infection of the surgical incision and mesh) are more frequent secondary to extensive detachment of subcutaneous tissue from the fascia increasing dead space. Wound complications are less frequent with the sublay and underlay mesh repair techniques because the mesh is removed from contact with the subcutaneous tissue and skin [12, 23, 24, 55]. In the underlay technique, the mesh is in contact with abdominal contents and increases risk for complications, such as intestine adhesion, obstruction, erosion, and fistula formation [13, 15, 22, 55].

Hassan et al. examined retrospectively 70 patients with umbilical hernia, CTP B and C liver cirrhosis, and ascites who underwent elective repair with retrorectus placement of mesh. The wound infection rate was 2.9% with an overall complication rate of 10%. There were no perioperative deaths. The recurrence rate was 1.4% [23].

Ammar et al. randomized 80 adult patients with CTP A or B liver cirrhosis and a complicated (incarcerated, inflamed, or ruptured hernia) umbilical hernia to an onlay mesh or standard fascial suture repair of the hernia. There were no differences between groups regarding preoperative factors. Surgical site infections (SSIs) were higher in the mesh group (16.2% vs 8.5%), but this was not statistically significant, and no mesh needed to be explanted. The recurrence rate for the mesh group was significantly lower (2.7% vs 14.2%) at 6 months [1]. Therefore, one needs to balance risk of infection and risk of recurrence in deciding whether to use mesh in patients with liver cirrhosis who present with umbilical hernia [10].

Laparoscopic

Laparoscopic inguinal and ventral hernia repairs have become more common for repair of hernias in the general population. Although still a matter of debate, multiple retrospective studies demonstrated an association between laparoscopic ventral hernia repair (LVHR) and less pain in the immediate postoperative period, a lower incidence of surgical site infection, decreased hernia recurrence, shorter length of stay, and shorter recovery time [28, 56]. However, data of laparoscopic repair in patients with liver disease is limited.

Belli et al. performed laparoscopic-assisted ventral hernia repair with mesh in 14 CTP A patients with cirrhosis. The morbidity rate was 79% and all were minor with only one wound complication. There was no perioperative mortality and no recurrences at a mean follow-up of 8 months [6].

As discussed previously, the ACS NSQIP database was used to identify 18,360 patients with liver disease who underwent inguinal hernia repair. That study included 4006 patients with liver disease that had a laparoscopic repair. These repairs occurred even in patients with significantly elevated MELD scores. As noted previously, there were very low complication and mortality rates at 2.35% and 0.12%, respectively. Decreased wound complications are a frequently cited advantage to laparoscopic repair in patients without liver disease. However, in this study having a laparoscopic repair did not result in decreased wound complications when compared to open procedure. It is possible the underlying risk related to the liver disease outweighs the benefit of one technique over the other [42].

The ACS NSQIP database was again utilized to identify patients with at least moderate chronic liver disease as defined by MELD score of 9 or greater who underwent elective open or laparoscopic ventral hernia repair. A total of 3594 patients were identified. 3058 underwent open repair and 536 underwent laparoscopic repair. The mean MELD score of the entire cohort was 14 but had a relatively low rate of ascites 15.6%. The laparoscopic group was associated with lower comorbidity scores, lower presence of incarceration/strangulation, less ascites, less varices, higher serum albumin, and a lower MELD score. Thirty-day mortality was significantly higher for open versus laparoscopic repair (0.4% vs 0.2%). This difference appeared to be more related to factors other than approach when multivariate analysis was used. Similar to other studies, MELD, age, comorbidity index, and albumin level were predictive of mortality risk. Wound-related complications were significantly lower in the laparoscopic group compared to the open

group (4.8% vs 0.9%). This difference remained on multivariate analysis. Systemic complications occurred in 6.5% of the entire cohort and were not impacted by approach. Length of stay was significantly longer for open repair compared to laparoscopic (mean 5.0 days vs 3.7 days).

Conclusions

Hernia repair in patients with cirrhosis requires careful consideration. In well-selected patients, the morbidity and mortality can be acceptable. Patients with cirrhosis and umbilical/ventral hernias are at higher risk for incarceration/strangulation than patients without cirrhosis. Some studies have shown worse outcomes for patients undergoing emergent repairs when compared to elective repair. This has prompted some authors to recommend elective repair broadly. However, the differences in outcome between elective repair and emergent repair appear to be more related to the underlying degree of liver dysfunction than acuteness of the indication. This conclusion is based on larger database studies that can control for other factors. Therefore, degree of liver dysfunction, physiologic status, and comorbidities should be weighed carefully. Referral to specialized centers (transplant centers) with a multidisciplinary team who can assist in perioperative care of the patient undergoing hernia repair should also be considered. They can also ideally participate in the discussion for suitability of the patient for liver transplantation at which time the hernia could be addressed simultaneously. In patients undergoing surgery, the risk of recurrence and complications can be reduced by maximizing medical treatment of ascites, assessing nutrition, and careful surveillance for infection.

References

1. Ammar SA. Management of complicated umbilical hernias in cirrhotic patients using permanent mesh: randomized clinical trial. Hernia. 2010;14(1):35–8.
2. Arroyo AG. Randomized clinical trial comparing suture and mesh repair of umbilical hernia in adults. Br J Surg. 2001;88(10):1321–3.
3. Azoulay DB. Neoadjuvant transjugular intrahepatic portosystemic shunt: a solution for extrahepatic abdominal operation in cirrhotic patients with severe portal hypertension. J Am Coll Surg. 2001;193(1):46–51.
4. Baron HC. Umbilical hernia secondary to cirrhosis of the liver. Complications of surgical correction. N Engl J Med. 1960;263:824–8.
5. Belghiti J, Durand F. Abdominal wall hernias in the setting of cirrhosis. Semin Liver Dis. 1997;17(3):219–26.
6. Belli GD. Laparoscopic incisional and umbilical hernia repair in cirrhotic patients. Surg Laparosc Endosc Percutan Tech. 2006;16(5):330–3.
7. Carbonell AM. Poor outcomes in cirrhosis-associated hernia repair: a nationwide cohort study of 32,033 patients. Hernia. 2005;9(4):353–7.
8. Carbonell AM. Outcomes of synthetic mesh in contaminated ventral hernia repairs. J Am Coll Surg. 2013;217(6):991–8.
9. Chatzizacharias NA. Successful surgical management of ruptured umbilical hernias in cirrhotic patients. World J Gastroenterol. 2015;21(10):3109–13.
10. Cho SW, Bhayani N, Newell P, et al. Umbilical hernia repair in patients with signs of portal hypertension: surgical outcome and predictors of mortality. Arch Surg. 2012;147(9):864–9.
11. Choi SB. Management of umbilical hernia complicated with liver cirrhosis: an advocate of early and elective herniorrhaphy. Dig Liver Dis. 2012;43(12):991–5.
12. Coelho GR. Single-center transfusion rate for 555 consecutive liver transplantations: impact of two eras. Transplant Proc. 2013;45(9):3305–9.
13. Coelho JC. Umbilical hernia in patients with liver cirrhosis: a surgical challenge. World J Gastrointest Surg. 2016;8(7):476–82.
14. del Olmo JA, Flor-Lorente B, Flor-Civera B, et al. Risk factors for nonhepatic surgery in patients with cirrhosis. World J Surg. 2003;27(6):647–52.
15. Eker HH. A prospective study on elective umbilical hernia repair in patients with liver cirrhosis and ascites. Surgery. 2011;150(3):542–6.
16. Fagan SP. Management of complicated umbilical hernias in patients with end-stage liver disease and refractory ascites. Surgery. 2004;135(6):679–82.
17. Farnsworth NF. Child-Turcotte-Pugh versus MELD score as a predictor of outcome after elective and emergent surgery in cirrhotic patients. Am J Surg. 2004;188(5):580–3.
18. Forman LM, Lucey MR. Predicting the prognosis of chronic liver disease: an evolution from CHILD to MELD. Hepatology. 2001;33:473–5.
19. Gines PT. Randomized comparative study of therapeutic paracentesis with and without intravenous albumin in cirrhosis. Gastroenterology. 1988;94(6):1493–502.
20. Ginsburg BY. Spontaneous rupture of an umbilical hernia with evisceration. J Emerg Med. 2006;30(2):155–7.
21. Gray SH. Umbilical herniorrhapy in cirrhosis: improved outcomes with elective repair. J Gastrointest Surg. 2008;12(4):675–81.

22. Gurita RE. Umbilical hernia alloplastic dual-mesh treatment in cirrhotic patients. J Med Life. 2013;6(1):99–102.
23. Hassan AM. Outcome of sublay mesh repair in non-complicated umbilical hernia with liver cirrhosis and ascites. Int J Surg. 2014;12(2):181–5.
24. Holihan JL. Mesh location in open ventral hernia repair: a systematic review and network meta-analysis. World J Surg. 2016;40(1):89–99.
25. Horn TW. When a hernia is not a hernia: the evaluation of inguinal hernias in the cirrhotic patient. Am Surg. 2001;67(11):1093–5.
26. Hur YH. Inguinal hernia repair in patients with liver cirrhosis accompanied by ascites. J Korean Surg Soc. 2011;80(6):420–5.
27. Hurst RD. Management of groin hernias in patients with ascites. Ann Surg. 1992;216(6):696–700.
28. Juo YS. Laparoscopic versus open ventral hernia repair in patients with chronic liver disease. Surg Endosc. 2017;31(2):769–77.
29. Kathpalia PB. Indwelling peritoneal catheters in patients with cirrhosis and refractory ascites. Intern Med J. 2015;45(10):1026–31.
30. Kelly ME. The safety and efficacy of prosthetic hernia repair in clean-contaminated and contaminated wounds. Am Surg. 2002;68(6):524–8; discussion 528
31. Kirkpatrick S, Schubert T. Umbilical hernia rupture in cirrhotics with ascites. Dig Dis Sci. 1988;33(6):762–5.
32. Lemmer JH. Management of spontaneous umbilical hernia disruption in the cirrhotic patient. Ann Surg. 1983;198(1):30–4.
33. Leonetti JP. Umbilical herniorrhaphy in cirrhotic patients. Arch Surg. 1984;119(4):442–5.
34. Licari LS. The abdominal wall incisional hernia repair in cirrhotic patients. G Chir. 2018;XXXIX(1):20–3.
35. Maniatis AG. Therapy for spontaneous umbilical hernia rupture. Am J Gastroenterol. 1995;90(2):310–2.
36. Mansour AW. Abdominal operations in patients with cirrhosis: still a major surgical challenge. Surgery. 1997;122(4):730–5. discussion 735
37. Marsman HA. Management in patients with liver cirrhosis and an umbilical hernia. Surgery. 2007;142(3):372–5.
38. McKay AD. Umbilical hernia repair in the presence of cirrhosis and ascites: results of a survey and review of the literature. Hernia. 2009;13(5):461–8.
39. Nguyen MT. Comparison of outcomes of synthetic mesh vs suture repair of elective primary ventral herniorrhaphy: a systematic review and meta-analysis. JAMA Surg. 2014;149(5):415–21.
40. Oh HK. Inguinal hernia repair in patients with cirrhosis is not associated with increased risk of complications and recurrence. World J Surg. 2011;35(6):1229–33; discussion 1234
41. Patti RA. Inguinal hernioplasty improves the quality of life in patients with cirrhosis. Am J Surg. 2008;196(3):373–8. Am J Surg. 196(3):373–8.
42. Pei KY. A matched comparison of laparoscopic versus open inguinal hernia repair in patients with liver disease using propensity score matching. Hernia. 2018;22(3):419–26.
43. Perez-Ayuso RM. Randomized comparative study of efficacy of furosemide versus spironolactone in non-azotemic cirrhosis with ascites. Relationship between the diuretic response and the activity of the renin-aldosterone system. Gastroenterology. 1983;84(5 Pt 1):961–8.
44. Pescovitz MD. Umbilical hernia repair in patients with cirrhosis. No evidence for increased incidence of variceal bleeding. Ann Surg. 1984;199(3):325–7.
45. Rossle MO. A comparison of paracentesis and transjugular intrahepatic portosystemic shunting in patients with ascites. N Engl J Med. 2000;342(23):1701–7.
46. Saleh F, Okrainec A, Cleary SP, Jackson TD. Management of umbilical hernias in patients with ascites: development of a nomogram to predict mortality. Am J Surg. 2015;209(2):302–7.
47. Sanyal AJ. The North American study for the treatment of refractory ascites. Gastroenterology. 2003;124(3):634–41.
48. Shlomovitz E, Quan D, Etemad-Rezai R, McAlister VC. Association of recanalization of the left umbilical vein with umbilical hernia in patients with liver disease. Liver Transpl. 2005;11(10):1298–9.
49. Slakey DP. Umbilical hernia repair in cirrhotic patients: utility of temporary peritoneal dialysis catheter. Am Surg. 2005;71(1):58–61.
50. Stabilini CS. Mesh versus direct suture for the repair of umbilical and epigastric hernias. Ten-year experience. Ann Ital Chir. 2009;80(3):183–7.
51. Stanley MM. Peritoneovenous shunting as compared with medical treatment in patients with alcoholic cirrhosis and massive ascites. Veterans administration cooperative study on treatment of alcoholic cirrhosis with ascites. N Engl J Med. 1989;321(24):1632–8.
52. Teh SH. Risk factors for mortality after surgery in patients with cirrhosis. Gastroenterology. 2007;132(4):1261–9.
53. Telem DA. Complicated hernia presentation in patients with advanced cirrhosis and refractory ascites: management and outcome. Surgery. 2010;148(3):538–43.
54. Trotter JF. Incarceration of umbilical hernia following transjugular intrahepatic portosystemic shunt for the treatment of ascites. Liver Transpl Surg. 1999;5(3):209–10.
55. Vorst AL. Evolution and advances in laparoscopic ventral and incisional hernia repair. World J Gastrointest Surg. 2015;7(11):293–305.
56. Zhu XC. Totally extraperitoneal laparoscopic hernioplasty versus open extraperitoneal approach for inguinal hernia repair: a meta-analysis of outcomes of our current knowledge. Surgeon. 2014;12(2):94–105.

Part IX

Mesenteric Ischemia

28 Mesenteric Ischemia: When to Operate, What to Resect, and When to Reoperate

Dwight C. Kellicut and Kelli B. Ishihara

Introduction

Acute mesenteric ischemia (AMI) is a rare entity that occurs in less than 1% of all patients who present to the emergency room; however, it is notoriously difficult to diagnose. It is important to maintain a high clinical suspicion of this disease process as it is associated with an extremely high mortality rate (50–70% in some cases). Once diagnosed, AMI can be categorized based on etiology, which will ultimately guide management and treatment strategies. This chapter will review the etiologies of AMI and focus on operative interventions and general management strategies of these complex patients.

Epidemiology and Classification of AMI

Acute mesenteric ischemia is most commonly classified based on etiology. AMI can be due to arterial embolism, arterial thrombosis, non-occlusive mesenteric ischemia, and venous thrombosis. The most common etiology of AMI is arterial embolism, which occurs in approximately 40–50% of cases [1, 2]. The most common place for the emboli to obstruct is in the SMA given the large caliber and less acute takeoff angle from the aorta [1, 3]. Classically the emboli will lodge 3–10 cm distal to the SMA and spare the proximal jejunum and colon. Twenty percent of the emboli will be associated with concurrent emboli in other locations in the body [1, 2]. Arterial thrombosis is the next most common cause of AMI, representing approximately 25% of cases [1, 2]. Thrombosis typically occurs at the origin of the vessel and is usually a chronic process of worsening stenosis over time. Given that it is a chronic process, this allows for collateralization to occur. Non-occlusive mesenteric ischemia occurs in approximately 20–30% of cases and will typically present in a patient with a low flow state [1, 2]. It generally is a diffuse, global process that affects the entire bowel. Mesenteric venous thrombosis is the least common presentation, occurring in approximately 5–10% of cases [1, 2].

Presentation

As previously mentioned, AMI is a rare entity, and a high index of clinical suspicion is needed based on history and overall clinical picture to make the correct diagnosis. The textbook presentation for mesenteric ischemia will be a patient who complains of abdominal pain out of

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proportion to physical exam findings. Most patients will present with a constellation of nonspecific findings of nausea, vomiting, or diarrhea with or without blood. One study showed that 33% of patients present with a triad of abdominal pain, fever, and hemoccult-positive stool, but there is no specific physical exam finding that is characteristic of AMI [1]. If patients present with advanced mesenteric ischemia, they may present in septic shock and with diffuse peritonitis.

A key component to diagnosis of AMI is a thorough history, which will often help to delineate the etiology of the AMI based on certain risk factors. Patients who present with mesenteric arterial embolism will commonly present with a history of atrial fibrillation, endocarditis, or recent myocardial infarction with poor ejection fraction. All of these conditions represent physiologic conditions that predispose the body to creating emboli that can lodge into the mesenteric vessels. In fact, one-third of these patients will have a history of a prior arterial embolization event [2]. Patients with mesenteric arterial thrombosis usually have a history of chronic mesenteric ischemia, in which they will complain of weight loss due to "food fear" which develops as a result of the postprandial abdominal pain patients will experience. Patients who present with NOMI will generally present as a critically ill patient and generally in patients that are experiencing a low flow state. This can be due to severe heart failure, hypovolemia, or use of vasopressors. Patients with mesenteric venous thrombosis may present with history of hypercoagulability (genetic predisposition, oral contraceptive use, history of malignancy, etc.). They may also present with other conditions that will contribute to venous stasis or inflammation such as pancreatitis, portal hypertension, sepsis, or trauma [1, 2].

Diagnosis

In addition to a thorough history and physical examination, laboratory work can be used as an adjunct in making the diagnosis. There is no specific biochemical marker for AMI, and thus, there is a limited role for these studies. The most common lab abnormality found is a metabolic acidosis secondary to elevated lactate, which occurs in 88% of patients according to one study [1]. Other biochemical markers have been studied such as D-dimer and intestinal fatty acid binding protein, but neither of these markers alone are specific enough to diagnose AMI.

Previously, the gold standard for diagnosis of AMI was catheter-based angiography due to its ability to assess both the arterial and venous phases. However, the less invasive option of computed tomography angiography (CTA) has become a popular diagnostic modality more recently as it can be more readily and quickly performed. With the advent of multidetector CTA, the etiology of the AMI (arterial occlusion versus venous) is more readily identified with the added benefit of detecting findings associated with possible irreversible ischemia such as dilated bowel, bowel wall thickening, pneumatosis intestinalis, portal venous gas, and free air if there is a perforation.

Currently, there are no prospective, randomized controlled studies that compare the diagnostic accuracy of CTA versus catheter-based angiography. Previous studies have determined the sensitivity and specificity of catheter-based angiography to be between 74–100% and 100%, respectively [4–10]. This is comparable to two recent meta-analyses that determined the sensitivity and specificity of CTA to be approximately 93% and 95%, respectively [11, 12]. Though diagnostic accuracy appears to be similar, use of CTA has many additional benefits to include that it is widely available, does not require the skill or expertise of a vascular surgeon or interventional radiologist, and can rule out other causes of acute abdominal pain—making it now the diagnostic imaging modality of choice.

Initial Management

Initial management of AMI should consist of fluid resuscitation, broad-spectrum antibiotics, and anticoagulation with heparin and attempts at restoration of normal physiology. Judicious fluid administration is important in order to optimize

perfusion to the bowel and prevent the patient from developing abdominal compartment syndrome. Vasopressors should be avoided if possible, though if necessary there are studies that show dobutamine, low-dose dopamine, and milrinone have less effects on mesenteric blood flow than other vasopressors. AMI patients are at high risk for developing infections due to loss of mucosal barrier and bacterial translocation. Prompt initiation of heparin for therapeutic anticoagulation, unless otherwise contraindicated, can help to mitigate progression of bowel ischemia. These patients should be monitored closely and ICU admission is often indicated.

Early initiation of therapeutic anticoagulation, especially in the case of mesenteric venous thrombosis, has been shown to be associated with improved outcomes [13]. However, there are no established guidelines regarding the dosing and use of anticoagulation in the setting of mesenteric ischemia. A few studies in the literature have cited using a 5000-unit bolus of heparin followed by a continuous infusion with titration to maintain an activated partial thromboplastin time (aPTT) in the range of two to three times normal (approximately 60–90 seconds) [14, 15]. Currently, there is no consensus data or statement available regarding the use of low-molecular-weight heparin versus heparin or other novel agents in the treatment of mesenteric venous thrombosis. Common practice is the utilization of intravenous heparin as it is easily monitored with aPPP and has an available reversal agent.

When to Operate

In any patient demonstrating signs of advanced ischemia such as peritonitis, hemodynamic instability, or radiographic findings consistent with perforation, immediate operative exploration is indicated. Revascularization and resection of necrotic bowel should be attempted, which will be discussed in further detail below.

Timely intervention is critical in the management of patients diagnosed with AMI. Studies have shown that there is a direct relationship between delayed diagnosis and bowel viability. A large retrospective review demonstrated that in patients with less than 12 hours of symptoms, 100% of patients had viable bowel upon exploration [16].

In general, patients with arterial emboli and arterial thrombosis will need some sort of intervention to treat the occlusive lesion. Endovascular or open approaches may be considered for these patients. In highly specialized centers, combined endovascular and open approaches may be taken. In deciding which approach to utilize, one must consider the duration of symptoms, etiology, location and length of occlusive lesion, medical comorbidities of the patient, and overall clinical status.

In patients diagnosed with NOMI and mesenteric venous thrombosis, medical management is usually utilized first unless there are signs and symptoms concerning for advanced ischemia, in which case intervention must be taken. Patients who are undergoing medical management should be monitored closely and if there are any signs of worsening ischemia, should be taken for intervention.

What Approach to Take

Traditionally, patients diagnosed with AMI were taken urgently to the operating room for open revascularization and resection of nonviable bowel. However, with recent advances in endovascular approaches, utilization of endovascular approaches has increased significantly (from 11.9% in 2005 to 30% in 2009, in one study) [16]. The data is limited and conflicting regarding success rates and complications associated with endovascular approaches, but it has been described with reasonable success in the literature.

The theoretic advantages of an endovascular versus open approach include reducing the effects of the initial ischemic insult through faster revascularization when compared to open procedures. In theory if revascularization occurs through an endovascular approach prior to operative exploration, a period of adequate resuscitation may be given before examining the bowel. A large retrospective review that compared endovascular

intervention versus open intervention showed a significantly reduced mortality (24% vs 39%), decreased need for bowel resection (14% vs 33%), and shorter hospital stay [16]. This is confirmed by findings from several other case series [17, 18] and by a large retrospective review of NSQIP data. This study showed that there was a decreased risk of mortality and that 59% of patients that underwent endovascular intervention avoided an open procedure [18]. However, a prospective study performed at a specialized intestinal stroke center in France showed that 82% of patients that underwent initial endovascular revascularization for early AMI eventually required an open procedure at their institution [19]. Given the lack of prospective data available, it is difficult to say at this point if endovascular interventions alone are appropriate for treatment of AMI, though the approach is increasing in popularity and more data is surfacing in support of endovascular interventions for patient presenting without evidence of advanced ischemia.

In terms of endovascular interventions, the type of intervention will vary with the etiology of the AMI. If arterial embolization is suspected, then selective injection of thrombolytic agents, aspiration thrombectomy, and mechanical thrombectomy can be performed [2, 3]. Typical thrombolytic agents used include tissue plasminogen activator (tPA) or urokinase. Aspiration thrombectomy involves removal of a thrombus or embolus by suction. Mechanical thrombectomy can be performed utilizing specialized systems (such as the Rotarex or Penumbra) to remove the thrombus. A retrospective study conducted by Arthurs et al. demonstrated successful endovascular treatment of arterial embolization in 87% of cases with a significantly lower mortality rate than patients who underwent open approach (36% vs 50%) [3, 16, 17]. In thrombotic lesions, because there is often an area of atherosclerotic stenosis that is involved, percutaneous transluminal angioplasty (PTA) and stent placement may be performed in an antegrade or retrograde fashion. In the treatment of NOMI, endovascular therapies represent a key component of treatment. A bolus of papaverine, a potent vasodilator, can be directly injected into the SMA. A bolus dose of 45–60 mg is typically given, followed by a continuous infusion. For mesenteric venous thrombosis, multiple approaches can be taken to infuse thrombolytics. Percutaneous transhepatic or transjugular intrahepatic approaches allow for direct access to central clots. Alternatively the SMA approach can allow for indirect access [3]. Transhepatic approach can be taken, which is helpful for central clot burden within the mesenteric trunk; however, this is associated with increased incidence of intraperitoneal bleeding and liver injury [2].

In any endovascular case, a completion angiogram is performed to assess the inflow following interventions. If there is still poor flow following the angiogram or the patient continues to clinically worsen, open operative intervention is considered at this time.

In an open approach, revascularization and inspection of the bowel can be performed intraoperatively. Approach to revascularization will depend on the etiology of the ischemia. For arterial embolism, open embolectomy can be performed. In the case of arterial thrombosis, typically bypass is performed by a retrograde or antegrade fashion. Autologous-reversed saphenous vein can be used as a bypass conduit versus PTFE. In the setting of gross contamination, vein graft is obviously preferred to avoid potential graft infection if PTFE is utilized.

What to Resect

In any case of AMI, revascularization (whether it be through endovascular or open approach) should be ideally performed prior to bowel resection. If there are segments of the bowel that are obviously necrotic or perforated, these sections of the bowel can be resected prior to revascularization; however, the general practice is to allow for revascularization and reassessment of the bowel to avoid unnecessary resection of potentially salvageable bowel and to spare the patient from potentially developing short-gut syndrome.

Following surgical revascularization, inspection of the bowel should take place, and any areas with irreversible ischemia should be

resected. Ischemic bowel can be determined based on clinical appearance of the bowel. Intraoperative evaluation of bowel viability can be assessed with intravenous fluorescein dye and Wood's lamp or Doppler, though it is important to note there is no substantial evidence to support the use of these adjuncts in the assessment of marginalized bowel [20].

If revascularization is performed successfully and there is low suspicion for bowel necrosis, patients may be closely monitored with ongoing resuscitation. If they show no signs of clinical improvement, or worsening, then they should return to the operating room for laparotomy and assessment of bowel [21].

Principles of damage control surgery are often utilized if an open approach is taken and the patient is hemodynamically unstable. The patient can be left in discontinuity, and a temporary closure may be put in place until a second-look laparotomy can be performed in 24–48 hours after resuscitation and physiologic optimization. Temporary closure should be considered in any case given that it is common practice to plan for a second-look laparotomy. If primary closure is decided upon at the time of index operation, abdominal compartment pressure should be monitored.

If a vascular surgeon or interventional radiologist is unavailable, it is reasonable to resect necrotic bowel first, leave the patient with a temporary abdominal closure, further resuscitate the patient in the ICU, and arrange transfer for urgent interventional angiography or vascular surgery. Preferably, revascularization is performed first to prevent further ischemia from developing. Most commonly, the source of occlusion will be at the origin of the SMA; therefore, an open SMA embolectomy can be attempted prior to bowel resection [22].

When to Reoperate

As noted above, a second-look laparotomy is often necessary following initial revascularization and resection of ischemic bowel. This decision to return to the operating room is generally based on the surgeon's initial impression regarding appearance of the bowel on index surgery and on the patient's clinical status following index surgery. Assessment of the bowel on initial surgery is often inaccurate, thus prompting the inclination to reexamine the bowel after a period of resuscitation and stabilization. In general, a higher percentage of patients will undergo bowel resection at second look than at index presentation (53% vs 31%) [23]. In two retrospective reviews, 70–80% of patients underwent second-look laparotomy, and 14% underwent a third-look laparotomy in one study. 28–40% of these patients that underwent additional laparotomy required additional bowel resection [24, 25]. This data highlights the importance of close interval reassessment of the bowel to reduce the morbidity and mortality associated with missed ischemic bowel.

There is some literature that suggests a second-look laparoscopy can be reasonably performed in some patients. These authors cited reduced morbidity associated with re-laparotomy in patients that are often critically ill. The data primarily centers around utilization of second-look laparoscopy in the setting of NOMI, in patients that remain critically ill in the ICU. However there is a paucity of data regarding utilization of laparoscopy as a second-look intervention, and it is not a widely accepted practice to perform laparoscopy over laparotomy.

Conclusion

Acute mesenteric ischemia remains a difficult entity to diagnose; however, early recognition and intervention are keys to reducing the associated morbidity and mortality. With advances in endovascular techniques, both endovascular and open surgical techniques can be used for revascularization. Inspection and resection of the bowel should take place if there is concern for advanced ischemia. Second-look laparotomy is still a widely accepted practice due to high rates of ischemia detected on reassessment, necessitating further bowel resection. For those with limited

resources, damage control surgery can be done, and the bowel can be left in discontinuity. This would allow the patient to tolerate further resuscitation and stabilize the patient for transfer to a vascular surgeon and to a hospital setup for taking care of the higher acuity patients.

References

1. Bala M, et al. Acute mesenteric ischemia: guidelines of the World Society of Emergency Surgery. World J Emerg Surg. 2017;12:38. https://doi.org/10.1186/s13017-107-0150-5.
2. Stone J, Wilkins L. Acute mesenteric ischemia. Tech Vasc Interv Radiol. 2015;18(2):24–30.
3. Ierardi AM, et al. The role of endovascular therapy in acute mesenteric ischemia. Ann Gastroenterol. 2017;30:526–33.
4. Boley SJ, et al. Initial results from an aggressive roentgenological and surgical approach to acute mesenteric ischemia. Surgery. 1977;82(6):848–55.
5. Böttger T, et al. Value of preoperative diagnosis in mesenteric vascular occlusion. A prospective study. Langenbecks Arch Chir. 1990;375(5):278–82.
6. Clark RA, Gallant TE. Acute mesenteric ischemia: angiographic spectrum. AJR Am J Roentgenol. 1984;142(3):555–62.
7. Czerny M, et al. Acute mesenteric ischemia. Zentralbl Chir. 1997;122(7):538–44.
8. Naitove A, et al. Primary mesenteric venous thrombosis. Ann Surg. 1965;161:516–23.
9. Kaufman SL, et al. Superior mesenteric artery embolization: an angiographic emergency. Radiology. 1977;124(3):625–30.
10. Boos S, et al. Angiography of the mesenteric artery 1976 to 1991. A change in the indications during mesenteric circulatory disorders? Radiologe. 1992;32(4):154–7.
11. Menke J, et al. Diagnostic accuracy of multidetector CT in acute mesenteric ischemia: systematic review and meta-analysis. Radiology. 2010;256(1):93–101.
12. Cudnik MT, et al. The diagnosis of acute mesenteric ischemia: a systematic review and meta-analysis. Acad Emerg Med. 2013;20(11):1087–100.
13. Harnik IG, Brandt LJ. Mesenteric venous thrombosis. Vasc Med. 2010;15:407–18.
14. Kumar S, et al. Mesenteric venous thrombosis. N Engl J Med. 2001;345:1683–8.
15. Zhang J, et al. Acute mesenteric venous thrombosis: a better outcome achieved through improved imaging techniques and a changed policy of clinical management. Eur J Vasc Endovasc Surg. 2004;28(3):329–34.
16. Beaulieu R, et al. Comparison of open and endovascular treatment of acute mesenteric ischemia. J Vasc Surg. 2014;51(1):159–64.
17. Arthurs ZM, et al. A comparison of endovascular revascularization with traditional therapy for the treatment of acute mesenteric ischemia. J Vasc Surg. 2011;53(3):698–705.
18. Branco BC, et al. Endovascular therapy for acute mesenteric ischemia: an NSQIP analysis. Am Surg. 2015;81(11):1170–6.
19. Roussel A, et al. Revascularization of acute mesenteric ischemia after creation of a dedicated multidisciplinary center. J Vasc Surg. 2015;62(1):1251–6.
20. Bjork M, et al. Editor's choice – management of the diseases of mesenteric arteries and veins: clinical practice guidelines of the European Society of Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg. 2017;53(4):460.
21. Karkkainen JM, et al. Acute mesenteric ischemia (part II) – vascular and endovascular surgical approaches. Best Pract Res Clin Gastroenterol. 2017;31(1):27–38.
22. Acosta S. Surgical management of peritonitis secondary to acute superior mesenteric artery occlusion. World J Gastroenterol. 2014;20(29):2014.
23. Kougias P, et al. Determinants of mortality and treatment outcome following surgical interventions for acute mesenteric ischemia. J Vasc Surg. 2007;46:467–74.
24. Bjork M, et al. Revascularization of the superior mesenteric artery after acute thromboembolic occlusion. Br J Surg. 2002;89(7):923–7.
25. Ryer EJ, et al. Revascularization for acute mesenteric ischemia. J Vasc Surg. 2012;55(6):1682–9.

Radiology for Acute Mesenteric Ischemia

29

Bryan J. Stevens and Brian H. Ching

Introduction

Mesenteric ischemia is a medical condition that is precipitated by inadequate blood supply to the small intestine. The inadequacy of blood supply can lead to both reversible and irreversible injury to an affected small intestine segment. The ischemic injury progresses from cellular damage to intestinal necrosis and can ultimately cause death if left untreated with mortality rates between 30% and 90% [1, 2]. Mesenteric ischemia has both acute and chronic forms.

The acute form is associated with severe abdominal pain and can often result in death. The chronic form of mesenteric ischemia has a more gradual course and usually presents with gradually increasing postprandial, abdominal pain and unintentional weight loss. Inadequacy of blood perfusion to the small intestine can be due to a disruption of either venous or arterial blood supply. The disruption most commonly develops secondary to embolism and is followed by thrombosis, nonocclusive ischemia, and less frequently venous thrombosis. For patients with mesenteric venous thrombosis and nonocclusive mesenteric ischemia, treatment is most commonly a conservative measure unless the stage of ischemia is sufficiently advanced. In recent years, interventional radiology procedures have provided a potential lifesaving remedy to acute mesenteric ischemia (AMI) [1–4].

Epidemiology

Advanced age is a risk factor for mesenteric ischemia. Partially occlusive disease of the visceral arteries is a common finding in elderly patients and is due to atherosclerotic disease. Up to 10% of autopsy studies have shown atherosclerotic disease in the mesenteric vessels [5]. Females are affected more than males with a ratio of approximately 3:1 [6]. Other risk factors include smoking, hyperlipidemia, diabetes, and sedentary lifestyle [7]. The total number of deaths associated with AMI has declined from 12.9 to 5.3 per million from 2000 and 2012 [8]. Non-acute mesenteric ischemia can remain asymptomatic until two or more mesenteric vessels become involved secondary to the development of collateral vessels. The acute form typically involves acute thrombosis of the superior mesenteric artery (SMA).

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Relevant Anatomy

Imaging of the mesenteric viscera is commonly done using computed tomography or via angiography (Fig. 29.1). Table 29.1 is from the 2018 American College of Radiology Appropriateness Criteria in the imaging of acute mesenteric ischemia. Computed tomography angiography (CTA) is the preferred imaging modality for the assessment of acute mesenteric ischemia. At our institution, we prefer CTA over MRA given the faster acquisition time, less effect of respiratory artifact, and better assessment of atherosclerotic calcifications. MRA is useful in patients who are unable to receive iodinated contrast. A meta-analysis to determine the diagnostic accuracy of contrast agent-enhanced multi-detector computed tomography between 1996 and 2009 showed a pooled sensitivity of 93% and a pooled specificity of 96% [9]. The sensitivity and specificity of 3D contrast MRA are approximately 95% [10]. Limitations of MRI include limited number of MRI-compatible pacemakers, claustrophobia, lengthy examination time, and the inability to assess patients with mesenteric stents secondary to artifact.

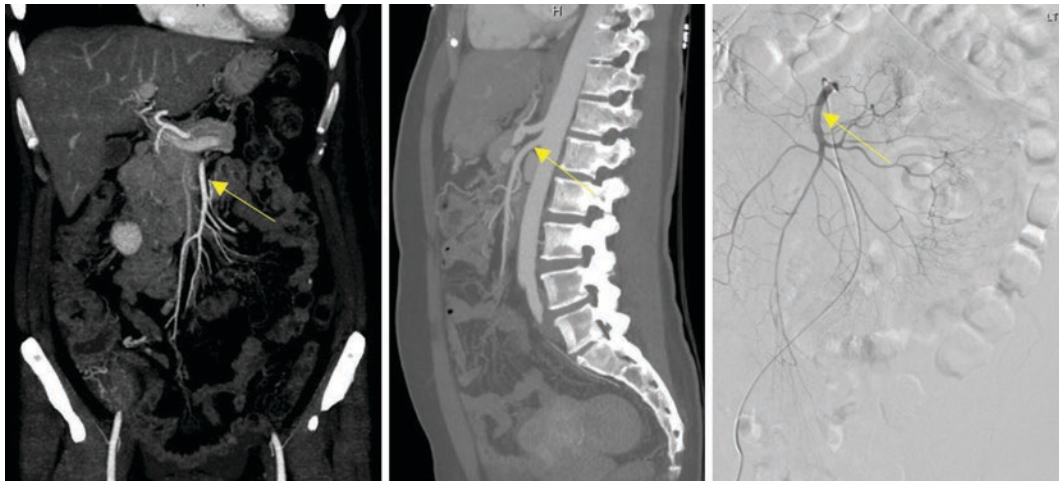

Fig. 29.1 Normal CT and angiogram appearance of the superior mesenteric artery (arrows)

Table 29.1 American College of Radiology ACR Appropriateness Criteria® Imaging of Mesenteric Ischemia. Variant 1, suspected acute mesenteric ischemia. Initial Imaging. Revised 2018

Procedure	Appropriateness Category	Relative Radiation Level
CTA abdomen and pelvis with IV contrast	Usually Appropriate	☢☢☢
CT abdomen and pelvis with IV contrast	May Be Appropriate	☢☢☢
Anteriography abdomen	May Be Appropriate (Disagreement)	☢☢☢
MRA abdomen and pelvis without and with IV contrast	May Be Appropriate (Disagreement)	○
X-ray abdomen	May Be Appropriate	☢☢
US duplex Doppler abdomen	May Be Appropriate	○
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☢☢☢
MRA abdomen and pelvis without IV contrast	Usually Not Appropriate	○

The relevant anatomy for AMI cases can be divided based upon the gut region supplied by specific arterial flow as well as the collateral flow.

- First, the foregut: Distal esophagus to the ampulla of Vater between the second and third portions of the duodenum supplied by the celiac artery with collateral connections from the pancreaticoduodenal arteries and far more rarely the arc of Buhler distally.
- Next, the midgut: Ampulla of Vater to the splenic flexure of the colon supplied by the SMA with collateral supply from pancreaticoduodenal arteries and occasionally the arc of Buhler proximally, the marginal artery of Drummond, and arc of Riolan distally (Figs. 29.2 and 29.3).
- The hindgut: Splenic flexure of the colon to the distal sigmoid colon supplied by the inferior mesenteric artery (IMA) with collateral supply from the marginal artery of Drummond proximally and the superior hemorrhoidal to middle hemorrhoidal arteries distally.
- Finally, the cloacal derivatives: Distal sigmoid colon to the anus supplied by branches of the internal iliac arteries with collateral supply from the middle and superior hemorrhoidal arteries proximally.

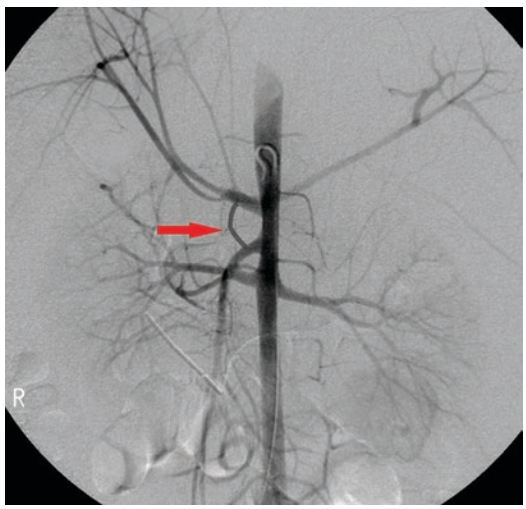

Fig. 29.2 Depiction of arc of Buehler (arrow)

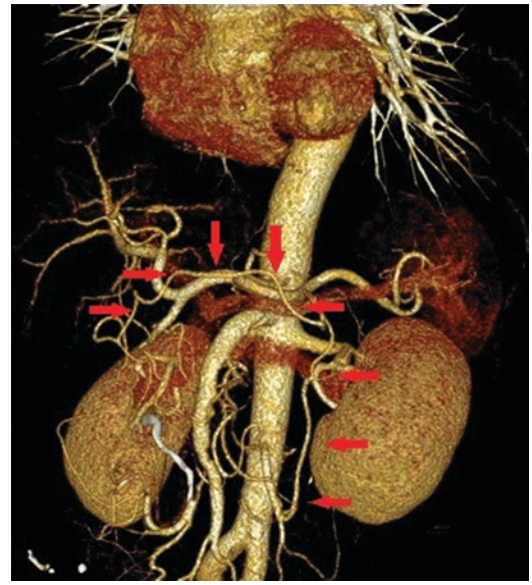

Fig. 29.3 Arc of Riolan (arrows)

Of note, the arc of Riolan is different from other collateral flows as it may provide flow in either direction between the proximal SMA and IMA. The flow to these regions accounts for 10–35% of resting cardiac output and can increase by as much as 200% postprandially [3].

The SMA is the most commonly affected artery in cases of AMI and its branches are often the ischemic culprit. The SMA originates from the anterior aspect of the abdominal aorta inferior to the celiac trunk. In adults it typically arises at the L1 vertebral level. The SMA then traverses in an anteriorly inferior manner and then passes posteriorly to the neck of the pancreas and splenic vein. Typically the superior mesenteric vein can also be found running to the right of the SMA. Once the SMA passes from under the neck of the pancreas, it then begins diverging into smaller branches. The first branch is the inferior pancreaticoduodenal artery, which supplies the head of the pancreas and the inferior portion of the duodenum. Next are various intestinal arteries that supply parts of the ileum and jejunum. The SMA also has three colic branches; however, some patients may not possess all three due to anatomic variance. The first colic branch is the ileocolic artery which supplies the distal ileum,

cecum, and appendix. Next is the right colic artery which typically supplies the ascending colon. Finally, the middle colic artery arises from the SMA and supplies the transverse colon. It is important to note that many patients may lack an artery and receive collateral supply from one or more alternative arteries [3].

Acute Mesenteric Ischemia

The advent of minimally invasive techniques and improved diagnostic capabilities has allowed for additional treatment options for patients with AMI. Although there is significant mortality and morbidity associated with AMI, it has become one of the leading diagnoses that is successfully treated with early endovascular technique. The majority of AMI cases are caused by arterial emboli from cardiac arrhythmias, such as atrial fibrillation, with one study quoting approximately 40–50% attributable to cardiac emboli [11]. Arterial thrombosis is the next most common cause for AMI where preexisting atherosclerotic lesions create a nidus for acute occlusion. This thrombosis accounts for roughly 25% of cases. The role of local thrombolysis is aimed at early intervention to prevent the formation of irreversible necrosis via prolonged ischemia due to embolic or thrombotic events. For this reason, in stable patients with AMI, it is paramount to acquire CT angiography to confirm diagnosis and follow with prompt intervention [3, 4, 11, 13]. The notable other forms of mesenteric ischemia are nonocclusive mesenteric ischemia (accounting for approximately 20% of cases) and venous mesenteric thrombosis (accounting for approximately 10% of cases) [12].

Clinical Presentation

The diagnosis of acute mesenteric ischemia is relatively uncommon, and subsequently recording data for its prevalence has been challenging. Many patients present with suspected AMI and are later found to have an alternative diagnosis. One study found that as little as 19% of suspected cases of AMI were actually confirmed to have AMI. Patients greater than the age of 65 are seemingly at the greatest risk of developing AMI with 20% of suspected cases, although patients between the ages of 35 and 65 accounted for 18%. One study indicates that alternative broad diagnoses such as gastrointestinal, hepatopancreaticobiliary, cardiopulmonary, genitourinary, and vascular conditions are far more common in patients less than the age of 35. Recent research indicates that there are no significant differences in diagnosis of AMI between men and women. Interestingly, one study concluded that inpatients were more likely to develop AMI than patients presenting to the emergency department [13].

Treatment Overview

Originally the treatment of mesenteric ischemia was limited to open surgical repair; however, in the last 15 years, development of endovascular procedures has provided an additional option for this disease. Endovascular treatment began with percutaneous dilation of the SMA in 1980 and sent placement in 1992 [14]. Catheter-directed thrombolysis has been a commonly used technique in SMA thrombolysis. However, given the long treatment interval needed to achieve lysis, suction embolectomy is becoming more popular [13].

Although new techniques have emerged that may benefit the patient, it is important to identify the cases that will provide maximal benefit with little risk. Patients with advanced stage disease, frank peritonitis, or hemodynamic instability may not benefit from an endovascular technique and are better suited for laparotomy.

With enhanced imaging techniques, the role of endovascular techniques for AMI has been instrumental for reducing morbidity and mortality for affected patients. Intestinal surgery for AMI is aimed at resecting necrosis. If the diagnosis is made before this process occurs, then endovascular techniques aimed at re-vascularizing the acute thrombosis can provide significant benefit. One study found that active endovascular-first strategy resulted in a 42% overall mortality rate – which is in stark contrast to a similar study in

Finland that produced a mortality rate of 82% without this intervention [15]. However, many studies have concluded that when AMI is significantly severe or present in fragile patients, supportive care is often the best therapy due to the futility of any surgical intervention [4, 13, 15].

Endovascular Treatments

The technical treatment of AMI has multiple endovascular modalities available. The most common are as follows: catheter-directed thrombolysis, suction embolotherapy, balloon angioplasty with or without stenting, and mechanical vacuum-assisted removal (AngioVac). To perform these procedures, the patient is positioned on the table, and sedation is typically required. Sterile technique is used to access the desired entry point, and a small incision is made at the access site, usually at the common femoral artery using the Seldinger technique [2, 16–19].

Catheter-directed thrombolysis is a technique that aims to improve blood flow by essentially dissolving obstructive blood clots. This technique requires a catheter to be advanced endovascularly from the accessed site into the SMA. The procedure is completed with cone beam CT-guided imagery to ensure proper placement. The catheter is then advanced to the area of poor circulation. Contrast is then injected through the catheter, and images are taken to precisely pinpoint the exact area of occlusion. Tissue plasminogen activator (tPA) is most commonly injected through an infusion catheter over the course of several hours to dissolve the embolus. Continued monitoring and imaging are carried out throughout the procedure to ensure revascularization is achieved. Once complete, the catheter is removed, and hemostasis is achieved at the access site via manual compression or a mechanical closure device [16, 19].

Suction embolotherapy has emerged as an additional option with the benefit of rapid restoration of blood flow to the bowel. This technique involves advancing a suction catheter through the incision site and traversing the circulatory system to the ischemic area of interest. Arterial access is again achieved using the Seldinger technique, usually through a common femoral or brachial artery approach. A sheath may or may not be used; however, many angiographers use them due to the necessity of multiple catheter changes. Imaging is vitally important for locating the area of interest, and digital subtraction angiography (DSA) has provided fast and accurate diagnoses in acute situations. End-hole catheters are utilized with an inner diameter and taper large enough to prevent occlusion by the embolic clot. Suction is then applied to the catheter and the clot is then removed [2, 18].

Balloon angioplasty is a third option. A guidewire is navigated to the area of occlusion, and a balloon catheter is then placed over the wire to reach the site. The stenotic area is then expanded via the balloon catheter. The process of inflating and deflating the balloon may be repeated multiple times to achieve the desired expansion of the vessel. As the balloon is inflated, the occlusive material is compressed against the arterial wall. Once this has been achieved, the patient may need a stent to maintain the scaffold structure of the vessel. Balloon-mounted stents are most commonly used. Once the balloon is inflated, the stent is then expanded on the arterial wall and subsequently left in place after the balloon is deflated [2, 19].

AngioVac or *mechanically assisted vacuum-assisted cannulation* is a relatively new technique that utilizes an external centrifugal pump to remove the embolic material. This procedure requires two insertion sites, one for the AngioVac cannula and one for the reinfusion cannula. A 22 French cannula with an expandable funnel tip is navigated to the ischemic site. Once imaging has confirmed that the tip is proximal to the embolus, the pump is engaged creating a vacuum. The embolus is removed externally, and the blood is reinfused after external filtration of the occlusive materials [2, 20].

Vasospasm has been cited as a cause of nonocclusive mesenteric ischemia. Continuous intra-arterial infusion of *vasodilator drugs* into the SMA has become a therapeutic option, although there is no strong evidence that this intervention prevents vasospasm [1]. Intravenous rather than

intra-arterial prostaglandin E1 (PGE1) has demonstrated efficacy in treatment of this vasospasm [21].

Outcomes

The complications from endovascular treatment of AMI range from relatively mild to death. A notably common complication of endovascular treatment of AMI is worsening of bowel necrosis. This is partly due to the inability of the interventional radiologist to visually inspect the bowel. Perhaps the greatest argument for treatment of AMI with an open technique is to allow for visual assessment of potentially affected bowel and signs of necrosis.

Despite early thrombolysis with an endovascular technique, the patient may still suffer bowel necrosis due to the obscure signs and distracting presentation of these critical patients. The rates of bowel resection remain quite high despite the higher rates of treatment of AMI with an endovascular technique [3]. As such the clinicians must still be wary of the need for surgical intervention to assess bowel viability.

Medical assessment of bowel necrosis has historically been monitoring lactate levels. However, several studies have found this lab value to be inaccurate at predicting the need for bowel resection (13). Yet, the amount of patients receiving bowel resection due to mesenteric ischemia has steadily declined since the late 1980s. Multiple studies have found that in the late 1980s, bowel resection rates were approximately 70%, and most recent data suggests 20% to 50% are receiving bowel resections (15). This is most likely attributed to the fact that diagnostic modalities are better at detecting AMI and the endovascular techniques available have provided prompt reperfusion that effectively prevents necrosis. The presentation of AMI is not standardized among patient populations, and there is a multifaceted approach to managing each case with personalized medical needs. However, it is clear that as both radiologic diagnostics and interventional techniques have evolved, patients are experiencing better outcomes [3, 13, 15].

Despite the advantages of endovascular techniques, there are complications to include access site injury (hematoma or pseudoaneurysm) and potential contrast agent-related complications (contrast agent-induced nephropathy and/or allergic reactions). In patients undergoing papaverine or vasodilator therapy, systemic hypotension may develop when the infusion catheter inadvertently disengages from the SMA. Thrombolysis-associated complications include access site bleeding, embolization, and stroke [22].

If angioplasty or stent placement is performed, vessel injury or distal embolization can occur. Factors associated with higher rates of distal embolization are mesenteric occlusion, severe calcification, and lesion length >30 mm [23].

Conclusion

Advanced radiologic modalities aid in the diagnosis of AMI and endovascular techniques can both treat AMI and reduce the need for surgery while improving overall morbidity and mortality. The decision to involve endovascular techniques requires a multidisciplinary approach with a vascular surgeon, a general surgeon, an interventional radiologist, and a critical care physician. As early intervention is best, it is recommended that appropriate consults be made when the suspicion arises and a CTA be obtained quickly to confirm the diagnosis. Patients who are in extremis are more likely to benefit from surgery or supportive care. Interventional and endovascular techniques seem to be best suited in patients who respond to resuscitation or who are hemodynamically normal; however, these patients still require prompt endovascular intervention and/or surgery to determine the viability of the bowel.

References

1. Bala M, Kashuk J, Moore EE, Kluger Y, Biffl W, Gomes CA, Ben-Ishay O, Rubinstein C, Balogh ZJ, Civil I, Coccolini F, Leppaniemi A, Peitzman A, Ansaloni L, Sugrue M, Sartelli M, Di Saverio S, Fraga GP, Catena F. Acute mesenteric ischemia: guidelines

of the world Society of Emergency Surgery. World J Emerg Surg. 2017;12:38.
2. Lerardi AM, Tsetis D, Sbaraini S, Angileri SA, Galanakis N, Petrillo M, Patella F, Panella S, Balestra F, Lucchina N, Carrafiello G. The role of endovascular therapy in acute mesenteric ischemia. Ann Gastroenterol. 2017;30(5):526–33.
3. Sise MJ. Acute mesenteric ischemia. Surg Clin North Am. 2014;94(1):165–81.
4. Henes FO, Pickhardt PJ, Herzyk A, Lee SJ, Motosugi U, Derlin T, Lubner MG, Adam G, Schon G, Bannas P. CT angiography in the setting of suspected acute mesenteric ischemia: prevalence of ischemic and alternative diagnoses. Abdom Radiol (NY). 2017;24(4):1152–61.
5. Foley MI, Moneta GI, About-Zamzam AM Jr, et al. Revascularization of the superior mesenteric artery alone for treatment of intestinal ischemia. J Vasc Surg. 2000;32(1):37–47.
6. Acosta S, et al. Modern treatment of acute mesenteric ischaemia. Br J Surg. 2014;101(1):e100–8.
7. Paterno F, et al. The etiology and pathogenesis of vascular disorders of the intestine. Radiol Clin N Am. 2008;46(5):877–85.
8. Zettervall SL, Lo RC, Soden PA, et al. Trends in treatment and mortality for mesenteric ischemia in the United States from 2000–2012. Ann Vasc Surg. 2016;42:111–9.
9. Menke J. Diagnostic accuracy of multidetector CT in acute mesenteric ischemia: systematic review and meta-analysis. Radiology. 2010;256(1):93–101.
10. Schaefer PJ, Pfarr J, Trentmann J, et al. Comparison of noninvasive imaging modalities for stenosis grading in mesenteric arteries. Rofo. 2013;185:628–34.
11. Jia Z, Jiang G, Tian F, Zhao J, Li S, Wang K, Wang Y, Jiang L, Wang W. Early endovascular treatment of superior mesenteric occlusion secondary to thromboemboli. Eur J Vasc Endovasc Surg. 2014;47(2):196–203.
12. Bobadilla JL. Mesenteris ischemia. Surg Clin North Am. 2013;93(4):925–40, ix.
13. Karkkainen JM, Acosta S. Acute mesenteric ischemia (Part I) – incidence, etiologies, and how to improve early diagnosis. Best Pract Res Clin Gastroenterol. 2017;31(1):15–25.
14. Finch IJ. Use of the Palmaz stent in ostial celiac artery stenosis. J Vasc Interv Radiol. 1992;3(4):633–5. discussion 636–7
15. Karkkainen JM, Acosta S. Acute mesenteric ischemia (Part II) – vascular and endovascular surgical approaches. Best Pract Res Clin Gastroenterol. 2017;31(1):27–38.
16. Bjornsson S, Bjorck M, Block T, Resch T, Acosta S. Thrombolysis for acute occlusion of the superior mesenteric artery. J Vasc Surg. 2011;54(6):1734–42.
17. Sugimoto K, Hofmann L, Razavi M, Kee S, Sze D, Drake M, Semba C. The safety, efficacy, and pharmacoeconomics of low-dose alteplase compared with urokinase for catheter-directed thrombolysis of arterial and venous occlusions. J Vasc Surg. 2003;37(3):512–7.
18. Suzuki M, Mizunari T, Iwamoto N, Morita A. Embolectomy through aneurysm wall for iatrogenic occlusion of M1 portion during coil embolization: technical note for transaneurysmal embolectomy. World Neurosurg. 2018 Jun;114:113–6.
19. Colleran R, Kastrati A. Percutaneous coronary intervention: balloons, stents and scaffolds. Clin Res Cadiol. 2018;107(suppl2):55–63.
20. Pasha AK, Elder MD, Khurram D, Snyder BA, Movahed MR. Successful management of acute massive pulmonary embolism using Angiovac suction catheter technique in a hemodynamically unstable patient. Cardiovasc Revasc Med. 2014 Jun;15(4):240–3.
21. Mitsuyoshi A, Obama K, Shinkura N, et al. Survival in non-occlusive mesenteric ischemia: early diagnosis by multidetector row computed tomography and early treatment with continuous intravenous high-dose prostaglandin E(1). Ann Surg. 2007;246(2):229–35.
22. Stone JR, Wilkins LR. Acute mesenteric ischemia. Tech Vasc Interv Radiol. 2015;18(1):24–30.
23. Oderich GS, Macedo TA, Malgor RD, Bower TC, Vritiska T, Duncan AA, et al. Natural history and predictors of mesenteric artery in-stent restenosis in patients with mesenteric ischemia. J Vasc Surg 2009;49(Suppl 1):A1–22. S1–58, e1–2

Part X

Acute Pancreatitis

Acute Pancreatitis

30

Andrew Han and Mark A. Gromski

Epidemiology

The incidence of acute pancreatitis in the United States ranges from 5 to 30 per 100,000 and appears to be increasing [1]. Acute pancreatitis is common in the United States, representing the third most common inpatient GI diagnosis [2]. The rising incidence likely reflects the increase in alcohol use as well as obesity, which increases the risk of gallstones. Acute pancreatitis therefore represents a large burden for healthcare in America, reaching over $2.6 billion per year in inpatient costs alone [2]. As such, the appropriate and timely diagnosis and management of acute pancreatitis remain critical, not just for patient outcomes but also for healthcare resources.

Definition

Pancreatitis is defined as acute or chronic, depending on a number of factors. The diagnosis of acute pancreatitis is made when at least two of the following criteria are met: characteristic abdominal pain, serum amylase or lipase >3 times the upper limit of normal, and/or radiographic evidence of pancreatitis on cross-sectional imaging [3]. Chronic pancreatitis may be detected by ductal or parenchymal abnormalities on imaging or diagnostic studies that are representative of chronic architectural changes of the pancreas. The scope of this chapter will focus on acute pancreatitis. Acute pancreatitis comprises two phases: early and late. The early phase of acute pancreatitis represents the first 2 weeks after disease onset, and the late phase can encompass weeks to months afterward [3].

Disease Severity

Once acute pancreatitis has been diagnosed based on the above criteria, it is often prudent to determine the severity of the pancreatitis. The Revised Atlanta Criteria represents the most commonly accepted and used classification to distinguish disease severity as mild, moderately severe, or severe. Mild pancreatitis is defined by no organ failure and no local nor systemic complications. Moderately severe and severe acute pancreatitis are defined by the presence of systemic and/or local complications, with moderately severe defined as limited to <48 hours of systemic complications and severe representing >48 hours of systemic complications. Systemic complications include organ failure and/or exacerbation of a

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chronic medical condition like heart failure or chronic obstructive pulmonary disease [4]. Local complications include peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocyst formation, and walled-off necrosis (sterile or infected) [3]. Eighty to eighty-five percent of acute pancreatitis episodes are mild, are interstitial, and resolve within 1 week without any significant sequelae. Interstitial pancreatitis manifests as homogeneous normal enhancement on a contrast-enhanced CT scan, indicating undisrupted perfusion to the gland (Fig. 30.1). By definition, the presence of any necrosis constitutes at least moderately severe acute pancreatitis. Patients who develop severe necrotizing pancreatitis, manifested as persistent organ failure, face up to 30% risk of mortality, contrasted with an overall case fatality rate of 5% for all acute pancreatitis [5]. Necrotizing pancreatitis appears as low attenuation on contrast-enhanced CT, indicating areas of hypoperfusion (Fig. 30.2). Given the high risk of potential mortality with severe pancreatitis, several markers have been studied to predict progression to severe acute pancreatitis. The most useful predictors appear to be elevated blood urea nitrogen (BUN), serum creatinine, and serum hematocrit, or more specifically, the failure to return to normal ranges in spite of adequate fluid resuscitation [6]. Besides the Atlanta Classification, several scoring systems to measure disease severity exist, such as Ranson's criteria, Bedside Index for Severity in Acute Pancreatitis (BISAP), and the Acute Physiology and Chronic Health Evaluation (APACHE-II) scale. These scales, however, are used primarily for research categorization and are of attenuated clinical utility due to high false-positive rates and/or complexity [7].

Risk Factors

Gallstones are the most common cause of acute pancreatitis, representing 40% of cases of acute pancreatitis. In context, the vast majority of patients with cholelithiasis remain asymptomatic, and cholelithiasis is typically identified incidentally. Only 3–7% of patients with cholelithiasis will develop acute pancreatitis. Behind gallstones, alcohol is the second most common cause with 30% of cases being attributed to it. However, as the prevalence of excessive alcohol use continues to rise in America, the number of cases of alcohol-related acute pancreatitis is likely to rise [8]. While gallstones are the most common cause of acute pancreatitis, the physiology can be applied broadly. The mechanism by which

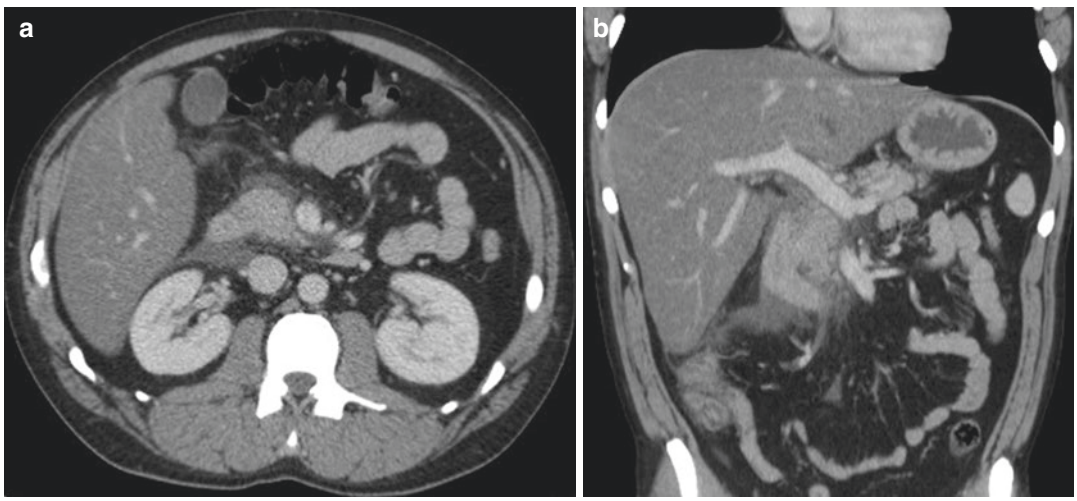

Fig. 30.1 Axial (**a**) and coronal (**b**) computed tomography (CT) scans demonstrating interstitial pancreatitis manifested as peripancreatic edema and peripancreatic stranding with homogenous enhancement of the pancreatic gland

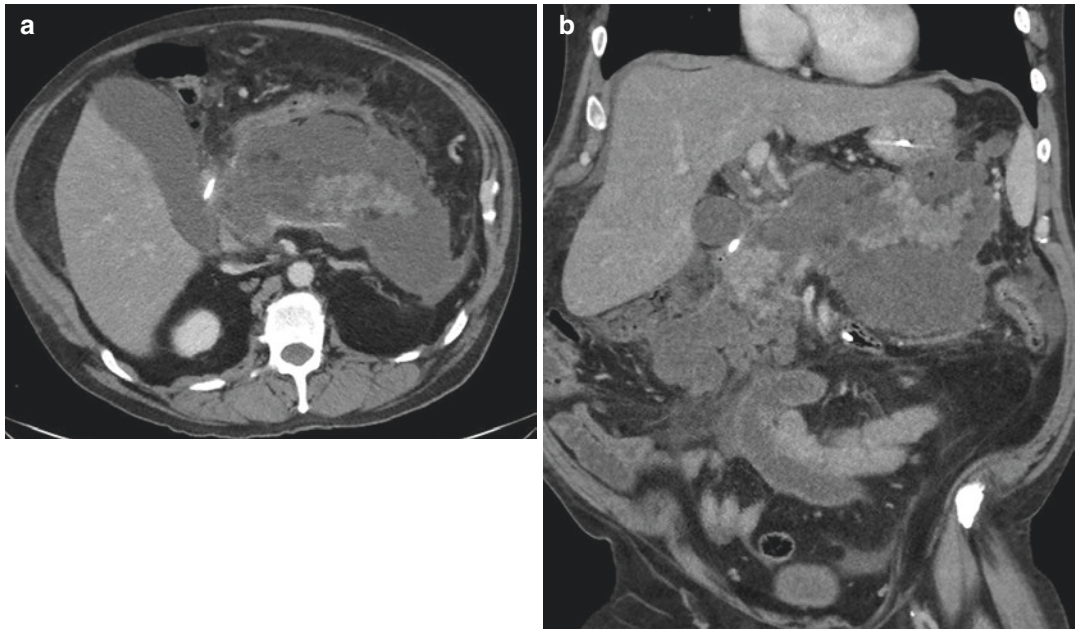

Fig. 30.2 Axial (**a**) and coronal (**b**) computed tomography (CT) scan demonstrating acute necrotizing pancreatitis. There are hypoenchancing regions of the pancreatic gland with acute necrotic collections in the pancreatic and peripancreatic areas

gallstones are thought to cause acute pancreatitis is by ampullary obstruction or periampullary edema from the passage of stones in the common bile duct. Therefore, smaller stones (less than 5 mm in diameter) are more likely to be culprits as they can more easily pass through the cystic duct and reach the ampulla. Aside from stones, malignancy can also cause obstruction of the pancreatic duct. Slow-growing tumors, such as main duct intraductal papillary mucinous neoplasms (IPMN) or ampullary neoplasms, can initially present with acute pancreatitis due to obstruction of the pancreatic duct. Other malignancies, such as metastatic disease from lung cancer, can lead to external compression of the ducts (Table 30.1).

Table 30.1 Risk factors for acute pancreatitis

Gallstones
Obstruction caused by malignancy
Alcohol
Hypertriglyceridemia
Diabetes mellitus
Hypercalcemia
Infection (CMV, EBV, mumps, parasites: Ascaris, *Clonorchis*)
Hypotension/ischemia
Trauma
Genetic/hereditary
Post-ERCP
Pancreas divisum
Sphincter of Oddi dysfunction
Medications
Idiopathic

All told, gallstones and alcohol account for approximately 70% of the cases of acute pancreatitis. Other etiologies of acute pancreatitis include hypertriglyceridemia, drugs/medications, infection, autoimmune disorders, hypercalcemia, hereditary pancreatitis, and penetrating duodenal ulcers, though these are significantly less common. Drug-induced pancreatitis is thought to comprise less than 5% of all acute pancreatitis cases, but is relevant given the vast numbers of patients on chronic medications with increasing age. The list of drugs implicated in acute pancreatitis numbers in the hundreds; however, the most common drugs associated with acute pancreatitis include

azathioprine, ACE inhibitors, 5-ASA, valproic acid, and mesalamine [4, 9]. Drug-induced pancreatitis usually occurs within 1–2 months of initiating the drug, so adequately evaluating other triggers for acute pancreatitis is important to minimize risk of recurrent episodes due to untreated etiologies. Typically, if a patient has been on the medication for >6 months, then drug-induced pancreatitis is less likely. Comorbid conditions, which increase the risk of developing acute pancreatitis, include morbid obesity, diabetes, and tobacco abuse. Pancreas divisum, a congenital condition in which the pancreas fails to rotate and form a single pancreatic duct during embryologic development (Fig. 30.3), has been thought to be a potential causative risk factor for acute pancreatitis. Recent studies have found that pancreas divisum may be an associated finding that predisposes patients to developing acute pancreatitis when combined with certain genetic mutations [10]. Finally, a significant proportion of patients with previously determined idiopathic acute pancreatitis or idiopathic recurrent acute pancreatitis have been found to have sphincter of Oddi dysfunction [11, 12]. After a thorough diagnostic work-up, if the etiology of pancreatitis is not determined, these cases are termed idiopathic acute pancreatitis, and the proportion of people with idiopathic pancreatitis increases with patient age [4].

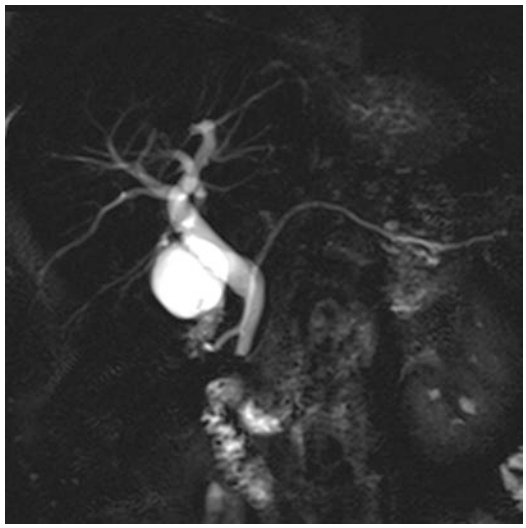

Fig. 30.3 Magnetic resonance cholangiopancreatography (MRCP) demonstrating pancreas divisum. The dominant dorsal duct of the pancreas is seen inserting into the duodenum in a discrete separate location (minor papilla) than the biliary insertion (major papilla)

Initial Management

Intravenous Fluids

Much of the disease course of acute pancreatitis is determined by the first 48–72 hours of management, and therefore accurate diagnosis, appropriate triage, and effective supportive care are critical to improving positive outcomes. Use of aggressive intravenous (IV) fluid resuscitation for the first 24 hours reduces mortality, and conversely, failing to identify acute pancreatitis or to initiate adequate fluid resuscitation on the onset of presentation can increase risk of poor outcomes [13]. Regarding which IV fluid to use, small studies have suggested lactated Ringer's solution may have therapeutic benefits over normal saline. However, there is insufficient evidence to support that any specific IV fluid is superior to another [14]. Regimens for initial IV fluid administration rates have been suggested, such as 5–10 mL/kg/hr., or 33% of body of total body weight, and commonly, rates such as 200–250 mL/hr are used in practice after an initial bolus. Given that elevated BUN and hematocrit are significant predictors for developing severe pancreatitis, these markers are typically monitored as surrogate indicators of adequate hydration [5]. Hydroxyethyl starch (HES)-containing IV fluids have also been studied in acute pancreatitis; however, the limited data available suggests HES may be harmful. Therefore, currently, consensus guidelines recommend against the use of HES fluids [14].

When using aggressive fluid resuscitation, clinicians must weigh the risks. The most immediate complication of aggressive IV hydration is fluid overload. As the population ages, the likelihood of pancreatitis patients having concomitant heart failure or renal insufficiency increases, raising the risks of prolonged aggressive resuscitation.

Therefore, close clinical monitoring and limiting aggressive hydration to the first 24 hours is important. Excessive fluid resuscitation presents risk of volume overload requiring intubation, intra-abdominal compartment syndrome, and death [15]. Even within the first 24 hours of resuscitation, IV hydration should be adjusted based on vital sign stability, BUN, and hematocrit.

Feeding

Long-standing paradigms of acute pancreatitis management include making patients *nil* per os (NPO) for the purposes of "pancreatic rest" as well as controlled introduction of clear liquids progressing to solid foods. However, more recent evidence supports early introduction of an oral diet within the first 24 hours of admission, even irrespective of type of diet in the case of mild acute pancreatitis, e.g., low fat vs. regular [16]. Early introduction of enteral nutrition is thought to be beneficial by promoting a healthy gut-mucosal barrier and thereby preventing bacterial translocation [17]. Symptoms such as abdominal pain and nausea do not need to necessarily be completely resolved prior to introducing an oral diet. However, in some cases, oral feeding may not be tolerated due to ongoing severe symptoms. Patients may be monitored for 3–5 days prior to initiating alternative nutrition, as early introduction of enteral tube feeding did not show any benefit over starting an oral diet after 3 days [18]. Furthermore, in the case of inability to tolerate oral diet, enteral tube feeding has shown clear benefit over parenteral nutrition in regard to reducing risks of complications in pancreatitis such as infected necrosis and single or multi-organ failure [14, 19]. Total parenteral nutrition (TPN) is associated with higher costs, higher risk of complications, and less clinical benefit [20]. Given the lack of benefit and increased risks associated with TPN, TPN should be reserved for when nutritional goals remain unmet despite trials of oral and enteral feeds (e.g., intestinal ileus or obstruction). Regarding whether to use nasogastric vs. nasojejunal feeding, the two appear to be similar without clear benefit for either modality. Intragastric feeding (orogastric, nasogastric) presents the benefit of more physiologic feeding, as well as more ease of tube placement, as compared to nasojejunal feeds. However, nasojejunal feeding may be preferred due to decreased risk of adverse events such as aspiration, especially in critically ill patients with severe pancreatitis who are intubated or who may have duodenal edema or obstruction from the acute pancreatitis [21].

Antibiotics

Decades ago, prophylactic antibiotics for severe acute pancreatitis were previously believed to reduce risk of infected necrosis as well as mortality. However, more recent, higher-quality studies have failed to demonstrate any benefit in overall mortality or risk of developing infected necrosis [22]. Therefore, unless strong evidence of infected necrosis exists, antibiotics should not be used, despite the presence of necrotizing pancreatitis or severe acute pancreatitis. Antibiotics have no role in the management of mild acute pancreatitis, unless for other concomitant infections. Unnecessary use of antibiotics increases the risk of comorbidities such as *Clostridium difficile* infection, drug-induced liver injury, allergic reactions, or development of resistant organisms.

Role of ERCP

Endoscopic retrograde cholangiopancreatography (ERCP) is an endoscopic procedure which allows for access to the pancreaticobiliary ductal anatomy. Fluoroscopic and endoscopic imaging guide therapeutic maneuvers. The role of ERCP in acute biliary pancreatitis is in the case of concurrent cholangitis (fever, jaundice, right upper quadrant pain) or persistent biliary obstruction as evidenced by continued direct bilirubinemia >5 mg/dL [23]. Other indications for ERCP include confirmed choledocholithiasis on imaging. With improvements in magnetic resonance imaging, the magnetic resonance cholangiopancreatography (MRCP) can help identify anatomy of the ducts, helping to provide a plan for ERCP

in the case where the index of suspicion for choledocholithiasis is moderate but not high. ERCP, while providing potential for immediate relief of biliary obstruction causing continued clinical deterioration, does carry risks, even in the hands of the most skilled endoscopists. Risks of ERCP include post-ERCP pancreatitis, which is reduced by the use of periprocedural rectal indomethacin and the use of prophylactic temporary pancreatic duct stents. Other potential risks of ERCP include post-sphincterotomy bleeding, infection, and perforation [23].

After ERCP, a sphincterotomy or temporary biliary stent can help to prevent recurrent episodes if there is incomplete clearance of stones in the biliary tree. However, cholecystectomy for appropriate patients is recommended to prevent recurrent gallstone pancreatitis. In the case of mild pancreatitis, the surgeon does not have to wait for the pancreas to recover, and the cholecystectomy should be done during the same admission. In the cases of moderate and severe pancreatitis, however, a waiting period (often up to 6 weeks) may be recommended until the pancreatic inflammation is resolved and the patient has recovered, prior to cholecystectomy.

The Step-Up Approach

In the late phase of pancreatitis, local complications need to be monitored for the need for interventional procedures. Acute pancreatic or peripancreatic fluid collections (APFC) should not be routinely accessed and drained unless they are clearly infected (i.e., air in collection on cross-sectional imaging), as the fluid collections may resolve spontaneously. In the case of an infected acute pancreatic fluid collection, the next step-up is a percutaneous approach done by an interventional radiologist. If the acute pancreatic or peripancreatic necrotic collections (ANC) are sterile, a waiting period is again recommended. In the early stages, typically viewed as within 4 weeks of development, the acute necrotic collections are comprised of heterogeneous material, and therefore no clear delineation can be made between necrosis and healthy pancreatic parenchyma. However, after a period of 4 weeks on average, the semisolid heterogeneous collections become more liquid and encapsulated by a rim, which is termed walled-off necrosis (WON) [4]. Similarly, acute pancreatic fluid collections will become encapsulated if they do not resolve spontaneously first, thereby becoming pseudocysts. At this point, if uninfected WON or pseudocysts are causing symptoms, drainage approaches using percutaneous, then endoscopic, and then, finally, surgical techniques are available. This is called the "step-up approach." Newer lumen-apposing metallic stents have made endoscopic transgastric or transduodenal access and drainage of pseudocysts and WON technically easier. Thus, there is some debate currently whether the first "step-up" of a mature WON or pseudocyst should be performed endoscopically or percutaneously – both are likely viable first steps depending on the location of the collection and local expertise. Surgery using minimally invasive approaches including VARD (video-assisted retroperitoneal debridement) and percutaneous or endoscopic approaches (Fig. 30.4) prior to open necrosectomy are preferred. These decisions should be approached in a multidisciplinary manner with the surgeon, endoscopist, interventional radiologist, internist, and perhaps the intensivist in attendance. This may vary based on local expertise [24, 25]. While direct comparison data between endoscopic and open surgical debridement is lacking, small studies investigat-

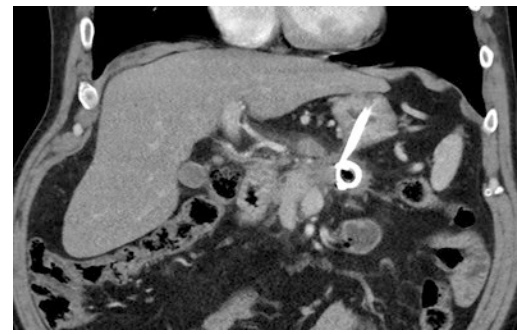

Fig. 30.4 Coronal computed tomography (CT) scan demonstrating transgastric double pigtail stent traversing a previously performed endoscopic cystgastrostomy, with one pigtail in the gastric lumen and the second draining a peripancreatic collection

ing using the step-up approach with percutaneous drainage were able to obviate need for open surgical debridement in 48–68.5% of patients with infected WON [26, 27].

When to Refer to Tertiary Care Center

Whereas the majority of mild acute pancreatitis patients can safely be managed on a medical-surgical hospital floor, clinicians should maintain a low threshold for admitting patients with acute pancreatitis to a closely monitored unit (e.g., progressive care unit or intensive care unit), as prompt implementation of the management paradigm as noted above and close monitoring for complications is crucial to optimal outcomes in this patient group. Any patients presenting with persistent systemic inflammatory response syndrome (SIRS), or any single or multi-organ dysfunction should be managed in either progressive care or intensive care units, as these markers represent risk of developing severe pancreatitis. As discussed previously, acute pancreatitis can develop various sequelae requiring intervention. As such, in the event that a patient develops any of the aforementioned sequelae such as WON or symptomatic pseudocysts, one may consider referral to a tertiary medical center with ERCP capabilities and hepatobiliary surgery support. Furthermore, if ready ERCP services are not available, referral to a tertiary care center is warranted in patients with suspected biliary pancreatitis that would warrant ERCP as noted above. The lack of a skilled nursing unit able to provide intensive or progressive level care should also warrant referral to a tertiary referral center given the increasing risk of mortality with severe pancreatitis.

Conclusion

Acute pancreatitis can present within a spectrum of disease from mild interstitial pancreatitis to severe, life-threatening pancreatitis. All patients who present with acute pancreatitis should be triaged and managed with a team approach including adequate nursing observation, clinical monitoring by physicians, and timely referral to tertiary care centers when appropriate technical capabilities are not present. The step-up approach will often prevent the need for surgical intervention in these patients who may be critically ill.

References

1. Krishna SG, et al. The changing epidemiology of acute pancreatitis hospitalizations: a decade of trends and the impact of chronic pancreatitis. Pancreas. 2017;46(4):482–8.
2. Peery AF, et al. Burden of gastrointestinal, liver, and pancreatic diseases in the United States. Gastroenterology. 2015;149(7):1731–1741.e3.
3. Banks PA, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102–11.
4. Forsmark CE, Vege SS, Wilcox CM. Acute pancreatitis. N Engl J Med. 2016;375(20):1972–81.
5. Yang CJ, et al. Predictors of severe and critical acute pancreatitis: a systematic review. Dig Liver Dis. 2014;46(5):446–51.
6. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013;13(4):e1–e15.
7. Mounzer R, et al. Comparison of existing clinical scoring systems to predict persistent organ failure in patients with acute pancreatitis. Gastroenterology. 2012;142(7):1476–82; quiz e15–6.
8. Grant BF, et al. Prevalence of 12-month alcohol use, high-risk drinking, and DSM-IV alcohol use disorder in the United States, 2001–2002 to 2012–2013: results from the national epidemiologic survey on alcohol and related conditions. JAMA Psychiat. 2017;74(9):911–23.
9. Nitsche C, et al. Drug-induced pancreatitis. Curr Gastroenterol Rep. 2012;14(2):131–8.
10. Bertin C, et al. Pancreas divisum is not a cause of pancreatitis by itself but acts as a partner of genetic mutations. Am J Gastroenterol. 2012;107(2):311–7.
11. Cote GA, et al. Similar efficacies of biliary, with or without pancreatic, sphincterotomy in treatment of idiopathic recurrent acute pancreatitis. Gastroenterology. 2012;143(6):1502–1509.e1.
12. Fischer M, et al. Endoscopic retrograde cholangiopancreatography and manometry findings in 1,241 idiopathic pancreatitis patients. Pancreatology. 2010;10(4):444–52.
13. Yamashita, T., et al. Large volume fluid resuscitation for severe acute pancreatitis is associated with reduced mortality: a multicenter retrospective study. J Clin Gastroenterol. Epub 2018 Apr 23.

14. Crockett SD, et al. American Gastroenterological Association Institute guideline on initial management of acute pancreatitis. Gastroenterology. 2018;154(4):1096–101.
15. Mao EQ, et al. Fluid therapy for severe acute pancreatitis in acute response stage. Chin Med J. 2009;122(2):169–73.
16. Lankisch PG, Apte M, Banks PA. Acute pancreatitis. Lancet. 2015;386(9988):85–96.
17. Windsor ACJ, et al. Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. Gut. 1998;42(3):431–5.
18. Bakker OJ, et al. Early versus on-demand nasoenteric tube feeding in acute pancreatitis. N Engl J Med. 2014;371(21):1983–93.
19. Vege SS, et al. Initial medical treatment of acute pancreatitis: American Gastroenterological Association Institute technical review. Gastroenterology. 2018; 154(4):1103–39.
20. Yi F, et al. Meta-analysis: total parenteral nutrition versus total enteral nutrition in predicted severe acute pancreatitis. Intern Med. 2012;51(6):523–30.
21. Ibanez J, et al. Incidence of gastroesophageal reflux and aspiration in mechanically ventilated patients using small-bore nasogastric tubes. JPEN J Parenter Enteral Nutr. 2000;24(2):103–6.
22. Tenner S, et al. American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol. 2013;108(9):1400–15; 1416.
23. Fogel EL, Sherman S. ERCP for gallstone pancreatitis. N Engl J Med. 2014;370(2):150–7.
24. van Brunschot S, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. Lancet. 2018;391(10115):51–8.
25. da Costa DW, et al. Staged multidisciplinary step-up management for necrotizing pancreatitis. Br J Surg. 2014;101(1):e65–79.
26. Babu RY, et al. Predictors of surgery in patients with severe acute pancreatitis managed by the step-up approach. Ann Surg. 2013;257(4):737–50.
27. Shenvi S, et al. Timing of surgical intervention in patients of infected necrotizing pancreatitis not responding to percutaneous catheter drainage. Pancreatology. 2016;16(5):778–87.

Part XI

Hypertensive Crisis: Pheochromocytoma

31 Perioperative and Hypertensive Crisis Management of Pheochromocytomas

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Pheochromocytomas are rare neuroendocrine tumors of the chromaffin cells of the adrenal medulla that secrete catecholamines. Clinical manifestations vary based on the type, quantity, and timing of catecholamine being secreted. Excessive catecholamines can cause symptoms of headache, anxiousness, and diaphoresis as well as hemodynamic effects such as hypertension and tachycardia that can develop into fatal arrhythmia and hypertensive crisis. Cases of catecholamine-induced complications that have been reported include myocardial infarctions, cerebrovascular stroke, Takotsubo-like cardiomyopathy [12], pulmonary edema [30], and multiorgan failure [34]. Due to its high morbidity and mortality, it is crucial that pheochromocytomas are recognized early so that appropriate medical management could be initiated in preparation for surgical cure.

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Epidemiology

With its rarity, non-specific symptoms, and paroxysmal nature, pheochromocytomas can be difficult to diagnose without an index of suspicion. Prevalence of pheochromocytomas is estimated to be 0.05–0.1% in the general population, with half of these being diagnosed at autopsy [9]. When looking at those with hypertension, the prevalence increases to 0.1–0.6% [9]. The most serious presentation of pheochromocytoma is pheochromocytoma crisis, defined as catecholamine-induced hemodynamic instability causing end-organ damage or dysfunction. The incidence of this hypertensive crisis at initial presentation has been reported to be between 7% and 18% in several retrospective series of post-adrenalectomy patients with the diagnosis of pheochromocytoma [13, 37]. Crises typically manifest as severe hypertension with evidence of end-organ damage such as catecholamine cardiomyopathy, but less commonly can result in hypotension, hyperthermia (temperature >40 °C), altered mental status, and multiorgan dysfunction [47]. Conversely, with the increasing availability and utilization of radiologic imaging, 30–64% of pheochromocytomas may present as adrenal incidentalomas [10, 21]. Because pheochromocytomas comprise approximately 5% of all adrenal incidentalomas [49], it is recommended that all adrenal incidentalomas are evaluated for catecholamine excess [11, 51]. Asymptomatic

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patients may also be found to have pheochromocytoma when screened as part of a genetic syndrome, such as multiple endocrine neoplasia (MEN) type 2B.

It was previously thought that 10% of pheochromocytomas were hereditary, but that estimation has increased as more associated gene defects are discovered. More recent studies have shown that as high as 40% of patients with catecholamine-producing tumors have genetic mutations associated with susceptibility for pheochromocytoma/paragangliomas, especially those who present as children [25, 27]. Detailed clinical exam and history may suggest a genetic syndrome such as MEN2, von Hippel-Lindau, and neurofibromatosis for targeted testing of the *RET*, *VHL*, or *NF1* gene mutation, respectively. In those without apparent syndromic pheochromocytoma, genetic testing should be considered in those under 45 years of age and in those with a bilateral tumor presentation or an extra-adrenal tumor [24].

Diagnosis and Localization

Diagnosis of pheochromocytoma is made by demonstrating pathological elevation of catecholamines and its metabolites, the metanephrines. Available biochemical tests include plasma free metanephrines and urine metanephrines. Diagnosis can be challenging as commonly used medications and sympathetic stimuli, including stress and upright positioning, can cause increases in plasma metanephrines, potentially leading to false-positive testing and misdiagnosis [25]. Medications such as tricyclic antidepressants and sympathomimetic drugs are known culprits and may need to be discontinued for testing. When interpreting these tests, special consideration needs to be made of the circumstances under which they were collected and to what medications the patient has been exposed. In cases when it is not feasible to get biochemical testing without confounders, such as in a critically ill patient, and suspicion is high for pheochromocytoma, then it is recommended to proceed with adrenal imaging for further evaluation [1].

Once biochemical confirmation is made, then localization is made radiographically. Pheochromocytomas can have a wide range of presentations on imaging but are usually well-defined with clear margins, larger than 3 cm, and heterogeneous with cystic areas [50]. For adrenal catecholamine-producing tumors, sensitivity of CT imaging is >90% [25]. On non-contrasted CT, they tend to have higher attenuation with Hounsfield units >10, usually >25, and on contrasted CT appear more vascular with <50% contrast washout at 10 min [50]. On MRI, pheochromocytomas are characterized as being enhancing masses with high signal intensity on T2-weighted imaging [5]. Unlike paragangliomas, which are extra-adrenal chromaffin cell tumors, pheochromocytomas are often localized with anatomic imaging alone. If anatomic imaging with CT and MRI is negative, then functional imaging with I-123 MIBG is useful. I-123 MIBG scintigraphy has sensitivity of 77–90% and specificity of 95–100% in pheochromocytomas, while I-123 MIBG SPECT outperforms that with nearly 100% sensitivity [5, 25]. In metastatic disease and paragangliomas, however, I-123 MIBG does not perform as well, and the Endocrine Society Clinical Practice Guidelines recommends 18F-FDG PET/CT scanning though newer studies have shown 18F-FDOPA, 61Ga-DOTATAE, and other pharmaceuticals to be superior [17, 24, 25].

Medical Management

The goal of medical management of pheochromocytoma is to normalize blood pressure and heart rate, restore volume depletion, decrease the risk for hypertensive crises, minimize bothersome symptoms, and prepare the patient for surgical cure. After diagnosis, management starts with preoperative alpha-adrenergic blockade prior to beta-adrenergic blockade. The rationale for this is to prevent the potential for hypertensive crisis if there are unopposed alpha-adrenergic actions without compensatory beta-2-adrenergic vasodilatory effects. While there are studies challenging whether this approach is necessary, this is consistent with the recommendations published

by both the Endocrine Society and the North American Neuroendocrine Tumor Society, which puts a higher value on reducing the risk for intraoperative hypertensive crises over the possible adverse effects from the medications [6, 24, 27]. It is also advised that after initiation of alpha-adrenergic blockade, fluid and sodium intake is liberalized to prevent perioperative hypotension that may occur once volume contraction is reversed with treatment [24]. Unfortunately, due to its rarity, there are no randomized controlled trials to base these recommendations.

The preferred drug of choice for alpha-adrenergic blockade is phenoxybenzamine (Table 31.1). Phenoxybenzamine is a nonselective, noncompetitive alpha-adrenergic antagonist that is essentially only used on the preoperative treatment of pheochromocytoma. It has a long-lasting effect that diminishes only after de novo alpha-adrenoreceptor synthesis. As pheochromocytoma cases are few, phenoxybenzamine may not be readily available and if available can be expensive. An alternative, including if patients are unable to tolerate the side effects of phenoxybenzamine, are selective alpha-1-adrenergic antagonists such as doxazosin or prazosin ([24, 27], ES). The selective alpha-1 adrenergic antagonists have less side effects than phenoxybenzamine as it is the alpha-2-adrenergic receptor blockade that results in more nasal congestion, reflex tachycardia, and orthostasis [33]. This allows for faster titration with less side effects compared to phenoxybenzamine. However, the selective alpha-1-adrenergic receptor antagonists are competitive antagonists so can theoretically be overcome by large amounts of catecholamines, which may occur during surgical manipulation [33]. Retrospective studies have also demonstrated improved perioperative parameters and postoperative hemodynamic recovery associated with use of selective alpha-1 adrenergic receptor antagonists [16]. Other studies comparing phenoxybenzamine to various selective alpha-1-adrenergic receptor antagonists have shown no clear superiority of one over another, and overall both appear to be safe methods for alpha-adrenergic blockade [33, 45]. Specific goals for alpha-blockade vary slightly by institutional practice and experience, as well as patient age and comorbidities. In general, a target blood

Table 31.1 Medications used for symptom management and pre-surgical blockade

Drug	Doses	Recommended use
Alpha-adrenergic blockers Phenoxybenzamine Prazosin Terazosin Doxazosin	10 mg 1–3 times daily 2–5 mg 2–3 times daily 2–5 mg per day 2–8 mg per day	Phenoxybenzamine is first choice for alpha-adrenergic receptor blockade Short-acting, specific, competitive alpha-adrenergic receptor blockers may be used in patients who cannot tolerate phenoxybenzamine and/or patients with mild hypertension
Beta-blockers Atenolol Metoprolol Propranolol	12.5–25 mg 2–3 times daily 25–50 mg 3–4 times daily 20–80 mg 1–3 times daily	To control tachyarrhythmia caused by catecholamines or alpha-adrenergic blockade
Calcium channel blockers Amlodipine Nicardipine Nifedipine Verapamil	10–20 mg per day 60–90 mg per day 30–90 mg per day 180–540 mg per day	To provide additional blood pressure control for patients on alpha blockers For patients who cannot tolerate alpha blockers For patients with intermittent hypertension
Catecholamine synthesis inhibitors Metyrosine	250 mg every 8–12 h for a total dose of 1.5–2 g per day	To provide additional blood pressure control for patients on adrenergic receptor blockade

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pressure of <130/80 mmHg with heart rate 60–70 bpm while sitting and >90 mmHg systolic with heart rate 70–80 bpm while standing is considered acceptable [24].

In patients already treated with alpha-adrenergic receptor blockers, the most common add-on drug class to further improve blood pressure control are calcium channel blockers. This class of drugs controls hypertension and tachyarrhythmias by blocking norepinephrine (NE)-mediated calcium influx into vascular smooth muscle and does not cause hypotension during normotensive periods [31]. Monotherapy is not recommended unless patients have mild preoperative hypertension or have intolerable side effects to adrenergic blockade [23].

Beta-adrenergic receptor antagonists are usually added 2 days after alpha-blockade is initiated if needed to control tachycardia and blood pressure. Selective beta-1-adrenergic blockers such as atenolol and metoprolol are preferred though propranolol is also often used. Beta-blockers that have alpha-adrenergic antagonist activity are generally not recommended because the beta-adrenergic antagonist activity exceeds that of the alpha-adrenergic blockade unless specific alpha-adrenergic blockade is initiated first [28, 31].

Metyrosine (alpha-methyl-para-tyrosine) can also be a considered adjunct. It works by decreasing catecholamine synthesis by inhibiting the enzyme tyrosine hydroxylase and can help control blood pressure. It is not recommended as preoperative monotherapy as it may not be adequate to control intraoperative hypertension on its own [43]. However, when metyrosine is used with an alpha-adrenergic receptor blocker, it has been shown to improve intraoperative hemodynamic stability and cardiovascular-specific complications compared to when alpha-adrenergic blocker is used alone [41, 46].

Management of Pheochromocytoma Crisis

In patients who present with pheochromocytoma crisis who are rapidly deteriorating, such as can be seen with tumor rupture or hemorrhage, some experts argue that emergent adrenalectomy is indicated [18, 44]. However, there is retrospective evidence to suggest better outcomes when first attempting medical stabilization and titration of alpha-blockade before surgical resection [20, 37, 47]. To do this, all patients who present with pheochromocytoma crisis should be managed in an intensive care setting, as they will by definition have hemodynamic instability and end-organ damage. In younger, otherwise healthy patients with limited hypertension and end-organ damage, arterial catheterization may be sufficient for blood pressure monitoring. In more severe crises threatening cardiopulmonary collapse, central venous access with pulmonary artery flotation catheter is appropriate to gauge filling pressures and cardiac output. Regular cardiac evaluation with tissue Doppler echocardiography can be used to monitor diastolic or systolic dysfunction or catecholamine-induced cardiomyopathy and help guide recovery [4, 29]. The first-line treatment for hypertension in this setting remains alpha-blockade to reverse the underlying pathologic process.

Non-adrenergic antihypertensive adjuncts may also include calcium channel blockers, magnesium sulfate, and sodium nitroprusside [47]. Additionally, intensive fluid resuscitation is of vital importance, as profound sympathetic vasoconstriction leads to intravascular hypovolemia. Patients who present in shock refractory to fluid and vasopressor administration have been effectively stabilized with intra-aortic balloon pumps and extracorporeal membrane oxygenation in numerous case reports. These treatments are often used as temporary cardiopulmonary support measures while their crisis recedes, allowing for delayed surgery as definitive management [8, 31, 35, 36, 40, 52].

Perioperative Management

In a symptomatic stable patient, it is largely accepted that surgical resection should be preceded by a 7–14-day titration of alpha-blockade, volume expansion, and any other adjuncts nec-

essary to control blood pressure and symptoms (e.g., beta-blockade or calcium channel blockers) as described above. Some controversy exists regarding whether asymptomatic patients require preoperative treatment [26, 39], but tradition and experience guide that all patients with functional pheochromocytomas should receive preoperative management to prevent hemodynamic instability. Patients with recent myocardial infarction, catecholamine-induced cardiomyopathy, or catecholamine-induced vasculitis may need a longer preoperative adrenergic blockade than 14 days prior to surgery in order to optimize medical status on an individualized basis [31].

Phenoxybenzamine is usually started at 10 mg twice a day and titrated up by 10 to 20 mg increments every 2 to 3 days until clinical symptoms are controlled or side effects, such as dizziness and nasal congestion, appear. A total daily dose of 1 mg/kg is generally sufficient, but some patients require much higher doses to prevent paroxysmal hypertensive episodes and to achieve normotension or mild hypotension. Another effective approach is to administer phenoxybenzamine by infusion (0.5 mg/kg/day) for 5 h per day for 3 days before the operation. In this situation, the use of metyrosine is limited due to short time frame to achieve maximal effect [7]. If other alpha-1 adrenergic blockers are used, it should be given the day of surgery due to its short half-life. Treatment should also include continuous administration of 1 to 2 liters of intravenous saline, at least the evening prior to surgery to reverse blood volume contraction. Patients admitted to the hospital prior to surgery should be monitored closely and placed on strict bed rest to prevent falls from hypotension.

Intraoperatively, it is not unusual for patients to have wide swings in blood pressure—even with incidentalomas, up to 50% of patients may have hemodynamic instability during pheochromocytoma resection [15]. This instability results from bursts of hormones released upon noxious stimuli such as intubation and tissue incision, as well as physical manipulation of the tumor with its extensive vascularity [38]. Numerous retrospective analyses have looked at factors that may predict the frequency and severity of hemodynamic instability, including tumor size, preoperative antihypertensive treatment, anesthetic drugs, genetic syndromes, amount and type of plasma catecholamine levels, and surgical approach, although many of these studies have conflicting results [32].

Postoperative Management

Postoperative management of all pheochromocytoma resections should also take place in the intensive care setting. Withdrawal of the tumor's catecholamine secretion classically results in hypotension, in part due to the residual antihypertensive medication, the relative intravascular hypovolemia, and possible downregulation of alpha- and beta-adrenergic receptors [42]. In addition to fluid resuscitation, many patients will require vasopressor support during early recovery; prolonged hypotension with mean arterial pressure <60 mmHg or ≥30 min of vasopressor support has been reported to occur in 39–48% of cases [48]. Hypotension may also be related to adrenal insufficiency, which should be closely watched for especially in patients who underwent bilateral resection or unilateral cortical-sparing adrenalectomy with prior contralateral adrenalectomy [25]. Furthermore, sudden catecholamine withdrawal can also lead to reactive hyperinsulinemia that may result in severe hypoglycemia [19]. Hourly blood sugar monitoring for the first 24–48 h following surgery should be performed in accordance with the Endocrine Society's clinical practice guidelines.

Persistent hypertension, on the other hand, may affect up to 25% percent of patients after pheochromocytoma removal [3]. The most common etiology in these patients is coexisting primary (essential) hypertension, but one must rule out iatrogenic renovascular damage such as renal artery ligation as well as residual pheochromocytoma. Indeed, plasma free or urinary fractionated metanephrines should be measured 14 days after surgery. Long-term surveillance for recurrent or metastatic disease involves annual measurement of plasma free or urinary fractionated

metanephrines [24]. This follow-up is lifelong, as tumor recurrence or metastatic disease may arise up to 40 years after resection [2]. In the absence of increased metanephrines, however, residual hypertension should be managed as primary hypertension [14].

Conclusion

Perioperative mortality in pheochromocytoma resections has decreased dramatically from 20% in 1951 to 2% recently [22]. Much of this improvement can be attributed to advances in minimally invasive procedures and improved perioperative management to control hemodynamic instability and prevent end-organ consequences of surgery-induced catecholamine storm. This has occurred despite a lack of prospective, randomized clinical trials to guide treatment options, as is often the case in such relatively rare diseases. Perioperative management continues to evolve, especially as certain medications with limited uses such as phenoxybenzamine become unavailable in certain countries (James 2015). Regardless, the improved outcomes of surgery underscore the importance of early recognition of pheochromocytoma. Clinical suspicion is vitally important as pheochromocytoma can mimic other diseases that might be treated with medications that can precipitate a crisis. To ensure ideal perioperative preparation, patients with pheochromocytomas should be evaluated and managed by multidisciplinary teams with close communication between endocrine, surgery, anesthesiology, and cardiology services. Complex cases involving pregnancy, metastatic disease, or cardiovascular decompensation should be referred to centers with appropriate expertise to ensure favorable outcomes.

References

1. Amar L, Eisenhofer G. Diagnosing phaeochromocytoma/paraganglioma in a patient presenting with critical illness: biochemistry versus imaging. Clin Endocrinol. 2015;83(3):298–302.
2. Amar L, Fassnacht M, Gimenez-Roqueplo AP, Januszewicz A, Prejbisz A, Timmers H, Plouin PF. Long-term postoperative follow-up in patients with apparently benign pheochromocytoma and paraganglioma. Horm Metab Res. 2012;44(05):385–9.
3. Amar L, Servais A, Gimenez-Roqueplo AP, Zinzindohoue F, Chatellier G, Plouin PF. Year of diagnosis, features at presentation, and risk of recurrence in patients with pheochromocytoma or secreting paraganglioma. J Clin Endocrinol Metabol. 2005;90(4):2110–6.
4. Agarwal G, Sadacharan D, Kapoor A, Batra A, Dabadghao P, Chand G, Mishra SK. Cardiovascular dysfunction and catecholamine cardiomyopathy in pheochromocytoma patients and their reversal following surgical cure: results of a prospective case-control study. Surgery. 2011;150(6):1202–11.
5. Castinetti F, Kroiss A, Kumar R, Pacak K, Taieb D. 15 YEARS OF PARAGANGLIOMA: imaging and imaging-based treatment of pheochromocytoma and paraganglioma. Endocr Relat Cancer. 2015;22(4):T135–45.
6. Chen H, Sippel RS, O'Dorisio MS, Vinik AI, Lloyd RV, Pacak K, et al. The north american neuroendocrine tumor society consensus guideline for the diagnosis and management of neuroendocrine tumors: Pheochromocytoma, paraganglioma, and medullary thyroid cancer. Pancreas. 2010;39(6):775–83.
7. Chew SL. Recent developments in the therapy of pheochromocytomas and paragangliomas. Ann N Y Acad Sci. 2004;1073:405–16.
8. Chao A, Yeh YC, Yen TS, Chen YS. Phaeochromocytoma crisis–a rare indication for extracorporeal membrane oxygenation. Anaesthesia. 2008;63(1):86–8.
9. Eisenhofer G, Pacak K, Maher ER, Young WF, de Krijger RR. Pheochromocytoma. Clin Chem. 2013;59(3):466–72.
10. Falhammar H, Kjellman M, Calissendorff J. Initial clinical presentation and spectrum of pheochromocytoma: a study of 94 cases from a single center. Endocr Connect. 2018;7(1):186–92.
11. Fassnacht M, Arlt W, Bancos I, Dralle H, Newell-Price J, Sahdev A, et al. Management of adrenal incidentalomas: European society of endocrinology clinical practice guideline in collaboration with the European network for the study of adrenal tumors. Eur J Endocrinol. 2016;175(2):G1–G34.
12. Gagnon N, Mansour S, Bitton Y, Bourdeau I. Takotsubo-like cardiomyopathy in a large cohort of patients with pheochromocytoma and paraganglioma. Endocr Pract. 2017;23(10):1178–92.
13. Guerrero MA, Schreinemakers JM, Vriens MR. Clinical spectrum of pheochromocytoma. J Am Coll Surg. 2009;209:727–32.
14. Hana NN, Kenady DE. Pheochromocytoma. In: Holzhemier RG, Mannick JA, editors. Surgical treatment: evidence-based and problem-oriented. Munich: Zuckschewerdt; 2001.

15. Hariskov S, Schumann R. Intraoperative management of patients with incidental catecholamine producing tumors: a literature review and analysis. J Anaesthesiol Clin Pharmacol. 2013;29(1):41–6.
16. Hoffman BB. Catecholamines, sympathomimetic drugs and adrenergic receptor antagonists. In: Goodman & Gillman's the pharmacological basis of therapeutics. Philadelphia: McGraw-Hill; 2001. p. 215–68.
17. Janssen I, Chen CC, Millo CM, Ling A, Taieb D, Lin FI, et al. PET/CT comparing (68)ga-DOTATATE and other radiopharmaceuticals and in comparison with CT/MRI for the localization of sporadic metastatic pheochromocytoma and paraganglioma. Eur J Nucl Med Mol Imaging. 2016;43(10):1784–91.
18. Kakoki K, Miyata Y, Shida Y, et al. Pheochromocytoma multisystem crisis treated with emergency surgery: a case report and literature review. BMC Res Notes. 2015;8:758.
19. Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. J Cardiothorac Vasc Anesth. 2002;16(3):359–69.
20. Kobayashi T, Iwai A, Takahashi R, Ide Y, Nishizawa K, Mitsumori K. Spontaneous rupture of adrenal pheochromocytoma: review and analysis of prognostic factors. J Surg Oncol. 2005;90:31–5.
21. Kopetschke R, Slisko M, Kilisli A, Tuschy U, Wallaschofski H, Fassnacht M, et al. Frequent incidental discovery of phaeochromocytoma: data from a German cohort of 201 phaeochromocytoma. Eur J Endocrinol. 2009;161(2):355–61.
22. Kwon SY, Lee KS, Lee JN, Ha YS, Choi SH, Kim HT, Kwon TG. Risk factors for hypertensive attack during pheochromocytoma resection. Investig Clin Urol. 2016;57(3):184–90.
23. Lebuffe G, Dosseh ED, Tek G, Tytgat H, Moreno S, Travernier B, Vallet B, Proye CA. The effect of calcium channel blockers on outcome following the surgical treatment of phaeochromocytomas and paragangliomas. Anesthesia. 2005;60(5):439.
24. Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, Grebe SK, Murad MH, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99(6):1915–42.
25. Lenders JWM, Eisenhofer G. Update on modern management of pheochromocytoma and paraganglioma. Endocrinol Metab (Seoul, Korea). 2017;32(2):152–61.
26. Lentschener C, Gaujoux S, Tesniere A, Dousset B. Point of controversy: perioperative care of patients undergoing pheochromocytoma removal-time for a reappraisal? Eur J Endocrinol. 2011;165:365–73.
27. Martucci VL, Pacak K. Pheochromocytoma and paraganglioma: diagnosis, genetics, management, and treatment. Curr Probl Cancer. 2014;38(1):7–41.
28. Mazza A, Armigliato M, Marzola MC, Schiavon L, Montemurro D, Vescovo G, et al. Anti-hypertensive treatment in pheochromocytoma and paraganglioma: current management and therapeutic features. Endocrine. 2014;45(3):469–78.
29. Meune C, Bertherat J, Dousset B, Jude N, Bertagna X, Duboc D, Weber S. Reduced myocardial contractility assessed by tissue Doppler echocardiography is associated with increased risk during adrenal surgery of patients with pheochromocytoma: report of a preliminary study. J Am Soc Echocardiogr. 2006;19(12):1466–70.
30. Muratori D, Pedrotti P, Baroni M, Belloni A, Quattrocchi G, Milazzo A, Giannattasio C, Roghi A. Catecholamine-induced myocarditis in pheochromocytoma. G Ital Cardiol (2006). 2017; 18(2):164-8.
31. Pacak K. Preoperative management of the pheochromocytoma patient. J Clin Endocrinol Metab. 2007;92(11):4069–79.
32. Ramachandran R, Rewari V. Current perioperative management of pheochromocytomas. Indian J Urol. 2017;33(1):19–25.
33. Randle RW, Balentine CJ, Pitt SC, Schneider DF, Sippel RS. Selective versus non-selective alpha-blockade prior to laparoscopic adrenalectomy for pheochromocytoma. Ann Surg Oncol. 2017;24(1):244–50.
34. Riester A, Weismann D, Quinkler M, Lichtenauer UD, Sommerey S, Halbritter R, et al. Life-threatening events in patients with pheochromocytoma. Eur J Endocrinol. 2015;173(6):757–64.
35. Ritter S, Guertler T, Meier CA, Genoni M. Cardiogenic shock due to pheochromocytoma rescued by extracorporeal membrane oxygenation. Interact Cardiovasc Thorac Surg. 2011;13(1):112–3.
36. Sakamoto K, Kojima S, Hokimoto S, Ogawa H. Pheochromocytoma multisystem crisis with transient stress cardiomyopathy due to ruptured pheochromocytoma. BMJ Case Rep. 2015;2015:bcr2015212456.
37. Scholten A, Cisco RM, Vriens MR, et al. Pheochromocytoma crisis is not a surgical emergency. J Clin Endocrinol Metab. 2013;98:581–91.
38. Scholten A, Vriens MR, Cromheecke G, Rinkes IHB, Valk GD. Hemodynamic instability during resection of pheochromocytoma in MEN versus non-MEN patients. Eur J Endocrinol. 2011;165(1):91–6. EJE-11.
39. Shao Y, Chen R, Shen ZJ, Teng Y, Huang P, Rui WB, et al. Preoperative alpha blockade for normotensive pheochromocytoma: is it necessary? J Hypertens. 2011;29(12):2429–32.
40. Smet M, Convens C, Verhelst J. Successful use of an intra-aortic balloon pump in an acute phaeochromocytoma crisis with severe catecholamine cardiomyopathy. Clin Intensive Care. 1998;9(4):167–9.
41. Steinsapir J, Carr AA, Prisant LM, Bransome ED Jr. Metyrosine and pheochromocytoma. Arch Intern Med. 1997;157(8):901–6.
42. Streeten DH, Anderson GH. Mechanisms of orthostatic hypotension and tachycardia in patients with pheochromocytoma. Am J Hypertens. 1996;9(8):760–9.
43. Thanapaalasingham K, Pollmann AS, Schelew B. Failure of metyrosine therapy for preoperative

management of pheochromocytoma: a case report. Can J Anaesth. 2015;62(12):1303–7.
44. Uchida N, Ishiguro K, Suda T, et al. Pheochromocytoma multisystem crisis successfully treated by emergency surgery: report of a case. Surg Today. 2010;40:990–6.
45. van der Zee PA, de Boer A. Pheochromocytoma: a review on preoperative treatment with phenoxybenzamine or doxazosin. Neth J Med. 2014;72(4):190–201.
46. Wachtel H, Kennedy EH, Zaheer S, Bartlett EK, Fishbein L, Roses RE, et al. Preoperative metyrosine improves cardiovascular outcomes for patients undergoing surgery for pheochromocytoma and paraganglioma. Ann Surg Oncol. 2015;22(Suppl 3):S646–54.
47. Whitelaw BC, Prague JK, Mustafa OG, et al. Phaeochromocytoma crisis. Clin Endocrinol. 2014;80:13–22.
48. Wu S, Chen W, Shen L, Xu L, Zhu A, Huang Y. Risk factors for prolonged hypotension in patients with pheochromocytoma undergoing laparoscopic adrenalectomy: a single-center retrospective study. Sci Rep. 2017;7(1):5897.
49. Young WF Jr. Management approaches to adrenal incidentalomas. A view from Rochester, Minnesota. Endocrinol Metab Clin N Am. 2000;29(1):159–85, x.
50. Young WF Jr. Clinical practice. The incidentally discovered adrenal mass. N Engl J Med. 2007;356(6):601–10.
51. Zeiger MA, Thompson GB, Duh QY, Hamrahian AH, Angelos P, Elaraj D, et al. American association of clinical endocrinologists and american association of endocrine surgeons medical guidelines for the management of adrenal incidentalomas: executive summary of recommendations. Endocr Pract. 2009;15(5):450–3.
52. Zhou X, Liu D, Su L, Long Y, Du W, Miao Q, Huang Y. Pheochromocytoma crisis with severe cyclic blood pressure fluctuations in a cardiac Pheochromocytoma patient successfully resuscitated by extracorporeal membrane oxygenation: a case report. Medicine. 2015;94(17):e790.

32 Hypertensive Crisis Due to Pheochromocytoma

Benjamin Tabak

Introduction

Pheochromocytomas are rare neuroendocrine tumors of the adrenal medulla, which may store excessive amounts of catecholamines, primarily norepinephrine, epinephrine, and dopamine. Hypertensive crisis is a feared and potentially fatal complication of pheochromocytoma, which may occur when these tumors release a surge of catecholamines into the bloodstream. The crisis may occur spontaneously but is more often provoked, either by certain medications, trauma, stress from non-adrenal surgery, or manipulation of the tumor during extirpation. Severe hypertension is the most commonly associated complication, but other sequelae include cardiac (myocardial infarction, arrhythmia, cardiomyopathy, aortic dissection), respiratory (pulmonary edema, acute respiratory distress syndrome), and neurologic (cerebrovascular accident) compromise, as well as resultant multisystem organ failures. Fortunately, these complications are uncommon.

Although the currently preferred management of hypertensive crisis is primarily medical optimization, the surgeon must be keenly aware of the perioperative management that is required to adequately prepare patients for surgery and the interventions recommended for treatment if the crisis occurs during surgery.

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Presentation

The classic triad of symptoms associated with pheochromocytoma includes diaphoresis, palpitations, and headache. Part of the challenge in addressing the prevention of hypertensive crises is that the triad rarely presents in classic fashion and patients often present in with nonspecific complaints. In one recent example, a 36-year-old female with anxiety and obesity presented to an emergency room with a 3-day history of headache, nausea, and vomiting [1]. Her initial blood pressure was 134/86 mmHg. She was administered intravenous metoclopramide (10 mg). Within 1 h, she developed severe headache and hypertension (223/102 mmHg). CT scan quickly identified a pheochromocytoma, but her preoperative hospital course was complicated by a myocardial infarction, acute respiratory distress syndrome requiring veno-venous extracorporeal membrane oxygenation (ECMO), cardiogenic shock, acute liver failure, and oliguric kidney injury requiring continuous renal replacement therapy. The literature is replete with similar examples of unsuspecting victims of hypertensive crisis. A list of drugs reported to induce hypertensive crises in pheochromocytoma patients is provided in Table 32.1, along with the proposed mechanisms.

Hypertensive crisis may also present in undiagnosed patients with pheochromocytoma undergoing surgery for unrelated conditions.

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Many inciting events during unrelated surgery have been proposed as mechanisms for instigating a crisis, including noxious stimuli such as laryngoscopy, endotracheal intubation, skin incision, insufflation, and abdominal exploration [2]. In any case, if a hypertensive crisis occurs, the priority should be to medically treat the crisis and abort the operation as soon as possible.

Table 32.1 Selected medications that may induce hemodynamic instability and cardiovascular events in patients with pheochromocytoma

Substance class	Proposed mechanism
Beta-blockers (e.g., propranolol, carvedilol)	Inhibition of beta-2-adrenoreceptor-mediated vasodilation; results in unopposed alpha-receptor stimulation
Dopamine D2 receptor antagonists (e.g., metoclopramide, droperidol)	Dopamine receptor antagonism
Antidepressants: tricyclic antidepressants (e.g., amitriptyline) and selective serotonin reuptake inhibitors (e.g., fluoxetine)	Inhibition of noradrenaline reuptake
Corticosteroid hormones (e.g., prednisone) and peptide hormones (e.g., glucagon)	Production and secretion of catecholamines by pheochromocytoma
Sympathomimetics (e.g., pseudoephedrine)	Stimulate catecholamine release

Adapted from Sonntagbauer et al. [17]

Preoperative Crisis Prevention/ Management

Once a pheochromocytoma has been diagnosed, a multidisciplinary team including the operating surgeon should develop a plan that focuses on medical optimization and prevention of a hypertensive crisis during surgery. The first goal in the preoperative period includes a thorough evaluation of the patient's overall health and functional capacity. In addition to basic serum laboratory tests, an electrocardiogram and an echocardiogram should be performed to establish a baseline and address any abnormalities already present. The catecholamine excess from pheochromocytoma can cause coronary artery vasoconstriction and cardiomyopathy that can be chronic (hypertrophic or dilated) or acute (also known as takotsubo) [2].

The second goal in the preoperative period is initiation of an antihypertensive regimen to prevent unpredictable intraoperative hemodynamic instability, even in patients who are normotensive at the time of diagnosis [2]. No randomized controlled trials have been performed to assess the efficacy of the myriad blood pressure control regimens utilized to prepare patients with pheochromocytoma for surgery. However, clinical practice guidelines have been established by the international Endocrine Society (Table 32.2). The details of medical management of blood pressure control were described in the previous chapter.

Table 32.2 Pre-surgical medical preparation

Drug	Starting time	Starting dose	Final dose
Preparation 1			
Phenoxybenzamine	10–14 days before surgery	10 mg BID	1 mg/kg/day
Or Doxazosin		2 mg/day	32 mg/day
Preparation 2			
Nifedipine	If needed for persistent HTN	30 mg/day	60 mg/day
Amlodipine		5 mg/day	10 mg/day
Preparation 3			
Propranolol	If needed for tachycardia; after at least 3–4 days	20 mg TID	40 mg TID
Atenolol		25 mg/day	50 mg/day

Adapted from Lenders et al. [11]
Abbreviations: *BID* twice daily, *TID* three times daily

Table 32.3 Roizen criteria to assess for adequate α-adrenergic blockade

No blood pressure reading >160/90 should be evident for 24 h before surgery
Orthostatic hypotension, with readings >80/45 mmHg, should be present
Electrocardiogram should be free of ST-T changes for at least 1 week
No more than 1 premature ventricular contraction every 5 min

Adapted from Roizen et al. [18]

Retrospective studies also support volume loading prior to surgery. This can be achieved by initiating a high-sodium diet a few days after the start of α-adrenergic blockade. Continuous administration of saline (1–2 liters) starting the night before surgery may also be considered. The goal is to reverse blood volume contraction and reduce the risk of significant hypotension after surgery. Caution is advised in patients with heart or renal failure (Table 32.3).

Intraoperative Crisis Prevention/ Management

The intraoperative management of a patient with pheochromocytoma is focused on preventing and preparing for a hypertensive crisis. The crisis can be precipitated at any part of the surgery, beginning with induction of general anesthesia, and so accurate monitoring capability must be established upfront. Invasive blood pressure monitoring via arterial cannulation is considered the gold standard for blood pressure monitoring in pheochromocytoma cases. A system for accurate volume status assessment is also necessary, given the volume depletion commonly associated with prolonged exposure to high catecholamine levels. Insertion of a central venous catheter is a generally accepted standard. However, central venous pressures may not accurately reflect left heart pressures, which may be discordant during tumor manipulation or rapid volume infusion. Swan-Ganz/pulmonary artery catheterization has fallen out of favor in recent years but is still used occasionally in pheochromocytoma cases at high-volume centers (8–24%) [3]. Transesophageal echocardiography has been suggested to provide superior assessment of intraoperative volume status but entails significant operator reliance to obtain and interpret data [4]. Due to the limitations of these more invasive techniques, alternative techniques have been used. Although not yet FDA-approved for use in children, the FloTrac/VigileoTM system has been reported in the use of pediatric pheochromocytoma cases as a technique to avoid complications of more invasive monitoring [5]. Whole-body bioimpedance cardiography using the Non-Invasive Cardiac System (NICaS), which requires only electrodes be placed on the upper extremity and contralateral lower extremity, has also been reported for monitoring in pheochromocytoma cases [6].

The choice of agents used for anesthesia may be important in preventing the onset of an intraoperative hypertensive crisis [2]. Sevoflurane is the typically used for maintenance of anesthesia in patient undergoing pheochromocytoma resection due to the low arrhythmogenic potential. Many induction agents have been used safely, including propofol and etomidate. Agents that may cause an increase in catecholamine levels (ketamine) or elicit histamine release (morphine) should be avoided. For neuromuscular blockade, succinylcholine has been used safely but should be used with caution as the fasciculations caused by administration could precipitate a catecholamine surge.

If a hypertensive crisis occurs, blood pressure is best treated with vasodilators, as the cause is most likely α-adrenergic stimulation from catecholamine release. The immediate onset, short duration (1–5 min), and easy titration ability have made sodium nitroprusside (0.5–3 μg/kg/min) and nitroglycerin the most commonly used agents. If tachycardia or tachyarrhythmia occurs during surgery, esmolol is a commonly used β1-antagonist that has a fast onset (1–2 min) and short duration (9 min) [2].

There are several agents that have gained more recent notoriety for perioperative management of pheochromocytomas [7]. Magnesium has several properties beneficial in this condition. It inhibits catecholamine release, directly inhibits catecholamine receptors, and has been shown to attenuate

the catecholamine release associated with noxious stimuli. It has also been proven to be effective in the management of pheochromocytomas in children, who comprise 20% of the pheochromocytoma population, as well as pregnant females, who also may have limited options for safe medication administration. Clevidipine is an ultrashort-acting arterial vasodilator, with an initial half-life of about 1 min. Due to its rapid onset and clearance, it has been referred to as the "esmolol" of calcium channel blockers. Finally, if hypotension occurs during or after tumor resection, intravenous fluid management is likely of benefit as patients are often volume contracted. However, if the hypotension does not respond to volume resuscitation, norepinephrine, phenylephrine, and dopamine have all been recommended. Vasopressin has also been used and has particular application to pheochromocytoma cases as it acts on V_1 receptors on smooth muscle and therefore does not rely on the availability of adrenergic receptors, which may be downregulated in these patients.

Surgical Crisis Prevention/ Management

Surgical resection is the treatment of choice for pheochromocytoma. However, a surgeon should not be fooled into acting on the commonly held belief that surgical resection is the treatment of choice for hypertensive crisis induced by these tumors. Several studies have demonstrated high mortality associated with emergency surgery performed in patients with ruptured pheochromocytoma or pheochromocytoma hemorrhage [8, 9]. Massive catecholamine release may occur during tumor manipulation of the tumor when abdominal exploration is made to stop bleeding, leading to dangerous hemodynamic instability. This concept was recently addressed in a retrospective study, entitled "Pheochromocytoma Crisis Is Not a Surgical Emergency." [10] Out of 25 patients presenting with crisis at a single institution, 15 patients were discharged and readmitted for elective surgery, and 10 patients were operated on urgently during the same hospitalization. None underwent emergency surgery. Surgery was delayed in all cases until medical stabilization and adequate α-blockade could be achieved. There were zero mortalities reported. Those patients who were operated on urgently (i.e., during the same hospitalization) had fewer intraoperative and postoperative complications. The median number of days from crisis to surgery was 57 days (range, 11–536 days), although the authors recommended surgery within 1 month of hospital discharge.

The operative technique of choice to minimize the chance of hypertensive crisis remains a matter of debate. Laparoscopy has fundamentally taken over as the operation of choice for most adrenal surgery. The Endocrine Society clinical practice guidelines recommend minimally invasive surgery for most adrenal pheochromocytomas [11]. In addition to the usual advantages of laparoscopic surgery (less pain, less blood loss, less surgical morbidity), there is some evidence that laparoscopic surgery may result in less intraoperative hemodynamic instability relative to open surgery, although the data quality to support that claim is weak [12]. The Endocrine Society guidelines recommend open resection for large tumors (e.g., >6 cm), in part due to concern that intraoperative hypertensive crises have been more often reported with tumors larger than 6 cm [13]. Recent studies, though, including a large prospective, nonrandomized controlled study of 51 large-sized (≥6 cm) pheochromocytomas, have demonstrated that laparoscopy may be safe and effective even for these larger-sized tumors [14]. Between the laparoscopic and open adrenalectomy groups, there was no significant difference in the frequency of intraoperative blood pressure fluctuation. All of the hemodynamic events were resolved by drug treatment, except for one case, in which the surgeons converted to an open procedure without adverse sequelae.

Robot-assisted laparoscopic surgery has also garnered significant popularity in its use for adrenal surgery and has recently been utilized in surgery for pheochromocytoma. In one study, robotic adrenalectomy was performed in 25 patients with pheochromocytoma, and the intraoperative hemodynamic parameters were similar to those in the preceding 40 cases which were done laparoscopi-

cally, without the use of the robot [15]. There were no adverse intraoperative hemodynamic events noted, and the authors thus proposed robotic surgery as a safe technique, which does not increase the risk of hypertensive crisis.

There are a couple of technical considerations applicable to the treatment of intraoperative hypertensive crisis during adrenalectomy. The first is that tumor manipulation should be avoided as much as possible, as this may provoke catecholamine expression and precipitate a hypertensive crisis. Secondly, the adrenal vein should be ligated as early as possible in the procedure, as this may prevent catecholamines from entering the systemic bloodstream if/when the tumor is manipulated. However, ligation/division of the adrenal vein tends to form the crux of adrenal surgery and may be the most technically challenging portion of the procedure, and so ultimately should be performed in the safest manner possible, whenever that may be. Whereas the arterial supply of the adrenal gland is diffuse, the venous supply is usually solitary [16]. The left adrenal vein is approximately 2 cm long and drains into the left renal vein after joining the inferior phrenic vein. The right adrenal vein is a potentially perilous structure to manage because it is short, wide, variable, and confluent with thin-walled, large-capacitance vessels (the inferior vena cava in more than 80% of cases, followed by the renal vein and, uncommonly, the right hepatic vein).

As a final note, when found outside the adrenal gland, these tumors are referred to as paraganglionomas and typically reside in the para-aortic sympathetic chain, although they can also be found in the mediastinum, heart, and urinary bladder. Paraganglionomas may or may not be biochemically active. Careful attention to prevention of hypertensive crisis should be given to these tumors as well, although the risk appears to be lower than in pheochromocytomas.

Conclusions

Patients with undiagnosed pheochromocytoma may present with a hypertensive crisis, which can result in severe morbidity if not quickly diagnosed and treated. Fortunately, this is a rare event. Emergent surgery is ill-advised for pheochromocytomas presenting with a hypertensive crisis. The patient's blood pressure and comorbidities should be controlled and optimized first before proceeding to surgery. Alpha-blockade and volume loading should be established in anticipation of surgery. Once the hypertensive crisis and its sequelae have been appropriately treated, surgery is the ultimate treatment for pheochromocytoma. The laparoscopic approach is favored, and surgery is generally recommended within 1 month after the hypertensive crisis is resolved.

References

1. Leonard JB, Munir KF, Kim HK. Metoclopramide induced pheochromocytoma crisis. Am J Emerg Med. 2018;36(6):1124.e1–2.
2. Naranjo JN, Dodd S, Martin YN. Perioperative management of pheochromocytoma. J Cardiothorac Vasc Anesth. 2017;31:1427–39.
3. Weingarten TN, Cata JP, O'Hara JF, et al. Comparison of two preoperative medical management strategies for laparoscopic resection of pheochromocytoma. Urology. 2010;76:508.e6–508.e11.
4. Seward JB, Khandheria BK, Oh JK, et al. Transesophageal echocardiography: technique, anatomic correlations, implementation, and clinical applications. Mayo Clinic Proc. 1988;63:648–80.
5. Jia X, Guo X, Zheng Q. Perioperative management of paraganglioma and catecholamine-induced cardiomyopathy in child – a case report and review of the literature. BMC Anesthesiol. 2017;17:142.
6. Matsuda Y, Kawate H, Shimada S, et al. Perioperative sequential monitoring of hemodynamic parameters in patients with pheochromocytoma using the Non-Invasive Cardiac System (NICaS). Endocr J. 2014;61:571–5.
7. Lord MS, Augoustides JGT. Perioperative management of pheochromocytoma: focus on magnesium, clevidipine, and vasopressin. J Cardiothorac Vasc Anesth. 2012;26:526–31.
8. Bruynzeel H, Feelders RA, Groenland TH, et al. Risk factors for hemodynamic instability during surgery for pheochromocytoma. J Clin Endocrinol Metab. 2010;95:678–85.
9. Brown H, Goldberg PA, Selter JG, et al. Hemorrhagic pheochromocytoma associated with systemic corticosteroid therapy and presenting as myocardial infarction with severe hypertension. J Clin Endocrinol Metab. 2005;90:563–9.
10. Scholten A, Cisco RM, Vriens MR, et al. Pheochromocytoma crisis is not a surgical emergency. J Clin Endocrinol Metabol. 2013;98:581–91.

11. Lenders JW, et al. Pheochromocytoma and paraganglionoma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99(6):1915–42.
12. Livingstone M, Duttchen K, Thompson J, et al. Hemodynamic stability during pheochromocytoma resection: lessons learned over the last two decades. Ann Surg Oncol. 2015;22:4175–80.
13. Conzo G, Musella M, Corcione F, et al. Laparoscopic treatment of pheochromocytomas smaller or larger than 6 cm. A clinical retrospective study on 44 patients. Laparoscopic adrenalectomy for pheochromocytoma. Ann Ital Chir. 2013;84:417–22.
14. Wang W, Li P, Wang Y, et al. Effectiveness and safety of laparoscopic adrenalectomy of large pheochromocytoma: a prospective, nonrandomized, controlled study. Am J Surg. 2015;210:230–5.
15. Aliyev S, Karabulut K, Agcaoglu O, et al. Robotic versus laparoscopic adrenalectomy for pheochromocytoma. Ann Surg Oncol. 2013;20:4190–4.
16. Townsend CM, Beauchamp RD, Evers BM, Mattox KL. Sabiston textbook of surgery: the biological basis of modern surgical practice. 20th ed. Philadelphia: Elsevier Saunders; 2017.
17. Sonntagbauer M, Koch A, Strouhal U, et al. Catecholamine crisis during induction of general anesthesia: a case report. Anaesthesist. 2018;67:209–15.
18. Roizen MF, Hunt TK, Beaupre PN, et al. The effect of alpha-adrenergic blockade on cardiac performance and tissue oxygen delivery during excision of pheochromocytoma. Surgery. 1983;94:941–5.

Part XII

Esophageal Occlusion

33

Esophageal Obstruction and Perforation: Incidence, Etiologies, Presentation, and Management

Mia DeBarros and Daniel G. Cuadrado

Introduction

Esophageal perforation or obstruction is overall a rare but serious entity with mortality rates as high as 30% in some types of presentations. Often discussed but rarely encountered, it requires correct and complex decision-making to ensure an optimal outcome for the patient. Throughout the literature, it is difficult to find all-encompassing discussions on esophageal perforation or obstruction and its management. The following chapters discuss etiologies for both entities and their diagnosis and management. The first chapter focuses on basic anatomy and physiology of the esophagus and the etiology of obstruction and perforation.

Anatomy and Physiology

The esophagus is a hollow muscular tube extending from the pharynx to the stomach whose function is to transfer swallowed material from the mouth to the stomach. There are three anatomic regions of the esophagus: cervical, thoracic, and abdominal [1]. The cervical esophagus is approximately 5 cm long and bordered by the trachea and vertebral column. The thoracic esophagus is approximately 20 cm long and enters the posterior mediastinum posterior to the aortic arch and to the right of the ascending aorta transitioning anteriorly to the aorta and entering the abdomen via the esophageal hiatus. The abdominal esophagus is 2–6 cm long and bordered by the inferior vena cava on the right, anterior to the aorta, and posterior to the left lobe of the liver. There are three anatomic narrowed areas in the esophagus. The first is at the level of the cricopharyngeus muscle and the narrowest. The second area occurs where the left main stem bronchus and aortic arch cross the esophagus. The third is the esophageal hiatus [1]. The upper esophageal sphincter (UES) is located at the junction of the inferior pharyngeal constrictor and cricopharyngeus muscles, but the cricopharyngeus muscle is the primary contributor to sphincter tone. The lower esophageal sphincter (LES) is located at the distal portion of the esophagus and is a 2–4-cm focus of contracted muscle. Both sphincters are contracted at rest [2].

The arterial and venous blood supply is segmented. Branches of the superior and inferior thyroid artery supply the cervical esophagus, and its venous drainage consists of inferior thyroid and brachiocephalic veins. Tracheal, bronchial, and sometimes intercostal arteries supply the thoracic esophagus. Venous drainage consists of the hemiazygos and azygos veins. Branches of the left gastric and splenic arteries supply the abdominal esophagus, and venous drainage occurs via left gastric and splenic arteries [3].

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Innervation of the esophagus is parasympathetic and sympathetic. The vagus nerve is parasympathetic and controls motor innervation, peristalsis, and sphincter relaxation. The spinal afferent nerves are sympathetic and control vasoconstriction [3]. The pharyngeal plexus and recurrent laryngeal nerve control UES innervation, whereas the vagus and splanchnic nerves innervate the LES.

Peristalsis is classified as primary, secondary, or tertiary. Peristalsis is controlled by the vagus nerve via the myenteric plexus. Primary peristalsis is triggered when a bolus of food is swallowed and propelled toward the stomach in a progressive circular contraction. Secondary peristalsis follows primary peristalsis to clear the esophagus of content and refluxed gastric contents and is triggered by sensory receptors present in the esophagus [2]. Tertiary peristalsis does not occur in conjunction with swallowing and represents isolated waves occurring simultaneously throughout the esophagus in a non-peristaltic manner.

I. Obstruction

Malignancy

Esophageal carcinoma remains one of the top ten global cancers and the seventh leading cause of death, and its incidence is increasing in the last 30 years [4]. There are two histological subtypes: adenocarcinoma and squamous cell. Globally, squamous cell carcinoma is still more prevalent, particularly in the so-called esophageal cancer belt, stretching from northern Iran through Central Asia to North and Central China [4]. The cause of squamous cell carcinoma (SCC) varies by global region but is attributed to lifestyle and dietary factors such as hot beverage consumption, malnutrition, fungal contamination of maize, and alcohol and tobacco use. In the United States and western countries, SCC incidence is declining, while adenocarcinoma cases are increasing secondary to increased prevalence of obesity, gastroesophageal reflux disease, and *H. pylori* eradication. Patients commonly present with rapidly progressive dysphagia, abdominal pain, and unintended weight loss [5]. The esophagus is highly distensible, accommodating up to two-thirds occlusion prior to symptom manifestation. This often prevents early detection, and the majority of patients are not candidates for curative resection due to the presence of advanced disease [6]. Malignant strictures are typically the progression in Barrett's esophagus, a precursor to the development of adenocarcinoma, but may represent local invasion of bronchogenic carcinoma or metastatic disease of breast, lung, or renal malignancies [7].

Foreign Body/Caustic Ingestions

The cause for foreign body ingestions varies by age, but the majority occurs in children less than 5 years of age [8]. In adults, the most common cause is meat impaction in the setting of a preexisting esophageal disorder causing luminal narrowing such as rings, strictures, or eosinophilic esophagitis. In the pediatric population, most foreign body impactions are from coin ingestion. Disc battery ingestion, although less common, deserves special mention due to the ability to discharge electrical current if both sides of the battery are in contact with the esophageal wall resulting in burns, stenosis, and perforation within hours of ingestion [9]. Food impactions are also common in the pediatric population, especially those with eosinophilic esophagitis, atresia repair, or Nissen fundoplication. Both adult and pediatric populations also have intentional ingestion subpopulation including psychiatric patients, prison inmates, and drug smugglers [10].

Caustic ingestions unfortunately occur more frequently than foreign body ingestions in children less than 5 years of age, representing 66% of all caustic ingestions reported in 2016 [8]. Household cleaners, containing sodium hypochlorite, are most the commonly ingested. Other alkali agents include hydrogen peroxide, boric acid, and lye (potassium or sodium hydroxide). Common household acids are hydrochloric acid, sulfuric acid, and phosphoric acid. In children, the ingestion is usually accidental and a corresponding lower morbidity and mortality. However, in adults and adolescents, intentional ingestion is more common and characterized by a higher volume and toxicity of agent ingested with resultant higher morbidity and mortality. The

injury to the mucosa is dependent on pH, concentration, viscosity of the agent, and location and time of contact. Alkali agents are colorless and odorless. They cause liquefaction necrosis resulting in saponification of lipids and deeper penetration of the mucosa into the submucosa and muscularis causing thrombosis, fibrosis, and perforation. Acids cause coagulation necrosis with less penetration, decreasing risk of perforation. Acids typically have a lower viscosity resulting in a faster clearance of the esophagus but higher rates of gastric injury and hemorrhage. Acids are less likely to be ingested due to their bitter taste.

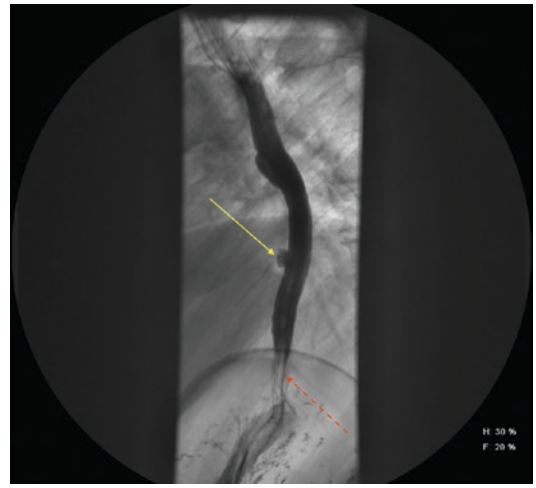

Fig. 33.1 Barium swallow demonstrating achalasia with narrowing in the distal esophagus (red, dashed arrow) and a pulsion epiphrenic diverticulum (yellow, solid arrow)

Dysmotility

Esophageal motility disorders are rare entities characterized by dysphagia, regurgitation of undigested food, chest pain, and, less commonly, obstruction. Due to the indolence and rarity of these disorders, they are frequently misdiagnosed and taking years to identify. The most common motility disorder is achalasia with a reported prevalence of 0.025–0.01% [11]. The underlying etiology is unknown but thought to be either autoimmune or neurodegenerative. On histology, there is destruction of ganglion cells in the myenteric plexus leading to absence of nitric oxide and vasoactive intestinal polypeptide. Patients typically report a gradual dysphagia to solids and eventually liquids, accompanied by sitophophia, weight loss, and malnutrition. Diagnostic workup begins with a contrast esophagram followed by upper endoscopy and manometry. Contrasted imaging demonstrates a dilated esophagus with a tapering at the LES (the classic "bird's beak") (Fig. 33.1). Manometry is the gold standard for diagnosis, and classic manometric findings of achalasia are failure of the lower esophageal sphincter (LES) to relax and an aperistaltic esophageal body.

Pseudoachalasia or secondary achalasia is a disorder that clinically and diagnostically mimics achalasia but is the result of an underlying disorder such as malignancy, paraneoplastic syndrome, or Chagas disease. The most common cause is malignancy, usually adenocarcinoma of the gastric cardia; however, there are reports of association with lymphoma, prostate, liver, and lung cancers [11]. Small-cell lung cancer is associated with paraneoplastic syndromes and pseudoachalasia. Patients with suspected small-cell lung cancer and achalasia should be tested for type-1 antineuronal nuclear autoantibody (ANNA-1) [12]. Chagas disease is a neurodegenerative disorder due to infection of the parasite *Trypanosoma cruzi* causing diffuse myenteric destruction and an aperistaltic megaesophagus [12].

With the advent of high-resolution manometry (HRM), diagnosis of esophageal dysmotility disorders is now diagnosed using the Chicago Classification [13]. Currently, three subtypes classify achalasia. Type I is classic achalasia as described above with aperistalsis and a nonrelaxing LES. Type II is the most common with a favorable prognosis to both medical and surgical treatments. Here, there is aperistalsis but are also intermittent periods of segmental esophageal contractions. Type III is the least common and a least favorable prognosis to any treatments and is hallmarked by well-defined spastic contractions [13]. Other less common dysmotility disorders include hypercontractile states (diffuse esophageal spasm and jackhammer or nutcracker esophagus) and hypocontractile states (scleroderma esophagus and aperistalsis). These dysmotility disorders are typically managed by medical therapy with surgical intervention as a last line therapy.

Peptic Strictures

Peptic strictures are the most common strictures, representing 70–80% of all benign strictures. The incidence of peptic strictures continues to decline with the widespread use of proton pump inhibitors [14]. Long-standing untreated gastroesophageal reflux disease (GERD) leads to chronic inflammatory and fibrotic changes of the esophagus creating a stricture. The stricture is typically located within 4 cm of the LES. Patients report progressive dysphagia, odynophagia, chest pain, or food impaction although 25% of patients are symptomatic at presentation [7]. Diagnosis is made on endoscopy and management includes treatment of the underlying cause.

Paraesophageal Hernia and Gastric Volvulus

Paraesophageal hernia (PEH) is a subtype of hiatal hernia and occurring less than 10% of hiatal hernias [15]. The hernia consists of gastric fundus herniating into the thoracic cavity and occurs in isolation (type II) or concomitantly with the gastroesophageal junction (type III) or other organs (type IV). There are several dominant theories in the literature on the etiology of this hernia [1]: increased intra-abdominal pressure [2], congenital or acquired shortening of the esophagus, and [3] widening of the diaphragmatic hiatus secondary to congenital or acquired changes in the crura or diaphragm [15].

Symptoms associated with a PEH are dependent on the subtype and related to hernia anatomy. Type II hernia patients have dysphagia, but not reflux because the gastroesophageal sphincter is in normal anatomic position, whereas types III and IV are more likely to present with dysphagia and reflux secondary to displacement of both stomach and gastroesophageal junction into the chest. Other related symptoms are mechanical in nature and include obstruction, volvulus, strangulation, ulcers (Cameron's ulcers), perforation, symptomatic anemia, and pulmonary symptoms such as aspiration and dyspnea. True asymptomatic patients are rare, and most "asymptomatic" patients upon careful questioning elicit subtle pulmonary or reflux symptoms. Workup and diagnosis begin with imaging, either an esophagram or CT of the chest and abdomen depending on surgeon preference (Fig. 33.2). Both studies provide adequate information on the size and location of the gastroesophageal junction (and therefore hiatal hernia subtype); however, CT also provides the size and location of the hernia [16]. Endoscopy (EGD) is also performed to evaluate the gastric and esophageal mucosa and identify Barrett's esophagus, Cameron's ulcers, or malignancy. Manometry is also recommended to evaluate for dysmotility disorders prior to undertaking surgical repair, which often includes a fundoplication [15].

Gastric volvulus is a malrotation of the stomach and a rare but life-threatening condition with a bimodal distribution occurring at less than 1 year of life and in the fifth decade [17]. Clinical presentation depends on the chronicity of the volvulus. Acute presentation is the classic Borchadt's triad (chest or upper abdominal pain, severe retching, and inability to pass a nasogastric tube) and present in 70% of cases [17]. Hematemesis is also present and represents ischemia or mucosal tears from retching. Chronic volvulus is more difficult to diagnosis due its non-specific and transient symptoms of chest or abdominal pain, dysphagia, and bloating. It is commonly misdiagnosed as peptic ulcer disease.

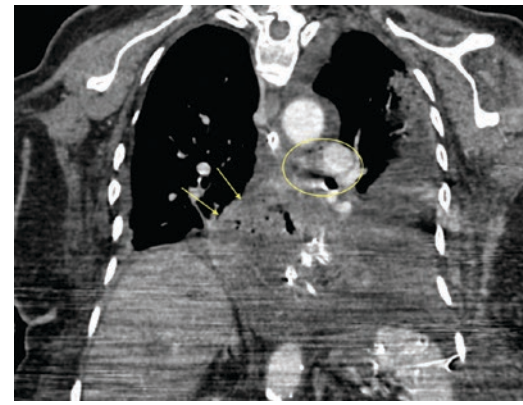

Fig. 33.2 Paraesophageal hernia (solid yellow arrows) with gastric volvulus and necrosis with free air (yellow circle) and mediastinal and left pleural contamination

The volvulus is classified by etiology or axis of rotation. The primary subtype is caused by malignancy or abnormalities in the anchoring points of the stomach (the ligaments, gastroesophageal junction, and pylorus), preventing malrotation. The secondary subtype is due to abnormalities in gastric anatomy or function or dysfunction of adjacent organs. This subtype is commonly associated with paraesophageal hernias in adults, but diaphragmatic dysfunction is also implicated. Classification by axis of rotation includes organoaxial, mesenteroaxial, and combined. Organoaxial is the most common, accounting for 60% of gastric volvulus and characterized by rotation of the greater curvature around a longitudinal axis resulting in the greater curvature superior to the lesser curvature. Mesenteroaxial rotation occurs when the pylorus and antrum are rotated anterior and superior to the gastroesophageal junction. The combined volvulus is both organoaxial and mesenteroaxial axial rotation and the most rare [17].

Miscellaneous

Schatzki's rings were first described in 1944 and are found in 6–14% of routine barium esophagrams. Although mostly asymptomatic, these entities are considered the most common cause of episodic dysphagia for solids and adult food impaction. Rings are frequently found in association with other esophageal disorders such as eosinophilic esophagitis, webs, and hiatal hernias particularly in symptomatic patients [18].

Eosinophilic esophagitis is a chronic, immune-mediated inflammatory disease of the esophagus primarily mediated by eosinophils causing strictures, occlusion, perforation, and malnutrition [19]. For unknown reasons, prevalence is increasing in the last 10 years, occurring in 12–23% of patients undergoing endoscopy for dysphagia. A recent meta-analysis of 1293 patients reported suspected or biopsy-proven eosinophilic esophagitis in 54% of cases of food impaction requiring endoscopic intervention [20]. Various causes for eosinophilic esophagitis cited include food allergens, increased aeroallergens, *H. pylori* eradication, increased proton pump inhibitor therapy, and early-life exposures [21].

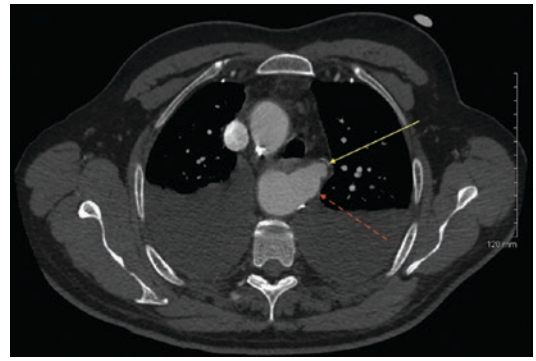

Fig. 33.3 CT angiogram demonstrating right-sided aortic arch with aberrant left subclavian artery (yellow, solid arrow) with Kommerell diverticulum (red, dashed arrow)

Dysphagia lusoria is compression of the esophagus due to a congenital aortic arch abnormality containing an aberrant right subclavian artery (Fig. 33.3). It is present in 0.5–1.8% of the population, and common symptoms of this rare entity include dysphagia, retrosternal chest pain, dyspnea, and weight loss [22]. Esophageal occlusion is even more rare and only reported as case reports [23].

II. Perforation

Iatrogenic

Iatrogenic injury is the most common cause of esophageal perforation, reported as the mechanism of injury in 60–70% of reported cases [24, 25]. Endoscopic perforation occurs at sites of luminal narrowing such as the cricopharyngeus, aortic knob, gastroesophageal junction, and pathologic sites where tumor or strictures are present. The reported risk of perforation during a diagnostic esophagogastric duodenoscopy (EGD) is 0.03% but increases with therapeutic procedures, particularly in variceal sclerotherapy (1–6%), laser and photodynamic therapy (4–6%), dilations (1–6%), and stent placement. Perforations also occur during blind placement of transesophageal probes used for ECHO [25]. Patients typically present with neck or chest pain

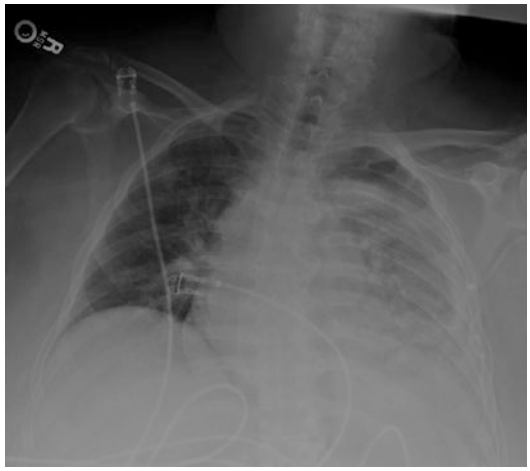

Fig. 33.4 Chest X-ray demonstrating esophageal perforation with left-sided pleural effusion

and dysphagia and may have crepitus if the perforation is located in the cervical esophagus. Chest X-ray demonstrates pleural effusion (Fig. 33.4). Traditional diagnostic imaging begins with thin barium esophagram; however, CT chest and abdomen with contrast provides location and defines anatomy and is an alternative first-line imaging choice (Fig. 33.5a, b).

Boerhaave's Syndrome

Described in 1724 by the Dutch physician, Herman Boerhaave, Boerhaave's syndrome is spontaneous esophageal perforation occurring after forceful vomiting [26]. This rare type of perforation is barotrauma secondary to a rapid rise in intraluminal pressure associated with vomiting. The perforation occurs in the lower third, left posterolateral portion of the esophagus, a localized anatomic weakness. Diagnosis is often delayed due to non-specific symptoms such as hypotension, shock, chest pain, and dyspnea prompting a workup for myocardial infarction, aortic dissection, pulmonary embolus, and peptic ulcer disease, resulting in higher morbidity and mortality of 20–40% due to delay in diagnosis [26]. A thin barium esophagram is the traditional diagnostic test of choice, but CT provides more rapid diagnosis and assists in exclusion of other diagnosis.

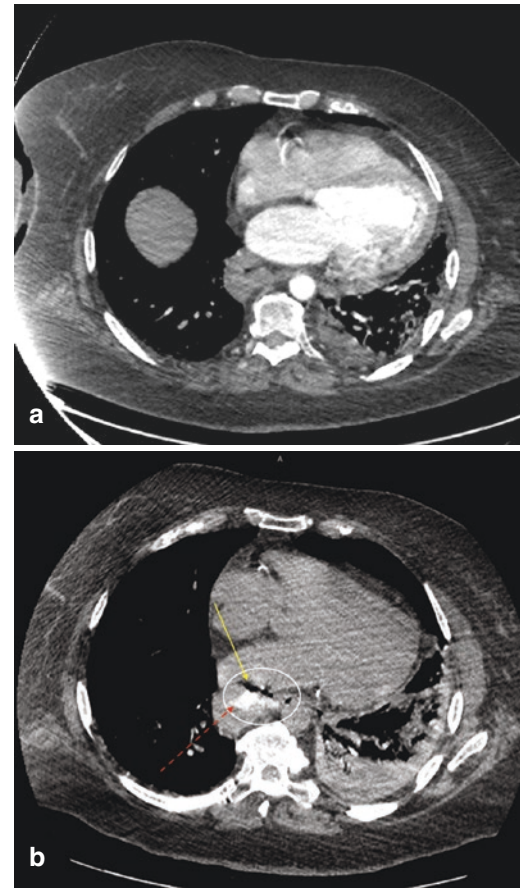

Fig. 33.5 (**a**) CT chest with contrast demonstrating esophageal perforation with left-sided pleural contamination. (**b**) CT chest with contrast in same patient with esophageal perforation with extravasation of contrast (red, dashed arrow) and free air (yellow, solid arrow) with left-sided pleural contamination

Trauma

Traumatic esophageal is rare, occurring in less than 10% of blunt and penetrating traumas, but associated with high morbidity and mortality [24]. The most recent literature reviews of the National Trauma Data Bank report indicate penetrating injuries account for 50% of all esophageal traumas. Gunshot wounds represent the most common injury (35.7%) followed by stab wounds (14.9%). The type of weapon and muzzle velocity determines the extent of injury. High-velocity weapons (>1500 fps) result in injury at the site of penetration and surrounding destruction from cavitation and blast effect, while low-velocity

bullets and stab wounds do not [24]. For blunt trauma, the most common mechanism is motor vehicle accidents (19%) followed by falls (7.7%) and assault (4.1%) [27]. The thoracic esophagus was the most common portion affected (64.9%) and associated with higher morbidity and mortality likely due to uncontained bacterial contamination into the mediastinum as well as the severity of the trauma itself with 80% having ISS > 15 [27]. Injury occurs when there is a horizontal deceleration compressing the esophagus against the vertebral column. This commonly occurs as the sternum strikes the steering wheel, compressing the esophagus against the thoracic spine. Other less common mechanisms occur during cardiopulmonary resuscitation, Heimlich maneuver, or barotrauma [24]. Cervical esophagus injuries are less common (35.1%) and associated with penetrating trauma. Diagnosis is made via triple endoscopy: bronchoscopy, direct laryngoscopy, and esophagoscopy. CT chest and abdomen with contrast is also a helpful adjunct diagnostic study.

Tracheoesophageal Fistula

Tracheoesophageal fistula (TEF) represents an abnormal connection between the esophagus and the trachea but is also used to describe a fistulous connection between the esophagus and the lung or bronchus. It is broadly classified by its underlying cause: malignant or nonmalignant. Malignant TEF occurs due to tumor invasion and is commonly associated with esophageal cancer (5–15% in most series); however, it is also associated with bronchiogenic (1%), lung (0.16%), and thyroid and laryngeal carcinomas (15%) [28]. Nonmalignant TEF is caused by surgery, granulomatous infections such as tuberculosis or histoplasmosis (particularly in immunocompromised patients), post-intubation injury, and mechanical ventilation. Post-intubation injury represents the most common cause of nonmalignant TEF, as high as 80% in some reviews of the literature [29].

Overall, TEF is a rare disorder with most TEF occurring in the upper and middle trachea and esophagus. Patients present with stridor, frequent cough, aspiration, frequent fever, and pneumonia. A relevant history often reveals patients with a history of malignancy including recent chemotherapy, radiation therapy to the mediastinum, recent esophageal or tracheal surgery, recent esophageal instrumentation including laser therapy, or prolonged mechanical ventilation and tracheostomy [30]. Diagnosis is made with thing barium swallow followed by direct endoscopic evaluation using flexible bronchoscopy and esophagoscopy (Fig. 33.6). Imaging such as computed tomography is helpful in defining anatomy, but swallow studies utilizing gastrografin are contraindicated due to potential transfer of gastrografin into the respiratory tract causing chemical pneumonitis [28]. If granulomatous disease or HIV is suspected as the cause of the TEF, then relevant testing should be pursued during workup.

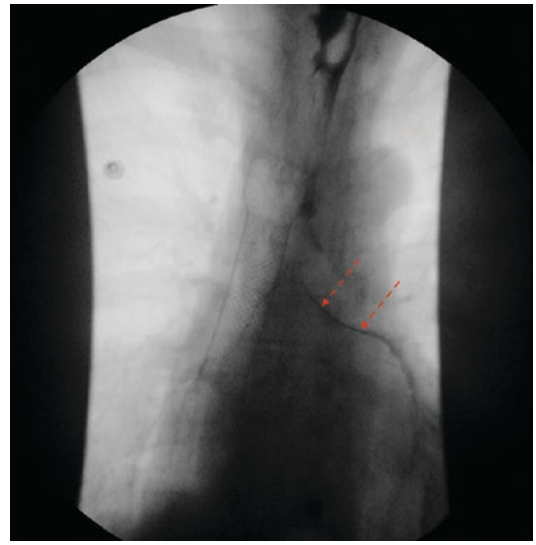

Fig. 33.6 Barium esophagram demonstrating failed stent placement in setting of tracheoesophageal fistula with contrast extravasating into the left main stem bronchus (red, dashed arrows)

Acute Management of Perforation

The acute management of esophageal perforation is dictated by location of the injury, underlying comorbid conditions, and the level of physiologic derangement. Presenting symptoms are varied, non-specific, and dependent on the location of

perforation. Diagnostic imaging often begins with a chest x-ray (CXR) due to non-specific presenting symptoms of chest pain and dyspnea. The CXR often demonstrates pleural effusion depending on the level of perforation but is not specific or sensitive for determining the location of the perforation. Commonly, a middle third perforation causes a right-sided effusion, and a lower third perforation causes a left-sided perforation, particularly in the setting of Boerhaave's syndrome. Bilateral pleural effusions are also possible. Other findings seen on CXR include pneumomediastinum, mediastinal air-fluid levels, and free air under the diaphragm. Definitive diagnosis is made with a thin barium swallow. The authors prefer thin barium to gastrografin because of risk of chemical pneumonitis; however barium contamination into the peritoneal cavity requires abdominal exploration and washout. CT scan of the chest and abdomen is also an excellent alternative choice to delineate the level of perforation and define anatomy [31]. The role of upper endoscopy in the management of perforation is diagnostic and potentially therapeutic. Therapeutic endoscopy is discussed elsewhere and beyond the scope of this chapter. For planned surgical repairs of perforation, the use of endoscopy includes final confirmation of level and extent of perforation, assessment for associated pathology such as distal obstruction, and insufflation testing after primary repair.

The tenets of surgical repair of all esophageal perforations begin with complete circumferential mobilization and encirclement of the esophagus with a Penrose drain or umbilical tape. The muscular defect is enlarged longitudinally exposing the full extent of the mucosal tear. All devitalized tissue is debrided. Mucosal repair is performed with absorbable sutures. The authors' preference is 4-0 interrupted PDS. Following repair, the overlying esophageal musculature is closed with interrupted silk sutures. In setting of heavy contamination, the skin edges of the wound are left open, and the subcutaneous tissue is packed with wet-to-dry gauze.

Injuries to the cervical esophagus typically present with neck pain, dysphagia, and possibly crepitus in the neck and shoulders. The mechanism of injury is often iatrogenic in the setting of a structurally abnormal esophagus. Patients with underlying dysmotility disorders and pulsion diverticulum such as Zenker's or epiphrenic diverticulum from achalasia are particularly susceptible [32].

Although cervical perforation is often the easiest to manage, mediastinal soilage and mediastinitis may progress rapidly. Prompt initiation of NPO status, broad-spectrum antibiotics, and fluid resuscitation are the mainstay of initial treatment. Operative intervention consists of either cervical drainage alone or primary repair following endoscopic evaluation [33].

The operative approach to the cervical esophagus is best achieved through a left neck exploration. Incision along the anterior border of the sternocleidomastoid muscle and lateral retraction of the carotid sheath provides excellent exposure to the posterior mediastinum. Division of the omohyoid muscle and middle thyroid vein facilitates this exposure. Care must be taken to identify the recurrent laryngeal nerve as it travels between the trachea and esophagus. Failure to identify the recurrent nerve should prompt the surgeon to perform operative drainage alone instead of primary repair as a nerve injury greatly increases the risk of postoperative aspiration and long-term morbidity [34–36]. Operative drainage consists of developing the prevertebral and retrosternal planes with blunt dissection, facilitating wide drainage of the anterior and posterior mediastinum. Jackson Pratt and Blake closed suction drain placement are the preferred method of drainage. In the presence of heavy contamination, all layers of the cervical incision are opened to the esophagus manner similar to post-esophagectomy cervical leak management. A Penrose drain can be left to facilitate drainage from the neck. Once the perforation heals, endoscopic evaluation is performed for symptomatic patients with dysphagia to assess for strictures.

The initial diagnostic evaluation and resuscitation are the same in thoracic and abdominal perforations. Operative approach to the injury is dictated by location and determined by imaging and intraoperative endoscopic evaluation. Perforation to the mid-thoracic esophagus is approached through a right posterolateral thoracotomy and the distal esophagus and

gastroesophageal (GE) junction through a left posterolateral thoracotomy. Although video-assisted thoracoscopic (VATS) and robotic approaches are described for operative repair, they should only be considered in centers with expertise in minimally invasive approaches [37]. The thoracotomy approach is the most reliable approach with excellent exposure of the posterior mediastinum for the majority of acute care surgeons.

The mid-thoracic esophagus 5th intercostal space providing excellent exposure. For GE junction and distal esophageal injuries, the left chest is accessed via the 6th or 7th intercostal space. An intercostal muscle pedicle flap to buttress the esophageal repair is harvested prior to inserting a self-retaining retractor. Lysis of the inferior pulmonary ligament and anterior retraction of the lung exposes the posterior mediastinum. Division of the azygos vein in the right chest should be performed liberally to facilitate exposure, if needed. The pleural space is cleared of debris and all devitalized tissue debrided (Fig. 33.7).

Esophageal mobilization and localization of the perforation are performed in a similar fashion to cervical perforation. The esophageal muscle is opened longitudinally to visualize the full extent of the perforation. Repair of the mucosal defect followed by muscular closure of the esophagus is performed. The intercostal muscle flap is secured to the repair as a tissue buttress. In cases in which an intercostal muscle flap is not harvested, or is nonviable, a pericardial fat pad or pleural flaps are alternatives. An endoscopic leak test, if performed, is completed prior to buttressing the repair [38].

Following completion, the pleural space is widely drained and the lung decorticated as necessary to ensure full re-expansion. At a minimum, thoracostomy tubes are placed in the posterior mediastinum and along the diaphragm. An anterior tube is placed if decortication is performed to manage air leaks. A nasogastric tube is placed with care taken not to disrupt the repair. Enteral access is deferred in the majority of case but is an option in chronically malnourished patients. Gastric feeding tubes are avoided to preserve the stomach as a future esophageal conduit if more extensive resection is required. Entering the abdomen to place a feeding jejunostomy should be deferred from the index operation and, if required, can be placed laparoscopically once the patient recovers from the initial physiologic insult. It should not be done endoscopically to avoid injury to the newly repaired esophagus. The presence of a contralateral pleural effusion warrants placement of a thoracostomy tube in that space.

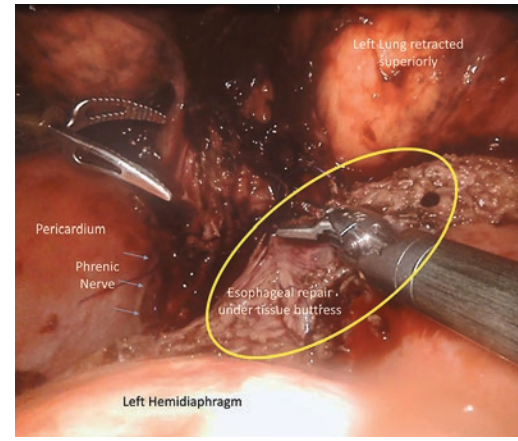

Fig. 33.7 Completed esophageal primary repair. Intercostal muscle flap is being secured for tissue buttress

Upon successful completion of a primary esophageal repair, the patient is supported with nutritional supplementation, parenteral antibiotics, and early aggressive mobilization. If a jejunal feeding tube was not placed intraoperatively, total parenteral nutrition may be utilized. Although no formal recommendations exist, antibiotics are continued for 7–10 days and adjusted based on intraoperative cultures. A barium esophagram is obtained on postoperative days 5 through 7. Oral feeding begins following confirmation of an intact repair. In cases where a leak is identified, a covered stent should be considered (see next paragraph). A small leak well controlled by the operatively placed drains warrants a prolonged course of NPO status and enteral feeds. The leak rate in urgently repaired esophageal perforations in adults is dependent on time of presentation, degree of contamination, and underlying etiology. Following surgical repair, the incidence of radiographically apparent leak is about 30%, and upward of 40% of patients may require further

interventions [39]. It is the authors' preference to place laparoscopic jejunostomy tubes only in cases where the patient is unable to begin oral feeds based on the postoperative day 5 swallow study. Surgical drains are removed if no leak is identified on the swallow study.

A full discussion of endoscopic management of esophageal perforations is beyond the scope of chapter and is discussed elsewhere. However, covered esophageal stents should be considered in select patients. The presence of an injury crossing the GE junction, within 5 cm of the cricopharyngeus, or spanning a length greater than 5 cm is associated with a higher risk of stent failure [40]. In patients with contamination of the pleural space, drainage via tube thoracostomy or VATS is performed even with successful endoluminal coverage.

Perforation in the presence of malignancy presents a significant management challenge. Proceeding with an esophageal resection in a patient with significant physiologic derangement is a decision not to be taken lightly. Primary repair of an esophageal tear in the presence of a distal obstruction is doomed to fail. In these situations, based on the availability of advanced endoscopic techniques and technical expertise in esophageal resection, temporizing measures are recommended. Endoscopic management with a covered esophageal stent followed by VATS drainage of the mediastinum is an excellent option if the capabilities exist. Wide mediastinal drainage through a thoracotomy with placement of a T-tube through the perforation and large bore chest tubes are excellent temporizing measures allowing for continued resuscitation and transfer to a higher level of care [41, 42]. In centers experienced with esophageal cancer, primary resection can be performed with either simultaneous or delayed reconstruction [43, 44]. If possible, it is best to perform a cervical anastomosis to place the anastomosis out of the contaminated field. Although these techniques are applicable to nonmalignant perforations, primary repair or endoscopic stenting with mediastinal drainage is the preferred approach for definitive management. These diversion techniques are best utilized for patients with severe physiologic derangements in a damage control approach to nonmalignant perforation.

Esophageal diversion is becoming less common due to the advent of endoscopic and improved surgical techniques. In hemodynamically unstable patients, in the setting of a large defect or nonviable esophageal tissue, diversion is necessary [42]. Depending on the level of perforation, the esophagus mobilized through a right or left thoracotomy and the devitalized segment resected. The resection is carried distally to include the GE junction and proximally to the level of the aortic arch if on the left and the azygos vein if on the right. The diaphragm hiatus is closed to prevent herniation. Both gastrostomy and jejunostomy tubes are placed transabdominally. The gastrostomy is to vent the intestinal tract and the jejunostomy is for enteral access. The cervical stump is left as long as possible and placed on the anterior chest for drainage and fitted with an ostomy appliance. Reconstruction is only attempted after a period of recovery and nutritional support. This usually requires either a gastric conduit or a colonic interposition be performed through a retrosternal or subcutaneous tunnel, as the posterior mediastinum will be inaccessible.

Acute Management of Obstruction

Food Impaction

The management of food impaction is managed in a systematic fashion beginning with airway assessment. Once the airway is secure, localization of the foreign body and its removal can occur. Plain film upright X-rays are often not helpful unless bone material is present within the foreign body, but a non-contrasted computed tomography (CT) is more sensitive and able to identify 80–100% of foreign bodies and therefore the recommended study of choice [45]. In hemodynamically stable patients with a patent airway, relief of impaction can start with administration of pharmacological agents in the emergency department. The most common agent is intravenous glucagon (1–2 mg IV in adults, 0.02–0.03 mg/kg in children

less than 20 kg, max dose 0.05 mg), relaxing the esophagus and allowing passage of food into the stomach [46]. Although a common pharmacological maneuver, it is not well studied, and it is unclear if its success is related to certain subpopulations [10]. Another common agent is intravenous diazepam (2.5–10 mg IV), often utilized as a second-line agent. Other pharmacological agents, administered with and without glucagon, include water and gas-forming agents (simethicone, sodium bicarbonate, citric acid, and carbonated beverages). These agents use gravity and increased luminal pressure from carbon dioxide formation to push the bolus into the stomach, respectively; however perforations are reported and these agents must be used with caution. Calcium channel blockers (verapamil and nifedipine) and nitrates such as isosorbide nitrate (5 mg sublingual) are reported, but not routinely used [47]. Proteolytic enzymes such as papain and chymotrypsin were previously popular but have fallen out of favor due to complications such as esophageal erosion, necrosis, and perforation and pulmonary complications if aspirated [48].

Endoscopic retrieval is recommended in patients who are in distress or failed medical management. For conscious patients with complete obstruction, they are positioned upright and secretions managed with suction. Asymptomatic patients are given a trial of observation, but endoscopic retrieval should not be postponed more than 24 h to prevent progression to perforation. Flexible endoscopy is recommended over rigid endoscopy due to need for general anesthesia and higher risk of perforation; however, it may be beneficial in impacted foreign bodies in the pediatric population or in impactions occurring at the level of the upper esophageal sphincter or hypopharyngeal region [49]. A variety of endoscopic tools including forceps, snares, nets, baskets, and overtubes should be readily available. The push technique involves gentle pressure at the center of the bolus to push it into the stomach; however, it is avoided in patients with large, firm food bolus with bone material, prolonged impaction, or suspected or known eosinophilic esophagitis [45, 46, 49]. The extraction technique is the preferred method in patients with abnormal esophageal anatomy or function. The bolus is often broken into smaller pieces and either removed or pushed into the stomach using a combination of snares, forceps, graspers, and forceps [46]. If a stricture or ring is found at the site of impaction, dilation can be performed during the same procedure; however, if an abnormality such as eosinophilic esophagitis is suspected, biopsies of the distal esophagus proximal and distal should be performed and dilation deferred [10, 45, 49].

Malignancy

Esophageal cancer has seen a 21-fold increase internationally worldwide and is responsible for over 400,000 deaths per year [50]. The incidence is three times more common in men than woman [50]. Chronic reflux and being overweight or obese are risk factors for the development of esophageal adenocarcinoma and explain the increase in incidence in the United States over squamous cell carcinoma [51–53]. Over 90% of patients with esophageal cancer present with advanced disease, and 5-year survival is 10–15% [54].

Patients with malignant obstruction typically have advanced disease. The malnutrition accompanying obstruction independently increases mortality and dramatically reduces the ability to tolerate chemoradiotherapy [55]. Palliative enteral access is important to allow patients to receive chemotherapy and radiation therapy. A retrospective study looking at NPO and supportive care versus a fluoroscopic placed NGT versus esophageal stenting found a median survival of 51 days, 122 days, and 133 days, respectively [56]. In practical terms, patient median survival is on the order of months, and their management is approached with the mindset of providing palliation with minimal morbidity.

Esophageal stents provide potential for obstruction relief and the restoration of normal oral intake. The self-expandable metallic stents (SEMS) can be effective tools in managing dysphagia symptoms and allowing for oral feeding [57–61]. The interventions are not low-risk and must be performed by an experienced endosco-

pist. Life-threatening complications such as bleeding, perforation, pneumonia, and bronchoesophageal fistulas can occur, as well as intractable pain and reflux. The rates of post-stent mortality range from 3.9% to 27.2% [59, 62–65].

In the evaluation of patients with a suspected malignant obstruction, ensuring a secure airway is the first priority. Radiographic evaluation with a CXR to assess for pleural effusions, air-fluid levels within the esophagus, or aspiration pneumonia is a useful initial study. In patients unable to tolerate secretions, a CT scan of the chest and abdomen is preferred to a contrast esophagram. CT scan is also useful to evaluate the size and location of the obstruction and evidence of distant disease.

Patients with complete or near-complete esophageal obstruction require prompt endoscopic evaluation. The goals of this initial evaluation are the following [1]: clearance of any obstructing foreign bodies [2], evaluation of the location and degree of obstruction, and [3] obtaining adequate tissue for pathologic diagnosis. The ability to traverse the obstruction provides useful information for further therapeutic planning. In cases in which an adult-sized endoscope cannot pass, a pediatric scope is an alternative. For any attempt at using a guidewire to help traverse the lesion, fluoroscopic guidance is mandatory to prevent iatrogenic perforation. However for the initial endoscopic evaluation, intervention on the obstruction is deferred in favor obtaining adequate tissue for diagnosis and the use of a multidisciplinary approach involving medical and radiation oncology, gastroenterology, and a discussion with the patient and their family.

Subsequent interventions on the occlusion should take into account the level of occlusion, pathologic subtype, and patient preference. SEMS for cervical occlusion is controversial, as these tumors tend to be squamous and are very responsive to radiation therapy. Limited series demonstrate improvement in symptoms with complications rates similar to more distal occlusions, so expert consultation is advised [66]. In general, though, lesions within 4 cm of the upper esophageal sphincter should not be stented.

Performance of SEMS requires either an endoscopy suite or a standard operating room. Fluoroscopy is integral for visualization of the guide wire and correct stent positioning. Numerous stent options are commercially available, and a detailed product description is beyond the scope of this chapter. Once the lesion is traversed, length measurements are performed using the endoscope or fluoroscopic markers (Figs. 33.8 and 33.9). Balloon dilation of the

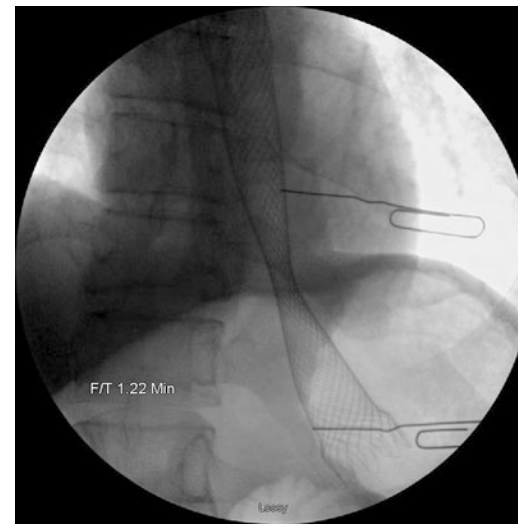

Fig. 33.8 Stent deployment under fluoroscopy in the setting of a malignancy with use of paper clips as markers

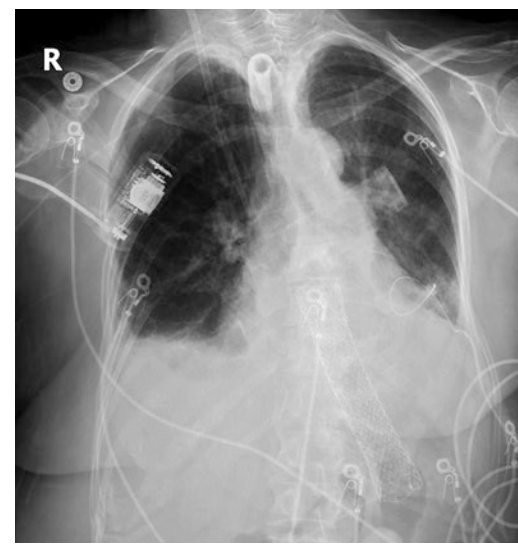

Fig. 33.9 Stent deployment in a patient with esophageal perforation at GE junction secondary to stomach necrosis from paraesophageal hernia and gastric volvulus

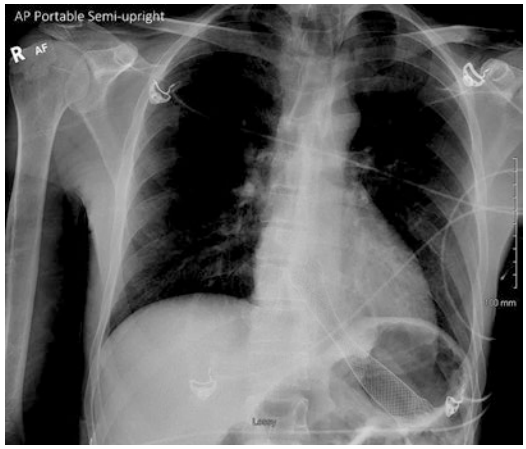

Fig. 33.10 Stent migration

obstruction is performed to facilitate passage of the stent across the lesion. One advantage of balloon dilation over Savary bougies is the ability to post-dilate through the stent following deployment with less concern for stent migration.

Postoperatively, patients are typically started on clear liquids; however, there is a low threshold for obtaining an esophagram if there are concerns for perforation. Patients are counseled with strict return precautions if obstructive symptoms recur and to expect some degree of reflux symptoms. Stent migration occurs over time or as the tumor responds to therapy and retrieval is typically managed endoscopically (Fig. 33.10). In high-grade obstructions, additional enteral access is obtained in order to maintain adequate nutrition. Consideration for the possibility of future esophagectomy with gastric conduit reconstruction determines whether a gastric or intestinal feeding tube is selected. A nasogastric tube can be placed through the stent if the patient desires and understands the risks of tube dislodgement.

Tracheoesophageal Fistula

A fistulous connection can occur between the esophagus and trachea with some occlusions. Treatment is aimed at treating the underlying cause, and surgery is first-line therapy often involving resection of the tract, reconstruction, and coverage of the fistulous tract with healthy tissue; however, most patients are too deconditioned at time of presentation to undergo surgery. Treatments such as covered self-expanding stents, fibrin glue, degradable stents, Amplatzer plugs, endobronchial one-way umbrella valves, septal buttons, and mesenchymal stem cell transfer are all reported therapies with various success rates, all dependent on the etiology, size, and location of the TEF [28].

Management of Chronic Occlusive Conditions

Strictures

Untreated, esophageal strictures lead to progressively worsening obstruction and symptoms of dysphagia. The majority of strictures are due to GERD; however a benign stricture is a diagnosis of exclusion. Eosinophilic esophagitis may also lead to the development of stricture. Management of meat impaction and malignant obstruction has been previously discussed. As submucosal resection for the management of Barrett's has increased, patients can develop strictures as a consequence [67]. Post-anastomotic strictures following esophagectomy may also occur.

After airway assessment and imaging with either CT scan or esophagram, the mainstay of management is endoscopic dilation. Endoscopic dilation is performed as an outpatient treatment with either bougie or balloon dilation. As these strictures present a chronic problem, patients can be taught to self-dilate [68]. Bleeding and perforation are well-known complications of dilation and must be considered in the periprocedural period.

Esophageal stents for benign disease are not recommended because the lowest success rates for esophageal stenting are in patients with benign disease. The treatment success rate for refractory benign strictures is 33.3% with stent migration rate of 40% [69]. Patients with symptoms refractory to endoscopic dilation should be considered for esophagectomy.

Dysmotility Disorders

Patients with achalasia presenting with symptoms of obstruction are best managed acutely with endoscopy for removal of any obstructing foreign bodies and dilation. A full diagnostic evaluation including manometry is necessary for those without a firm diagnosis. Multiple therapeutic options exist for treatment including intrasphincteric botulinum toxin injection, dilation, per-oral endoscopic myotomy (POEM), or Heller myotomy. This is discussed at length in other chapters. In the absence of inoperable medical comorbidities, Heller myotomy has the best long-term results [11–13, 70–72]. Any associated pathology such as epiphrenic diverticuli can be addressed at the time of surgery.

Vascular Rings

Dysphagia lusoria presenting as an acute occlusion is a rare presentation of this uncommon entity [23, 73, 74]. After acute stabilization and management of any retained foreign bodies, treatment involves vascular division at the origin of the aorta to prevent future enlargement of a Kommerell diverticula [75] (Figs. 33.11, 33.12, and 33.13). The need for revascularization of the

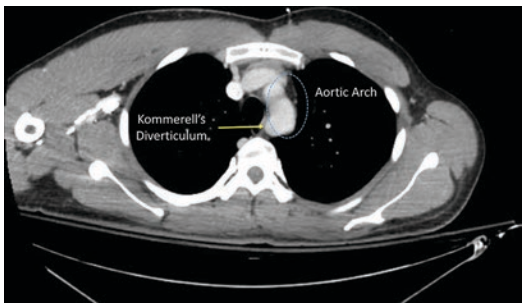

Fig. 33.11 Axial image denotes takeoff aberrant right subclavian artery with a retroesophageal course in a patient with dysphagia. The origin of the aberrant artery is Kommerell's diverticulum (yellow arrow)

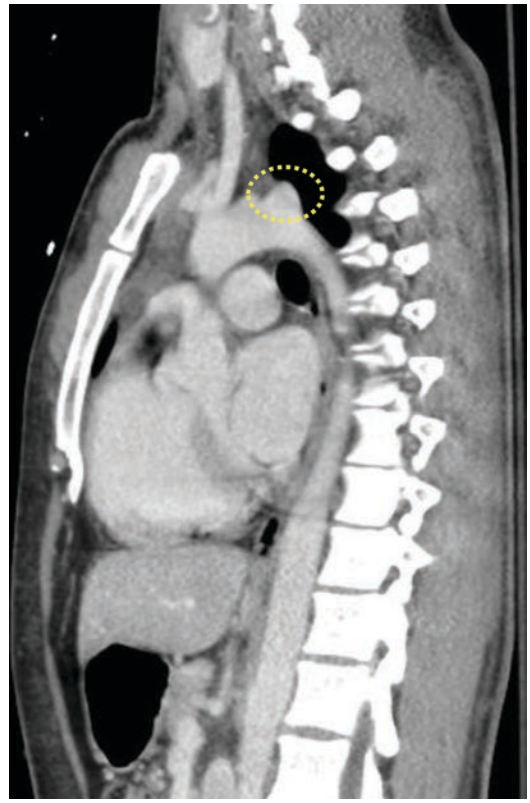

Fig. 33.12 Sagittal view in the same patient better illustrating the aneurysmal dilation of Kommerell's diverticulum (yellow-dashed circle)

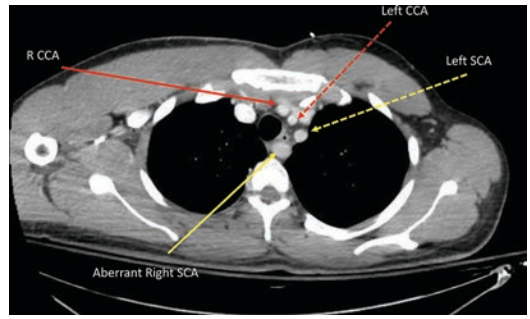

Fig. 33.13 Axial image denoting the retroesophageal course in the same patient of the aberrant right subclavian artery (solid yellow arrow). This demonstrates the external compression of the esophagus with pathognomonic of dysphagia lusoria. The patient is currently undergoing evaluation for surgical repair

aberrant subclavian is uncommon and should be based on the patient's arterial anatomy and may require carotid-subclavian bypass.

Conclusion

Esophageal obstruction and perforation are rare but associated with high morbidity and mortality if not diagnosed and treated early. Each etiology is associated with a different patient population, highlighting the importance of a thorough history to aid in directing appropriate diagnostic studies and management. Obstruction is commonly the result of malignancy but also seen in dysmotility disorders, food impaction, caustic injection, foreign bodies, paraesophageal hernias, volvulus, and strictures. Perforation most commonly occurs as iatrogenic injury from endoscopy but also occurs in Boerhaave's syndrome, trauma, and tracheoesophageal fistula (TEF).

Esophageal perforations are acutely managed with NPO status and initiation of intravenous fluids and broad-spectrum antibiotics. Diagnostic imaging is by thin barium esophagram, but CT abdomen and pelvis is an excellent alternative. Select patients can be managed with covered stent placement, but pleural or mediastinal contamination must be drained. Primary repair is usually possible and esophageal diversion is rarely necessary. Obstructions are initially managed with securing the airway and then using diagnostic imaging to determine the cause. Food impaction is managed endoscopically or pharmacologically. Malignant obstruction management requires a multimodal approach, to include chemoradiation therapy options, and primary resection is not to be undertaken in the acute care setting given the frailty of most patients in this population. For esophageal cancer, esophagectomy is usually reserved for stage T1b–3, N0–1, M0 disease, but these patients do not typically present acutely. The acute patient usually has locally advanced disease and as such may do better with a temporizing measure and subsequent chemoradiation therapy. Chronic obstructive pathology such as strictures and dysmotility disorders is primarily managed with endoscopy with surgical intervention reserved for young, fit patients or those who fail endoscopic therapy. Chronic obstructions do not typically present as a perforation.

References

1. Oezcelik A, DeMeester SR. General anatomy of the esophagus. Thorac Surg Clin. 2011;21(2):289–97. x
2. Patel D, Vaezi MF. Normal esophageal physiology and laryngopharyngeal reflux. Otolaryngol Clin N Am. 2013;46(6):1023–41.
3. Rice TW, Bronner MP. The esophageal wall. Thorac Surg Clin. 2011;21(2):299–305, x.
4. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends – an update. Cancer Epidemiol Biomark Prev. 2016;25(1):16–27.
5. Lagergren J, Smyth E, Cunningham D, Lagergren P. Oesophageal cancer. Lancet. 2017;390(10110):2383–96.
6. Bharat A, Crabtree T. Management of advanced-stage operable esophageal cancer. Surg Clin North Am. 2012;92(5):1179–97.
7. Smith CD. Esophageal strictures and diverticula. Surg Clin North Am. 2015;95(3):669–81.
8. Gummin DD, Mowry JB, Spyker DA, Brooks DE, Fraser MO, Banner W. 2016 annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 34th annual report. Clin Toxicol (Phila). 2017;55(10):1072–252.
9. Kurowski JA, Kay M. Caustic ingestions and foreign bodies ingestions in pediatric patients. Pediatr Clin N Am. 2017;64(3):507–24.
10. Triadafilopoulos G, Roorda A, Akiyama J. Update on foreign bodies in the esophagus: diagnosis and management. Curr Gastroenterol Rep. 2013;15(4):317.
11. Stavropoulos SN, Friedel D, Modayil R, Parkman HP. Diagnosis and management of esophageal achalasia. BMJ. 2016;354:i2785.
12. Uppal DS, Wang AY. Update on the endoscopic treatments for achalasia. World J Gastroenterol. 2016;22(39):8670–83.
13. Bowers SP. Esophageal motility disorders. Surg Clin North Am. 2015;95(3):467–82.
14. Pregun I, Hritz I, Tulassay Z, Herszenyi L. Peptic esophageal stricture: medical treatment. Dig Dis. 2009;27(1):31–7.

15. Andolfi C, Jalilvand A, Plana A, Fisichella PM. Surgical treatment of paraesophageal hernias: a review. J Laparoendosc Adv Surg Tech A. 2016;26(10):778–83.
16. Schieman C, Grondin SC. Paraesophageal hernia: clinical presentation, evaluation, and management controversies. Thorac Surg Clin. 2009;19(4):473–84.
17. Rashid F, Thangarajah T, Mulvey D, Larvin M, Iftikhar SY. A review article on gastric volvulus: a challenge to diagnosis and management. Int J Surg. 2010;8(1):18–24.
18. Muller M, Gockel I, Hedwig P, Eckardt AJ, Kuhr K, Konig J, et al. Is the Schatzki ring a unique esophageal entity? World J Gastroenterol. 2011;17(23):2838–43.
19. Furuta GT, Katzka DA. Eosinophilic esophagitis. N Engl J Med. 2015;373(17):1640–8.
20. Hiremath GS, Hameed F, Pacheco A, Olive A, Davis CM, Shulman RJ. Esophageal food impaction and eosinophilic esophagitis: a retrospective study, systematic review, and meta-analysis. Dig Dis Sci. 2015;60(11):3181–93.
21. Dellon ES. Epidemiology of eosinophilic esophagitis. Gastroenterol Clin N Am. 2014;43(2):201–18.
22. Polguj M, Chrzanowski L, Kasprzak JD, Stefanczyk L, Topol M, Majos A. The aberrant right subclavian artery (arteria lusoria): the morphological and clinical aspects of one of the most important variations – a systematic study of 141 reports. Sci World J. 2014;2014:292734.
23. Okumus M, Ozkan F, Bozkurt S, Dogan M, Tokur M, Kapci M. Arteria lusoria: a very rare cause of esophageal obstruction in a hypoxemic patient. Turk J Gastroenterol. 2014;25(4):433–4.
24. Petrone P, Kassimi K, Jimenez-Gomez M, Betancourt A, Axelrad A, Marini CP. Management of esophageal injuries secondary to trauma. Injury. 2017;48(8):1735–42.
25. Kaman L, Iqbal J, Kundil B, Kochhar R. Management of Esophageal Perforation in adults. Gastroenterology Res. 2010;3(6):235–44.
26. de Schipper JP, Pull ter Gunne AF, Oostvogel HJ, van Laarhoven CJ. Spontaneous rupture of the oesophagus: Boerhaave's syndrome in 2008. Literature review and treatment algorithm. Dig Surg. 2009;26(1):1–6.
27. Aiolfi A, Inaba K, Recinos G, Khor D, Benjamin ER, Lam L, et al. Non-iatrogenic esophageal injury: a retrospective analysis from the National Trauma Data Bank. World J Emerg Surg. 2017;12:19.
28. Hurtgen M, Herber SC. Treatment of malignant tracheoesophageal fistula. Thorac Surg Clin. 2014;24(1):117–27.
29. Reed MF, Mathisen DJ. Tracheoesophageal fistula. Chest Surg Clin N Am. 2003;13(2):271–89.
30. Zhou C, Hu Y, Xiao Y, Yin W. Current treatment of tracheoesophageal fistula. Ther Adv Respir Dis. 2017;11(4):173–80.
31. Nirula R. Esophageal perforation. Surg Clin North Am. 2014;94(1):35–41.
32. Obeso Carillo GA, Blanco Ramos M, Garcia Fontan EM, Perez Pedrosa A, Gil Gil P. Perforated pharyngoesophageal diverticulum as a cause of cervical infection with mediastinal extension. Cir Esp. 2012;90(8):533–5.
33. Brinster CJ, Singhal S, Lee L, Marshall MB, Kaiser LR, Kucharczuk JC. Evolving options in the management of esophageal perforation. Ann Thorac Surg. 2004;77(4):1475–83.
34. Cheng Q, Liu B. Treatment of cervical esophageal perforation. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi (Journal of Clinical Otorhinolaryngology, Head, and Neck Surgery). 2013;27(18):989–90, 94.
35. Zenga J, Kreisel D, Kushnir VM, Rich JT. Management of cervical esophageal and hypopharyngeal perforations. Am J Otolaryngol. 2015;36(5):678–85.
36. Mann W, Munker G. Drainage of deep mediastinal infections following perforation of the cervical esophagus (author's transl). HNO. 1975;23(11):355–7.
37. Nakano T, Onodera K, Ichikawa H, Kamei T, Taniyama Y, Sakurai T, et al. Thoracoscopic primary repair with mediastinal drainage is a viable option for patients with Boerhaave's syndrome. J Thorac Dis. 2018;10(2):784–9.
38. Pezzetta E, Kokudo T, Uldry E, Yamaguchi T, Kudo H, Ris HB, et al. The surgical management of spontaneous esophageal perforation (Boerhaave's syndrome) 20 years of experience. Biosci Trends. 2016;10(2):120–4.
39. Bufkin BL, Miller JI Jr, Mansour KA. Esophageal perforation: emphasis on management. Ann Thorac Surg. 1996;61(5):1447–51; discussion 51–2.
40. Freeman RK, Ascioti AJ, Giannini T, Mahidhara RJ. Analysis of unsuccessful esophageal stent placements for esophageal perforation, fistula, or anastomotic leak. Ann Thorac Surg. 2012;94(3):959–64; discussion 64–5.
41. Nakabayashi T, Kudo M, Hirasawa T, Kuwano H. Successful late management of esophageal perforation with T-tube drainage. Case Rep Gastroenterol. 2008;2(1):67–70.
42. Naylor AR, Walker WS, Dark J, Cameron EW. T tube intubation in the management of seriously ill patients with oesophagopleural fistulae. Br J Surg. 1990;77(1):40–2.
43. Abu-Daff S, Shamji F, Ivanovic J, Villeneuve PJ, Gilbert S, Maziak DE, et al. Esophagectomy in esophageal perforations: an analysis. Dis Esophagus. 2016;29(1):34–40.
44. Seo YD, Lin J, Chang AC, Orringer MB, Lynch WR, Reddy RM. Emergent esophagectomy for esophageal perforations: a safe option. Ann Thorac Surg. 2015;100(3):905–9.
45. Bekkerman M, Sachdev AH, Andrade J, Twersky Y, Iqbal S. Endoscopic management of foreign bodies in the gastrointestinal tract: a review of the literature. Gastroenterol Res Pract. 2016;2016:8520767.
46. Ko HH, Enns R. Review of food bolus management. Can J Gastroenterol. 2008;22(10):805–8.
47. Khayyat YM. Pharmacological management of esophageal food bolus impaction. Emerg Med Int. 2013;2013:924015.

48. Ageno W, Gallus AS, Wittkowsky A, Crowther M, Hylek EM, Palareti G, et al. Oral anticoagulant therapy: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S–88S.
49. Committee ASoP, Ikenberry SO, Jue TL, Anderson MA, Appalaneni V, Banerjee S, et al. Management of ingested foreign bodies and food impactions. Gastrointest Endosc. 2011;73(6):1085–91.
50. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65(2):87–108.
51. Kinsinger S. Elevated cancer risk perceptions among patients with Barrett's esophagus: do psychological factors play a role? Dis Esophagus. 2018;31(4).
52. Spechler S. Barrett esophagus and risk of esophageal cancer: a clinical review. JAMA. 2013;310(6):627–36.
53. Thrift AP. Barrett's esophagus and esophageal adenocarcinoma: how common are they really? Dig Dis Sci. 2018;63(8):1988–96.
54. Lim H, Kim DH, Jung HY, Gong EJ, Na HK, Ahn JY, et al. Clinical significance of early detection of esophageal cancer in patients with head and neck cancer. Gut Liver. 2015;9(2):159–65.
55. Dewys WD, Begg C, Lavin PT, Band PR, Bennett JM, Bertino JR, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. Am J Med. 1980;69(4):491–7.
56. Yang CW, Lin HH, Hsieh TY, Chang WK. Palliative enteral feeding for patients with malignant esophageal obstruction: a retrospective study. BMC Palliat Care. 2015;14:58.
57. Knyrim K, Wagner HJ, Bethge N, Keymling M, Vakil N. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. N Engl J Med. 1993;329(18):1302–7.
58. Cwikiel M, Cwikiel W, Albertsson M. Palliation of dysphagia in patients with malignant esophageal strictures. Comparison of results of radiotherapy, chemotherapy and esophageal stent treatment. Acta oncologica (Stockholm, Sweden). 1996;35(1):75–9.
59. Dai Y, Li C, Xie Y, Liu X, Zhang J, Zhou J, et al. Interventions for dysphagia in oesophageal cancer. Cochrane Database Syst Rev. 2014;10:Cd005048.
60. Dicle O, Goktay AY, Akbaylar H. Palliation of malignant esophageal strictures: initial results with self-expanding uncovered nitinol coil stents. Eur Radiol. 1999;9(7):1418–22.
61. Bassi M, Luigiano C, Fabbri C, Ferrara F, Ghersi S, Alibrandi A, et al. Large diameter fully covered self-expanding metal stent placement for palliation of proximal malignant esophageal strictures. Dis Esophagus. 2015;28(6):579–84.
62. Iwasaki H, Mizushima T, Suzuki Y, Fukusada S, Kachi K, Ozeki T, et al. Factors that affect stent-related complications in patients with malignant obstruction of the esophagus or gastric cardia. Gut Liver. 2017;11(1):47–54.
63. Wang MQ, Sze DY, Wang ZP, Wang ZQ, Gao YA, Dake MD. Delayed complications after esophageal stent placement for treatment of malignant esophageal obstructions and esophagorespiratory fistulas. J Vasc Interv Radiol (JVIR). 2001;12(4):465–74.
64. Homann N, Noftz MR, Klingenberg-Noftz RD, Ludwig D. Delayed complications after placement of self-expanding stents in malignant esophageal obstruction: treatment strategies and survival rate. Dig Dis Sci. 2008;53(2):334–40.
65. Sumiyoshi T, Gotoda T, Muro K, Rembacken B, Goto M, Sumiyoshi Y, et al. Morbidity and mortality after self-expandable metallic stent placement in patients with progressive or recurrent esophageal cancer after chemoradiotherapy. Gastrointest Endosc. 2003;57(7):882–5.
66. Poincloux L, Sautel C, Rouquette O, Pereira B, Goutte M, Bommelaer G, et al. The clinical outcome in patients treated with a newly designed SEMS in cervical esophageal strictures and fistulas. J Clin Gastroenterol. 2016;50(5):379–87.
67. Lian JJ, Ma LL, Hu JW, Chen SY, Qin WZ, Xu MD, et al. Endoscopic balloon dilatation for benign esophageal stricture after endoscopic submucosal dissection for early esophageal neoplasms. J Dig Dis. 2014;15(5):224–9.
68. Zehetner J, DeMeester SR, Ayazi S, Demeester TR. Home self-dilatation for esophageal strictures. Dis Esophagus. 2014;27(1):1–4.
69. Suzuki T, Siddiqui A, Taylor LJ, Cox K, Hasan RA, Laique SN, et al. Clinical outcomes, efficacy, and adverse events in patients undergoing esophageal stent placement for benign indications: a large multicenter study. J Clin Gastroenterol. 2016;50(5):373–8.
70. Clayton SB, Castell DO. Multiple good options are available for achalasia management. J Clin Gastroenterol. 2015;49(3):194–8.
71. Pandolfino JE, Gawron AJ. Achalasia: a systematic review. JAMA. 2015;313(18):1841–52.
72. Patti MG, Fisichella PM. Controversies in management of achalasia. J Gastrointest Surg. 2014;18(9):1705–9.
73. Polguj M, Chrzanowski L, Kasprzak JD, Stefanczyk L, Topol M, Majos A. The aberrant right subclavian artery (arteria lusoria): the morphological and clinical aspects of one of the most important variations–a systematic study of 141 reports. ScientificWorldJournal. 2014;2014:292734.
74. von Segesser L, Faidutti B. Symptomatic aberrant retro-esophageal subclavian artery: considerations about the surgical approach, management and results. Thorac Cardiovasc Surg. 1984;32(5):307–10.
75. Tanaka A, Milner R, Ota T. Kommerell's diverticulum in the current era: a comprehensive review. Gen Thorac Cardiovasc Surg. 2015;63(5):245–59.

Esophageal Occlusive Disease: Endolumenal Therapy

34

Nicholas R. Crews, Mark A. Gromski, and Mohammad A. Al-Haddad

Introduction

Etiologies of esophageal occlusive disease are broad. Intrinsic esophageal occlusion is associated with locally advanced esophageal neoplasia and benign stricturing conditions. Also, extrinsic compression from bulky lymphadenopathy or mass and postsurgical anastomotic stricture or post-fundoplication stenosis can create esophageal occlusion. This chapter focuses on the available endolumenal therapies for these conditions.

The hallmark symptom of esophageal occlusion is progressive dysphagia to solid foods; however, patients typically do not experience dysphagia until the esophageal luminal diameter has been decreased by at least 50%, or <13 mm [1]. Consequently, occlusive esophageal cancer is not recognized until it is locally advanced in the majority of cases, with 50% of patients having unresectable disease at the time of diagnosis [2]. The incidence of esophageal cancer in the United States continues to rise, with 17,290 cases newly diagnosed in 2017. Mortality rates for this disease remain high (15,850 deaths in 2017), with an overall 5-year survival rate of approximately 20% [3–5]. Current guidelines for early esophageal adenocarcinoma (EAC, stages T0–T1a, N0, M0) include endoscopic management with endoscopic mucosal resection (EMR) and/or ablative therapies. The most common approach for resectable cancer (stages T1b–3, N0–1, M0) is esophagectomy after neoadjuvant chemoradiation, which may be deferred in low-risk lesions [6–8]. Patients with unresectable advanced esophageal neoplasms can be offered palliative chemoradiation and general palliative care. Esophagectomy conduit complications including fistula development, anastomotic leaks, and strictures occur with a reported incidence of 1–6%. Although rare, these complications can cause significant morbidity [9–12]. Benign esophageal occlusion is most commonly caused by chronic erosive esophagitis, although it can also be caused by eosinophilic esophagitis or achalasia. Since the early 1990s, however, the incidence of peptic esophageal stricture, a complication of GERD, has decreased. This parallels and is likely associated with the widespread use of proton-pump inhibitors [13]. Esophageal occlusion, perforation, leak, and/or fistula development are also known rare complications of endoscopic esophageal therapeutic maneuvers (including stricture dilation, EMR,

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endoscopic submucosal dissection (ESD), peroral endoscopic myotomy (POEM)), or other foregut surgeries (including gastric bypass or fundoplication) [14].

Clinical Presentation and Evaluation

The clinical presentation for patients with esophageal occlusive disease is typically similar regardless of etiology. Symptoms of progressive dysphagia, odynophagia, or unexplained weight loss should prompt further evaluation, particularly if reported by patients who have increased risk for esophageal cancer (males, age >50 years, Caucasians, presence of central obesity, chronic [>5 years] gastroesophageal reflux symptoms, history of smoking, or family history of Barrett's esophagus (BE) or EAC) [7, 15]. Conventional esophagogastroduodenoscopy (EGD) with mucosal biopsies remains the standard diagnostic modality to determine the etiology of esophageal occlusion, demonstrated in Fig. 34.1. Diagnostic EMR is recommended for polypoid lesions, masses, or other mucosal irregularities as it is superior to routine mucosal biopsies in pathologic yield and frequently is sufficient to determine malignant invasion depth [7]. In obstructive malignancy, endoscopic traversability of the ste-

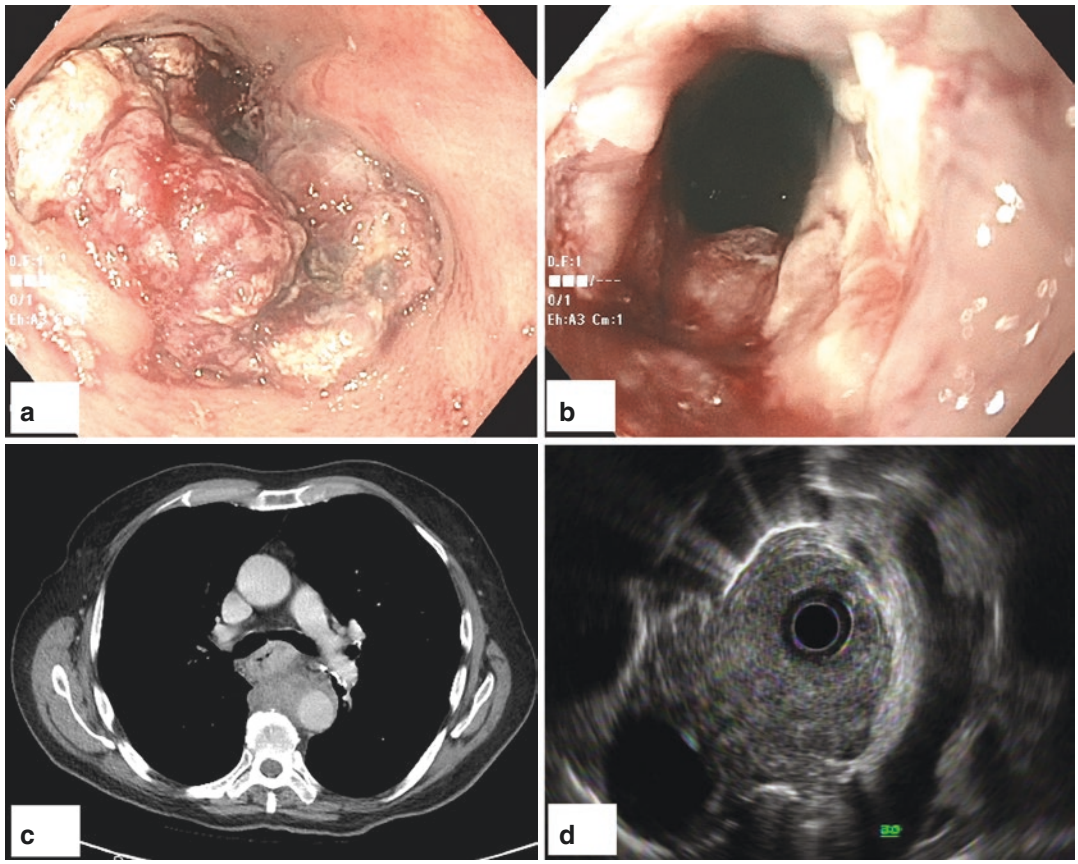

Fig. 34.1 Obstructive esophageal adenocarcinoma: (**a**) endoscopic images of invasive esophageal adenocarcinoma that is nearly completely obstructing. (**b**) The mass has caused moderate esophageal stenosis that was traversable with standard diagnostic endoscope. (**c**) CT chest images at the level of the gastroesophageal junction demonstrate soft tissue mass obliterating the normal esophageal anatomic structures. (**d**) Endoscopic ultrasound shows a discrete mass with complete loss of the interface between the neoplastic mass and the adventitia of the aorta indicating likely vessel encasement

nosis is a favorable prognostic factor, as it has been shown to be associated with significantly higher survival rate in patients with esophageal squamous cell carcinoma [16]. Contrasted esophagography is no longer routinely used prior to EGD for evaluation of dysphagia, though remains helpful in identification of esophagorespiratory fistulas, esophageal perforations, or anastomotic leaks prior to EGD.

Prior to EGD, patients should be evaluated thoroughly and kept nil per os (NPO), especially if there is concern for esophagorespiratory fistula or esophageal perforation. Interventions with high risk of bleeding, including EMR, are not recommended in the setting of coagulopathies or use of anticoagulants. Stent placement is considered safe in coagulopathic patients. Monitored anesthesia care during endoscopy is recommended for patients with severe cardiopulmonary disease, baseline use of supplemental oxygen, obesity, or previous intolerance to conscious sedation. Intubation for airway protection should be considered when there is an increased risk of aspiration, massive bleeding, esophagorespiratory fistula, or esophageal perforation. Endoscopy should be performed within 24 hours when there is concern for complication of esophageal conduit or iatrogenic complication of endoscopic therapies. If the patient is unstable from a cardiopulmonary standpoint, then the patient should be transferred to an intensive care unit and monitored closely and resuscitated prior to upper endoscopy.

The role of endoscopic ultrasound (EUS) in the evaluation of early-stage esophageal adenocarcinoma has been limited. The most recent ACG guidelines on BE management recommend considering EUS for evaluation and sampling for local lymph node involvement in stage T1b–T2 cancers [7, 17]. The routine use of EUS in EAC staging is no longer recommended due to lack of both sensitivity and specificity [18, 19]. EUS has demonstrated utility in measuring the maximum esophageal wall thickness of benign esophageal strictures, which may aid in predicting response to endoscopic dilation; however, its clinical role in this context remains uncertain and is not commonly employed [20].

Role of Esophageal Stenting

The use of self-expandable stents has been well-established for the successful palliative management of unresectable malignant esophageal strictures and fistulas. Endoscopic esophageal stenting may also be performed in benign conditions including benign refractory esophageal strictures, postoperative complications of an esophageal conduit, and esophageal perforations due to trauma, Boerhaave's syndrome, or iatrogenic causes.

Current commercially available stents include self-expandable metal stents (SEMS) that can be uncovered, fully covered, or partially covered (in which the two ends are uncovered), as well as self-expandable plastic stents (SEPS). Biodegradable stents are not currently available in the United States, but are in various stages of development and investigation. SEPS are not routinely used for malignant strictures due to increased complications compared to SEMS [21, 22]. A seminal prospective trial for palliation of malignant dysphagia reported by Kynrim et al. in 1997 showed lower rates of complications with similar rates of technical success and comparable dysphagia improvement scores with the use of SEMS compared to the standard plastic prostheses of the time [23]. The efficacy of SEMS has been demonstrated in numerous studies, showing 90–100% technical deployment success rate and rapid improvement in clinical dysphagia scores with 90–95% of patients able to tolerate at least liquids post-intervention [24–29]. However, durability of clinical response can be limited by stent complication or disease advancement. Covered SEMS patency rates have been shown to be 93%, 78%, and 67% at 30, 90, and 180 days, respectively, in a prospective study of 83 patients with unresectable malignant esophageal occlusive disease [30].

Covered SEMS also improve symptoms by fistulas by sealing malignant esophagorespiratory fistulas, which occur in 12–15% of locally advanced esophageal cancer cases. Initial clinical response has been shown to be 70–100% in several series, though redevelopment of fistulas due to cancer progression or stent complication is

seen in up to 35% of cases [2, 31–33]. Symptomatic esophageal occlusion or fistula due to local recurrence post-esophagectomy can be effectively palliated with SEMS placement with a success rate of 93–95% [34]. Head-to-head comparison studies analyzing the efficacy or safety of the available SEMS models have not been performed. Fully or partially covered SEMS are prioritized over uncovered SEMS in most circumstances for malignant dysphagia as they limit tumor ingrowth into the stent and have the capability of sealing fistulas [35].

Complications of Stenting

Stent complications are not uncommon, with most series reporting 30–35% overall complication rate [1]. Complications can occur immediately (airway compromise, esophageal perforation, chest pain) or be delayed (stent migration, tracheoesophageal fistula, or severe reflux symptoms particularly if the stent traverses the gastroesophageal junction). Figure 34.2 demonstrates stent migration and tracheoesophageal fistula. Stent migration and reflux symptoms are the most common. Severe reflux and nausea are typically managed with proton-pump inhibitors once or twice daily, and if needed an H-2 blocker or antiemetic can additionally be prescribed. We recommend that patients take typical reflux precautions (i.e., head of bed >30 degrees, do not lie supine less than 4 hours after eating, avoid alcohol) given the propensity for reflux in patients that have an esophageal stent traversing the gastroesophageal junction. Complication rates may be influenced in individual cases by SEMS diameter (larger diameters are typically associated with hemorrhage and fistula formation while smaller diameter associated with stent migration), tumor location and size, and concomitant or previous chemoradiation therapy [36, 37]. Uncovered SEMS can be limited by tumor ingrowth or overgrowth in 30% of cases, resulting in recurrent dysphagia and need for reintervention in 27–50% of cases [38, 39]. Stent obstruction with tumor can make stent removal difficult, though this task can be facilitated by destruction of ingrowing tissue via ablation or placing a fully covered SEMS within the initial stent [40]. Stent migration is a drawback for fully covered stents, occurring in 12–37% of cases compared to 0–7% for uncovered SEMS [39].

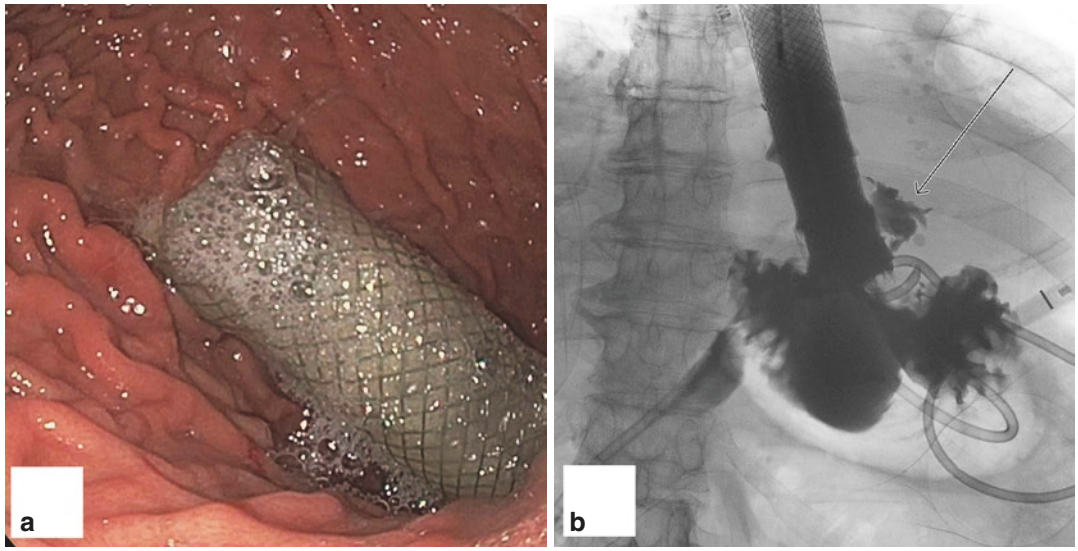

Fig. 34.2 Complications of stents: (**a**) stent migration into the stomach is a common complication, particularly of fully covered stents. (**b**) Stent failure to close esophagorespiratory fistulas (as in this case) or even cause esophagorespiratory fistulas to develop is another stent complication

Stent anchoring techniques to mitigate the risk for stent migration have been pursued. Through-the-scope (TTS) hemostatic clips have not been shown to be effective to reduce stent migration, due to limited closure strength. Over-the-scope clips (OTSC, Ovesco AG, Tubingen, Germany) are 85–93% effective; however, they are difficult to remove which can make stent retrieval challenging [41, 42]. Endoscopic suturing stay sutures into the SEMS with the Apollo OverStitch device (Apollo Endosurgery, Austin, TX, USA) has been shown to be effective in avoiding stent migration in 91% of 47 cases in a multicenter study [43]. Another multicenter study of 93 patients with locally advanced cancer receiving neoadjuvant chemoradiation therapy showed stent fixation with sutures significantly mitigated stent complications and reduced SEMS migration risk [44]. A recent study showed clinically significant migration rates decreased to 9% for sutured fully covered SEMS when compared to 39% for non-anchored fully covered SEMS [45]. A 2017 systematic review including 212 patients from 14 studies showed sutured SEMS migrated in 17% of cases, a reduction from known non-anchored SEMS migration rates [46].

The use of SEMS concomitantly with chemoradiation therapy (preoperative or palliative intent) or as a bridge to surgery remains controversial. Current guidelines recommend against the use of SEMS in these scenarios due to risk of increased SEMS complications (particularly hemorrhage and migration) frequently due to tumor shrinkage, tissue necrosis, or increasing chemoradiation toxicity [1, 2]. Nutritional supplementation has been recommended for patients that are malnourished (involuntary loss of 10% of usual body weight in 6 months or body mass index less than 18.5 kg/m^2). A multidisciplinary approach with a dietician is recommended, and enteral nutrition via a feeding jejunostomy tube should be considered if caloric requirements are unmet by oral intake. The stomach should be reserved as a conduit in case of the need for esophagectomy.

A 2014 systematic review showed increased risk for adverse events in this setting, including stent migration (32%) and chest pain (51%), though SEPS were used in 41% of patients in the review [47]. A large European study of 2944 patients showed a decreased proportion of R0 resections (71% vs. 85%) and reduced 3-year overall survival (25% vs. 44%) in patients in which SEMS was placed prior to esophagectomy compared to patients not stented prior to surgery [48]. Conversely, several studies have shown that the short-term use of fully covered SEMS concurrently with chemoradiation therapy can benefit dysphagia symptoms and improve nutritional status without significantly increasing complication risks [49–52]. A 2018 systematic review including 738 patients showed the SEMS plus chemoradiation therapy group had a lower risk of stent migration and restenosis with higher rates of pain, bleeding, and fistula formation compared to the SEMS alone group [53]. Studies have demonstrated the efficacy of SEMS and SEPS in symptom management as a bridge to esophagectomy (with or without preoperative chemotherapy). In these studies, stent removal occurred prior or during surgery with no reported stent-related surgical complications [54, 55]. Ultimately it appears that temporary use of stents with control of perforation or obstruction in the face of malignancy is efficacious and reasonable until more definitive care of either surgery, chemoradiation therapy, or both can be instituted. Complications of stents, though, can occur. These decisions should be made by a multidisciplinary team of surgeons, medical oncologists, radiation therapists, and gastroenterologists.

Management of Postoperative Complications

Complications of esophagectomy, including anastomotic dehiscence, leak, stricture, and fistula can be managed with endoscopic therapeutics, frequently avoiding significant morbidity of prolonged hospitalizations or reoperations that can be associated with high rates of morbidity and mortality [11, 12, 56]. Esophageal dilation, SEMS, OTS clips, and endoscopic suturing have all been shown to be efficacious for the management of foregut surgery complications, including

esophagectomy. Figures 34.3 and 34.4 portray the efficacy of SEMS and endoscopic suturing, respectively. Overall, outcomes are more favorable for early postoperative leaks or fistulas compared to less favorable success rates (20–40%) for chronic conditions (greater than 30 days from surgery) [43, 57, 58]. Specific endotherapies should be employed based on the features of the defect (size, location, surrounding tissue health) and expertise of the endoscopist and center.

Anastomotic stricture is a common complication, occurring in 10–23% of esophagectomies, and is particularly associated with upper esophagus reconstruction and transhiatal resection [59, 60]. Postoperative anastomotic leakage has been noted to be a risk factor for stricture development [61]. Bougie dilation and balloon dilation through the endoscope have both been shown to be effective methods of endoscopic dilation of benign anastomotic strictures, with initial symptom improvement in 93% of patients in one study [62]. Multiple dilation sessions (every 2–4 weeks) are commonly required to achieve adequate luminal patency. Dilation over 16 mm has been associated with prolonged period of symptom improvement compared to dilation to 16 mm or less [63]. Stricture recurrence is reported to be 43–50% in two series and more commonly associated with early (within 10 weeks of surgery) stricture development [62, 64]. Refractoriness to dilation is typically defined as lack of symptom improvement associated with the inability to

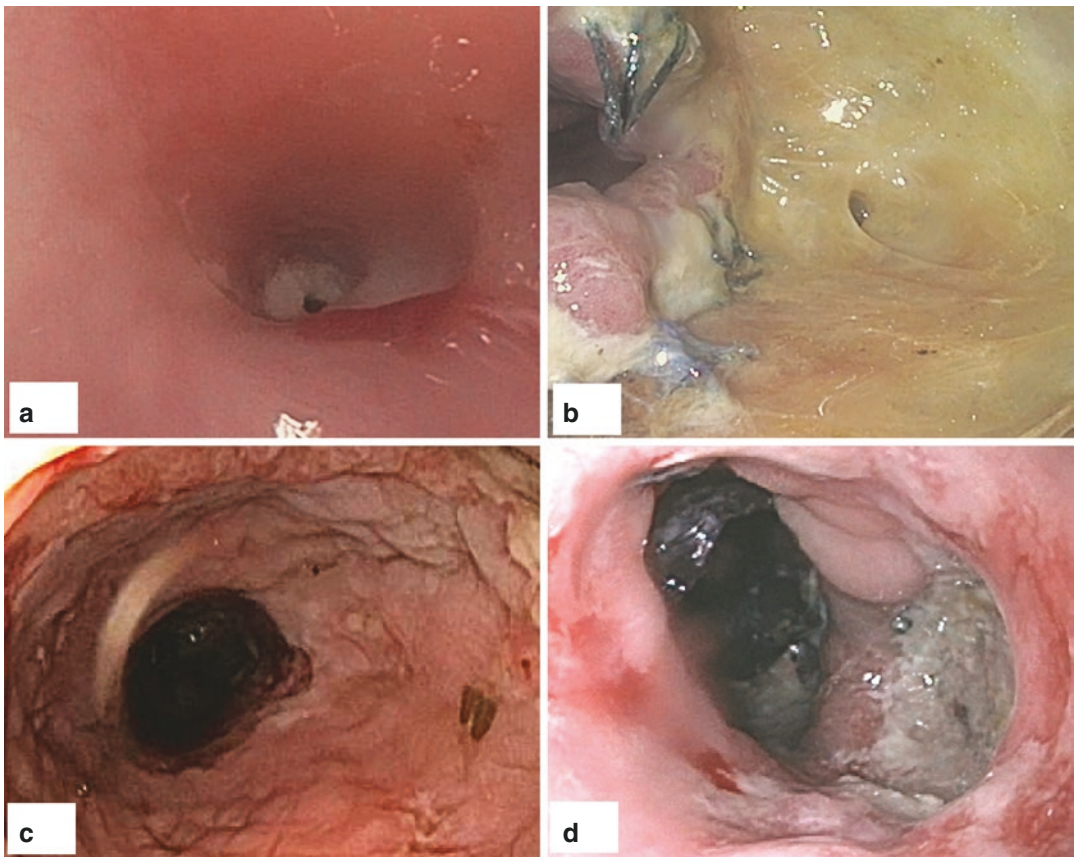

Fig. 34.3 Efficacy of stents: (**a**) severe benign esophageal stricture with inner diameter approximately 3 mm managed with esophageal dilation and SEM placement. (**b**) Anastomotic leak after esophagectomy with gastric pull-up for EAC managed with stent placement. (**c**) Esophageal stenosis from Image A is significantly improved after 11 weeks of stenting. (**d**) Healing anastomosis with cratered clean base ulcer after 8 weeks of stenting. No evidence of persistent anastomotic leak after stent is removed

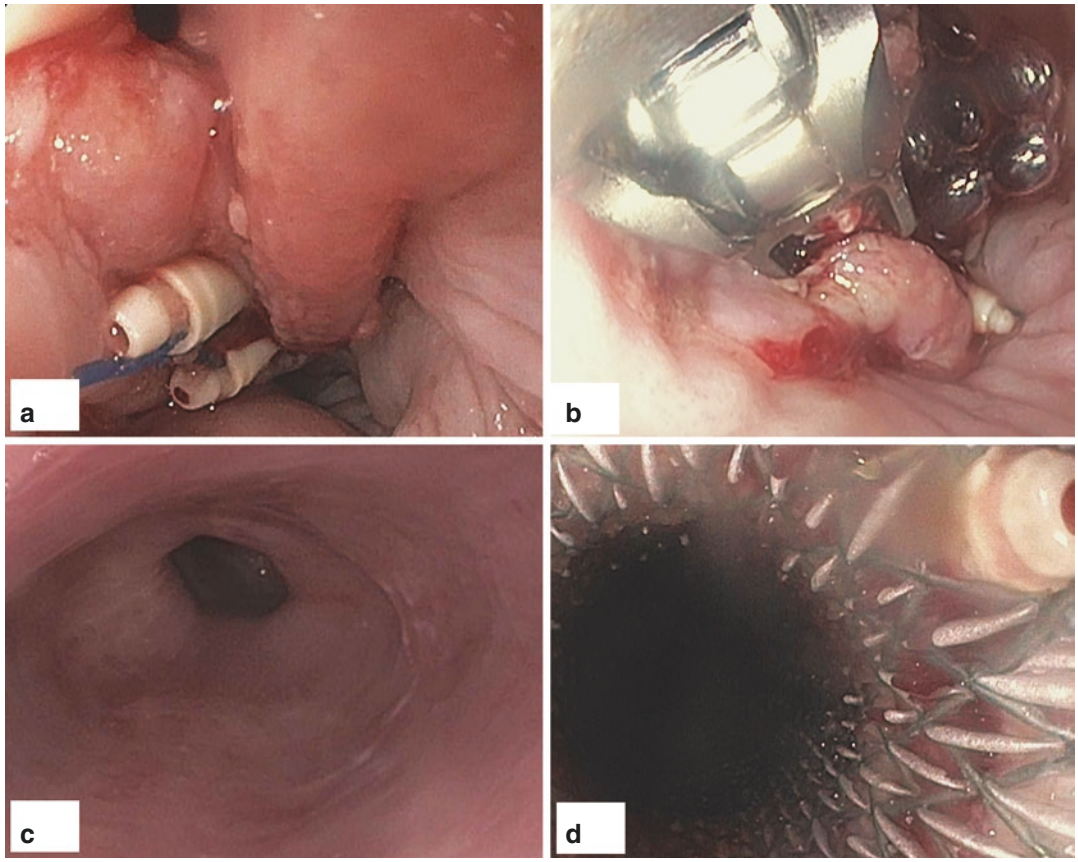

Fig. 34.4 Efficacy of suturing: (**a**) primary closure of spontaneous esophageal perforation with endoscopic suturing combined with stent placement for multimodality endoscopic approach. (**b**) Primary closure of tracheoesophageal fistula that was refractory to stenting. (**c**) Repeat endoscopy after stent removal shows complete resolution of spontaneous perforation from Image A. (**d**) Stent anchoring by endoscopically suturing stay sutures into the SEMS

maintain adequate luminal patency after four or more dilation sessions during 10–12 weeks. Endoscopic dilation with intramural steroid injection or SEMS placement are options for refractory strictures. Triamcinolone 50–100 mg dilute in 5 mL of saline is injected in 0.5 to 1 mL increments intramurally proximal and distal to the stricture. Intramural steroid injection into the esophagus is considered safe though may contribute very rarely to esophageal perforation.

The efficacy of SEMS therapy for foregut surgery complications is well established with multiple studies noting resolution of anastomotic leak, stricture refractory to dilation, or fistula in 71–100% of cases [65–71]. In these conditions, migration rates are higher (57–58%) for polyester-covered stents compared to non-anchored fully covered SEMS (22–42%) and partially covered SEMS (11–22%) [56, 65–71]. Stent replacement after migration was required in 36% of cases due to continued symptoms in one study [56]. Partially covered SEMS area associated with more adverse events and increased difficulty with stent removal in this setting [72]. Stent removal is recommend 4–6 weeks after insertion, though known complications may require premature stent removal including migration, stent intolerance (nausea, reflux symptoms, pain), hemorrhage, or aspiration.

In the last decade, newer endotherapies, including endoscopic suturing and over-the-scope clips, have become more popular as an

alternative primary therapy or adjunctive therapy to stenting for anastomotic dehiscence with leaks, perforations, or fistulas. Numerous studies have demonstrated the efficacy of these therapies; however, these studies are mostly small nonrandomized case series with significant heterogeneity, including variable techniques, multiple indications (postoperative complications, acute endoscopic perforations, or other chronic leaks), and a variety of locations (esophagus, stomach, and colorectal areas) [73]. Over-the-scope clips have shown to be clinically successful in closing 5–30 mm postoperative leaks in 68–73% of cases, but have produced mixed results (42–59% success rate) closing esophagorespiratory fistulas [58, 74, 75]. OTS clips have been associated with minimal noted complications, most frequently hemorrhage. Applications for endoscopic suturing are expanding, though postoperative leak and fistulas closure remain the current most common indications (in addition to stent anchoring as mentioned above) [76]. As opposed to OTS clips, endoscopic suturing has been shown to have clinical success in 80% of fistula closure, but only 27% of anastomotic leaks of a variety of foregut surgeries. Of note, in this study more patients (70%) with anastomotic leaks had failed prior therapies, whereas only 38% of patients in the fistula group had prior treatment failure [43]. Endoscopic suturing and OTS clips are frequently used together or with other concomitant therapies including stents, fibrin glue injection, and absorbable plugs [73, 77]. Ablation of the defect edges prior to clipping or suturing may increase the success of closure by starting the inflammatory and wound healing mechanistic cascades [78].

Conclusion

Endolumenal therapies have a prominent role in the setting of acute esophageal obstructions and perforations. Stenting and OTS clips have been used in benign disease, while stents have been used in the case of malignancy as well. In malignant situations, endolumenal therapy is important in establishing the diagnosis and possibly stabilizing the acute situation until more definitive therapy can occur. Significant complications from stents can occur, though, and they include migration, intolerance, reflux, bleeding, and aspiration. Ultimately the use of endolumenal techniques should be decided upon by a multidisciplinary team.

References

1. Sharma P, Kozarek R, Practice Parameters Committee of American College of G. Role of esophageal stents in benign and malignant diseases. Am J Gastroenterol. 2010;105(2):258–73; quiz 74.
2. Spaander MC, Baron TH, Siersema PD, et al. Esophageal stenting for benign and malignant disease: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy. 2016;48(10):939–48.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68(1):7–30.
4. Lagergren J, Mattsson F. Diverging trends in recent population-based survival rates in oesophageal and gastric cancer. PLoS One. 2012;7(7):e41352.
5. Crane SJ, Locke GR 3rd, Harmsen WS, Zinsmeister AR, Romero Y, Talley NJ. Survival trends in patients with gastric and esophageal adenocarcinomas: a population-based study. Mayo Clin Proc. 2008;83(10):1087–94.
6. Ajani JA, D'Amico TA, Almhanna K, et al. Esophageal and esophagogastric junction cancers, version 1.2015. J Natl Compr Cancer Netw. 2015;13(2):194–227.
7. Shaheen NJ, Falk GW, Iyer PG, Gerson LB. ACG clinical guideline: diagnosis and Management of Barrett's esophagus. Am J Gastroenterol. 2016;111(1):30–50.
8. Sharma P, Katzka DA, Gupta N, et al. Quality indicators for the management of Barrett's esophagus, dysplasia, and esophageal adenocarcinoma: international consensus recommendations from the American Gastroenterological Association symposium. Gastroenterology. 2015;149(6):1599–606.
9. Yimcharoen P, Heneghan HM, Tariq N, Brethauer SA, Kroh M, Chand B. Endoscopic stent management of leaks and anastomotic strictures after foregut surgery. Surg Obes Relat Dis. 2011;7(5):628–36.
10. Cassivi SD. Leaks, strictures, and necrosis: a review of anastomotic complications following esophagectomy. Semin Thorac Cardiovasc Surg. 2004;16(2):124–32.
11. Kobayashi S, Kanetaka K, Nagata Y, et al. Predictive factors for major postoperative complications related to gastric conduit reconstruction in thoracoscopic esophagectomy for esophageal cancer: a case control study. BMC Surg. 2018;18(1):15.
12. Licht E, Markowitz AJ, Bains MS, et al. Endoscopic management of esophageal anastomotic leaks after surgery for malignant disease. Ann Thorac Surg. 2016;101(1):301–4.

13. 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.
14. El H II, Imperiale TF, Rex DK, et al. Treatment of esophageal leaks, fistulae, and perforations with temporary stents: evaluation of efficacy, adverse events, and factors associated with successful outcomes. Gastrointest Endosc. 2014;79(4):589–98.
15. Crews NR, Johnson ML, Schleck CD, et al. Prevalence and predictors of gastroesophageal reflux complications in community subjects. Dig Dis Sci. 2016;61(11):3221–8.
16. Shin HJ, Moon HS, Kang SH, et al. Endoscopic traversability in patients with locally advanced esophageal squamous cell carcinoma: is it a significant prognostic factor? Medicine (Baltimore). 2017;96(51):e9441.
17. Thosani N, Singh H, Kapadia A, et al. Diagnostic accuracy of EUS in differentiating mucosal versus submucosal invasion of superficial esophageal cancers: a systematic review and meta-analysis. Gastrointest Endosc. 2012;75(2):242–53.
18. 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 71–3.
19. Bulsiewicz WJ, Dellon ES, Rogers AJ, et al. The impact of endoscopic ultrasound findings on clinical decision making in Barrett's esophagus with high-grade dysplasia or early esophageal adenocarcinoma. Dis Esophagus. 2014;27(5):409–17.
20. Rana SS, Bhasin DK, Singh K. Role of endoscopic ultrasonography (EUS) in management of benign esophageal strictures. Ann Gastroenterol. 2011;24(4):280–4.
21. Verschuur EM, Repici A, Kuipers EJ, Steyerberg EW, Siersema PD. New design esophageal stents for the palliation of dysphagia from esophageal or gastric cardia cancer: a randomized trial. Am J Gastroenterol. 2008;103(2):304–12.
22. 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.
23. Knyrim K, Wagner HJ, Bethge N, Keymling M, Vakil N. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. N Engl J Med. 1993;329(18):1302–7.
24. Acunas B, Rozanes I, Akpinar S, Tunaci A, Tunaci M, Acunas G. Palliation of malignant esophageal strictures with self-expanding nitinol stents: drawbacks and complications. Radiology. 1996;199(3):648–52.
25. Saxon RR, Morrison KE, Lakin PC, et al. Malignant esophageal obstruction and esophagorespiratory fistula: palliation with a polyethylene-covered Z-stent. Radiology. 1997;202(2):349–54.
26. Ell C, May A, Hahn EG. Gianturco-Z stents in the palliative treatment of malignant esophageal obstruction and esophagotracheal fistulas. Endoscopy. 1995;27(7):495–500.
27. Siersema PD, Hop WC, van Blankenstein M, et al. A comparison of 3 types of covered metal stents for the palliation of patients with dysphagia caused by esophagogastric carcinoma: a prospective, randomized study. Gastrointest Endosc. 2001;54(2):145–53.
28. Dai Y, Li C, Xie Y, et al. Interventions for dysphagia in oesophageal cancer. Cochrane Database Syst Rev. 2014;10:CD005048.
29. So H, Ahn JY, Han S, et al. Efficacy and safety of fully covered self-expanding metal stents for malignant esophageal obstruction. Dig Dis Sci. 2018;63(1):234–41.
30. Im JP, Kang JM, Kim SG, Kim JS, Jung HC, Song IS. Clinical outcomes and patency of self-expanding metal stents in patients with malignant upper gastrointestinal obstruction. Dig Dis Sci. 2008;53(4):938–45.
31. Hu Y, Zhao YF, Chen LQ, et al. Comparative study of different treatments for malignant tracheoesophageal/bronchoesophageal fistulae. Dis Esophagus. 2009;22(6):526–31.
32. Shin JH, Song HY, Ko GY, Lim JO, Yoon HK, Sung KB. Esophagorespiratory fistula: long-term results of palliative treatment with covered expandable metallic stents in 61 patients. Radiology. 2004;232(1):252–9.
33. Balazs A, Kupcsulik PK, Galambos Z. Esophagorespiratory fistulas of tumorous origin. Non-operative management of 264 cases in a 20-year period. Eur J Cardiothorac Surg. 2008;34(5):1103–7.
34. Van Heel NC, Haringsma J, Spaander MC, Didden P, Bruno MJ, Kuipers EJ. Esophageal stents for the palliation of malignant dysphagia and fistula recurrence after esophagectomy. Gastrointest Endosc. 2010;72(2):249–54.
35. Saranovic D, Djuric-Stefanovic A, Ivanovic A, Masulovic D, Pesko P. Fluoroscopically guided insertion of self-expandable metal esophageal stents for palliative treatment of patients with malignant stenosis of esophagus and cardia: comparison of uncovered and covered stent types. Dis Esophagus. 2005;18(4):230–8.
36. Verschuur EM, Kuipers EJ, Siersema PD. Esophageal stents for malignant strictures close to the upper esophageal sphincter. Gastrointest Endosc. 2007;66(6):1082–90.
37. Verschuur EM, Steyerberg EW, Kuipers EJ, Siersema PD. Effect of stent size on complications and recurrent dysphagia in patients with esophageal or gastric cardia cancer. Gastrointest Endosc. 2007;65(4):592–601.
38. Rozanes I, Poyanli A, Acunas B. Palliative treatment of inoperable malignant esophageal strictures with metal stents: one center's experience with four different stents. Eur J Radiol. 2002;43(3):196–203.
39. Vakil N, Morris AI, Marcon N, et al. A prospective, randomized, controlled trial of covered expandable metal stents in the palliation of malignant esophageal obstruction at the gastroesophageal junction. Am J Gastroenterol. 2001;96(6):1791–6.

40. Lagattolla NR, Rowe PH, Anderson H, Dunk AA. Restenting malignant oesophageal strictures. Br J Surg. 1998;85(2):261–3.
41. Irani S, Baron TH, Gluck M, Gan I, Ross AS, Kozarek RA. Preventing migration of fully covered esophageal stents with an over-the-scope clip device (with videos). Gastrointest Endosc. 2014;79(5):844–51.
42. Watanabe K, Hikichi T, Nakamura J, et al. Feasibility of esophageal stent fixation with an over-the-scope-clip for malignant esophageal strictures to prevent migration. Endosc Int Open. 2017;5(11):E1044–E9.
43. Sharaiha RZ, Kumta NA, DeFilippis EM, et al. A large multicenter experience with endoscopic suturing for Management of Gastrointestinal Defects and Stent Anchorage in 122 patients: a retrospective review. J Clin Gastroenterol. 2016;50(5):388–92.
44. Yang J, Siddiqui AA, Kowalski TE, et al. Esophageal stent fixation with endoscopic suturing device improves clinical outcomes and reduces complications in patients with locally advanced esophageal cancer prior to neoadjuvant therapy: a large multicenter experience. Surg Endosc. 2017;31(3):1414–9.
45. Bick BL, Imperiale TF, Johnson CS, DeWitt JM. Endoscopic suturing of esophageal fully covered self-expanding metal stents reduces rates of stent migration. Gastrointest Endosc. 2017;86(6):1015–21.
46. Law R, Prabhu A, Fujii-Lau L, Shannon C, Singh S. Stent migration following endoscopic suture fixation of esophageal self-expandable metal stents: a systematic review and meta-analysis. Surg Endosc. 2018;32(2):675–81.
47. Nagaraja V, Cox MR, Eslick GD. Safety and efficacy of esophageal stents preceding or during neoadjuvant chemotherapy for esophageal cancer: a systematic review and meta-analysis. J Gastrointest Oncol. 2014;5(2):119–26.
48. Mariette C, Gronnier C, Duhamel A, et al. Self-expanding covered metallic stent as a bridge to surgery in esophageal cancer: impact on oncologic outcomes. J Am Coll Surg. 2015;220(3):287–96.
49. Shin JH, Song HY, Kim JH, et al. Comparison of temporary and permanent stent placement with concurrent radiation therapy in patients with esophageal carcinoma. J Vasc Interv Radiol. 2005;16(1):67–74.
50. Siddiqui AA, Loren D, Dudnick R, Kowalski T. Expandable polyester silicon-covered stent for malignant esophageal strictures before neoadjuvant chemoradiation: a pilot study. Dig Dis Sci. 2007;52(3):823–9.
51. Kim JY, Kim SG, Lim JH, Im JP, Kim JS, Jung HC. Clinical outcomes of esophageal stents in patients with malignant esophageal obstruction according to palliative additional treatment. J Dig Dis. 2015;16(10):575–84.
52. Bower M, Jones W, Vessels B, Scoggins C, Martin R. Nutritional support with endoluminal stenting during neoadjuvant therapy for esophageal malignancy. Ann Surg Oncol. 2009;16(11):3161–8.
53. Lai A, Lipka S, Kumar A, et al. Role of esophageal metal stents placement and combination therapy in inoperable esophageal carcinoma: a systematic review and meta-analysis. Dig Dis Sci. 2018;63(4):1025–34.
54. Adler DG, Fang J, Wong R, Wills J, Hilden K. Placement of Polyflex stents in patients with locally advanced esophageal cancer is safe and improves dysphagia during neoadjuvant therapy. Gastrointest Endosc. 2009;70(4):614–9.
55. Brown RE, Abbas AE, Ellis S, et al. A prospective phase II evaluation of esophageal stenting for neoadjuvant therapy for esophageal cancer: optimal performance and surgical safety. J Am Coll Surg. 2011;212(4):582–8; discussion 8–9.
56. Chang J, Sharma G, Boules M, Brethauer S, Rodriguez J, Kroh MD. Endoscopic stents in the management of anastomotic complications after foregut surgery: new applications and techniques. Surg Obes Relat Dis. 2016;12(7):1373–81.
57. Eisendrath P, Cremer M, Himpens J, Cadiere GB, Le Moine O, Deviere J. Endotherapy including temporary stenting of fistulas of the upper gastrointestinal tract after laparoscopic bariatric surgery. Endoscopy. 2007;39(7):625–30.
58. 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.
59. Ahmed Z, Elliott JA, King S, Donohoe CL, Ravi N, Reynolds JV. Risk factors for anastomotic stricture post-esophagectomy with a standardized sutured anastomosis. World J Surg. 2017;41(2):487–97.
60. Rostas JW, Graffree BD, Scoggins CR, McMasters KM, Martin RCG. Long-term outcomes after hand-sewn versus circular-stapled (25 and 29 mm) anastomotic technique after esophagogastrectomy for esophageal cancer. J Surg Oncol. 2018;117(3):469–72.
61. Tanaka K, Makino T, Yamasaki M, et al. An analysis of the risk factors of anastomotic stricture after esophagectomy. Surg Today. 2018;48(4):449–54.
62. Mendelson AH, Small AJ, Agarwalla A, Scott FI, Kochman ML. Esophageal anastomotic strictures: outcomes of endoscopic dilation, risk of recurrence and refractory stenosis, and effect of foreign body removal. Clin Gastroenterol Hepatol. 2015;13(2):263–71.e1.
63. van Halsema EE, Noordzij IC, van Berge Henegouwen MI, Fockens P, Bergman JJ, van Hooft JE. Endoscopic dilation of benign esophageal anastomotic strictures over 16 mm has a longer lasting effect. Surg Endosc. 2017;31(4):1871–81.
64. Park JY, Song HY, Kim JH, et al. Benign anastomotic strictures after esophagectomy: long-term effectiveness of balloon dilation and factors affecting recurrence in 155 patients. AJR. 2012;198(5):1208–13.
65. 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(5):935–8; discussion 8–9.
66. Vanbiervliet G, Filippi J, Karimdjee BS, et al. The role of clips in preventing migration of fully covered

metallic esophageal stents: a pilot comparative study. Surg Endosc. 2012;26(1):53–9.
67. Blackmon SH, Santora R, Schwarz P, Barroso A, Dunkin BJ. Utility of removable esophageal covered self-expanding metal stents for leak and fistula management. Ann Thorac Surg. 2010;89(3):931–6; discussion 6–7.
68. Babor R, Talbot M, Tyndal A. Treatment of upper gastrointestinal leaks with a removable, covered, self-expanding metallic stent. Surg Laparosc Endosc Percutan Tech. 2009;19(1):e1–4.
69. 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(5):890–9.
70. 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.
71. Sharaiha RZ, Kim KJ, Singh VK, et al. Endoscopic stenting for benign upper gastrointestinal strictures and leaks. Surg Endosc. 2014;28(1):178–84.
72. Ngamruengphong S, Sharaiha R, Sethi A, et al. Fully-covered metal stents with endoscopic suturing vs. partially-covered metal stents for benign upper gastrointestinal diseases: a comparative study. Endosc Int Open. 2018;6(2):E217–E23.
73. Mennigen R, Senninger N, Laukoetter MG. Novel treatment options for perforations of the upper gastrointestinal tract: endoscopic vacuum therapy and over-the-scope clips. World J Gastroenterol. 2014;20(24):7767–76.
74. Lee HL, Cho JY, Cho JH, et al. Efficacy of the over-the-scope clip system for treatment of gastrointestinal fistulas, leaks, and perforations: a Korean Multi-Center Study. Clin Endosc. 2018;51(1):61–5.
75. Baron TH, Song LM, Ross A, Tokar JL, Irani S, Kozarek RA. Use of an over-the-scope clipping device: multicenter retrospective results of the first U.S. experience (with videos). Gastrointest Endosc. 2012;76(1):202–8.
76. Stavropoulos SN, Modayil R, Friedel D. Current applications of endoscopic suturing. World J Gastrointest Endosc. 2015;7(8):777–89.
77. Goenka MK, Goenka U. Endotherapy of leaks and fistula. World J Gastrointest Endosc. 2015;7(7):702–13.
78. Felsher J, Farres H, Chand B, Farver C, Ponsky J. Mucosal apposition in endoscopic suturing. Gastrointest Endosc. 2003;58(6):867–70.

Esophageal Occlusion: Role of Chemoradiation Therapy

35

Caroline E. Murphy and David Padro

Introduction

Esophageal cancer is a relatively uncommon malignancy in the United States, constituting a mere 1% of all new cancer cases annually. These cancers tend to be diagnosed late with the majority of esophageal cancers (71%) already spread to regional lymph nodes or distant sites [1]. As such, despite its relative rarity, esophageal cancer comprises a higher proportion of cancer deaths with less than 20% people surviving at 5 years after diagnosis, and it is currently the sixth leading cause of cancer deaths [2]. Surgery has historically been the mainstay of treatment and remains the only hope for a definitive cure; however, given the prevalence of advanced disease at diagnosis along with the high rates of locoregional and systemic recurrence, combined modalities have been integrated into the standard of care. Given the results of most recent clinical trials in locally advanced esophageal cancer, preoperative chemoradiotherapy has been established as the standard of care. This chapter will focus on the role of chemoradiation in locally advanced and palliative setting of esophageal cancer.

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Epidemiology and Presentation

Worldwide, esophageal cancer is estimated to be the cause of 1 in every 20 cancer deaths in 2018. There exists a stark predilection for men, with approximately 70% of cases occurring among men and a twofold to threefold difference in incidence and mortality rates between the sexes worldwide [3]. There exist two main histologic subtypes that lend themselves to varied mortality rates, adenocarcinoma and squamous cell carcinoma [4]. Squamous cell carcinoma is noted to be predominant in endemic regions such as Asia and sub-Sahara Africa and has been decreasing in prevalence, felt to be related to a decrease in cigarette smoking and dietary and economic gains in those regions. Adenocarcinoma is the subtype more common in the developed world, with gastroesophageal reflux disease (GERD), high rates of obesity, and Barrett's esophagus known to be risk factors [5]. Adenocarcinoma of the esophagus has demonstrated a steady climb in prevalence over the past decade. Unfortunately, there exists little data directly comparing treatment modalities for each histological subtype [6]. Clinically, patients with esophageal cancer will present with dysphagia on ingestion of solids, often progressing to difficulty with liquids and subsequent weight loss. As tumor invasion spreads into surrounding structures such as nerve bundles or the tracheobronchial tree, patients will experience symptoms of hoarseness or

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severe coughing spells that interfere with breathing. As such, esophageal cancer treatment is particularly challenging owing to the proximity of structures that are either vital for normal physiologic functions or for maintaining quality of life. The proximity of these structures dictates disease approach; the risk of surgery for cervical esophageal often precludes that modality, and it is treated with definitive chemoradiotherapy, similar to recommendations for head and neck cancer [7].

Treatment

Proper and accurate staging remains crucial for determining prognostic factors during each phase of treatment. Staging has improved beyond the traditional TNM tumor staging model with the eighth edition of the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) Cancer Staging Manual, which maintains cancer location, histopathologic cell type, and histologic grade and includes separate classifications for the clinical (cTNM), pathologic (pTNM), and postneoadjuvant pathologic (ypTNM) stage groups with improved mapping of esophageal lymph nodes. With these changes, stage is determined at each milestone as a patient progresses in their disease course and allows for a better analysis of treatment effect and, ultimately, control and survival (Fig. 35.1).

Historically, surgical resection is the only hope for curative treatment in locally advanced adenocarcinoma (AC) and squamous cell carcinoma (SCC) of the esophagus. Despite improvements in surgical approach, esophageal cancer suffers from high rates of local recurrence and systematic spread. As this chapter's focus is advanced disease, we will emphasize the treatment of disease beyond the scope of definitive surgery. Advanced disease necessitates utilizing a multidisciplinary approach of trimodality therapy including radiation, chemotherapy, and surgical resection.

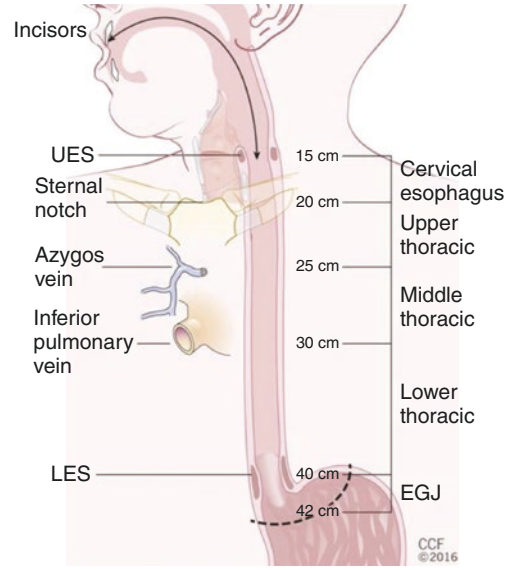

Fig. 35.1 Location of esophageal cancer primary site, including typical endoscopic measurements of each region measured from the incisors. LES lower esophageal sphincter, UES upper esophageal sphincter, EGJ esophagogastric junction. (Reprinted by permission from Elsevier: Rice et al. [8])

Early results of RT alone were disappointing with poor survival and high recurrence rates [9–13]. One landmark trial by the Radiation Therapy Oncology Group (RTOG) 8501 demonstrated that combined therapy significantly increased overall survival compared with RT alone. In the randomized part of the trial, at 5 years of follow-up, the overall survival for combined therapy was 26% (95% confidence interval [CI], 15–37%) compared with 0% following RT [14, 15]. Given these results, definitive RT alone has been reserved for patients not eligible for chemotherapy or surgery [15–24].

With the high rate of local and distant failure with radiation alone, attention turned to chemotherapy as a means to improve both local and systemic disease. Encouraged by the success of bimodality therapy of chemotherapy seen with other cancers of the gastrointestinal tract [25], combination therapy of a 5-fluorouracil (5-FU) and cisplatin was trialed with RT (50–60 Gy) preoperatively and produced promising results

with a pathologic clinical response (pCR) rate of 37% and overall 2-year survival of 30% [14, 26, 27]. Chemotherapy regimens are constantly evolving and improving, with fluoropyrimidines (5-FU or capecitabine) and a platinum-based therapy such as cisplatin or newer-generation oxaliplatin still shown to demonstrate some of the best outcomes without statistically significant outcomes to prefer one over the other [28–33]. Carboplatin and paclitaxel have also demonstrated excellent response rates as a chemotherapy regimen [34].

Focusing on the high rates of local recurrence in patients treated with chemoradiotherapy alone, and given it remained a promising option for patients unable to go to surgery, efforts have also been made to improve biological effectiveness of the radiation dose with fractionation and adjusting volume-boost doses. The 2002 RTOG 94-05 trial compared treatment response to concurrent chemoradiation using 64.8 Gy versus 50.4 Gy radiotherapy in patients with Stages I–III squamous cell carcinoma or adenocarcinoma; however, the study failed to show that high-dose radiotherapy with concurrent chemotherapy had any advantage over standard-dose radiotherapy with concurrent chemotherapy. A critique of this study, however, is that 7 of the 11 deaths in the high-dose arm occurred in patients who received 50.4 Gy or less; therefore, high-dose radiation was not responsible for the increased mortality in this group. More recent studies have shown that radiotherapy effectively relieves common symptoms of malignant obstruction such as dysphagia in about 90% of patients with SCC of the esophagus [35]. It was also noted that patients had a higher quality of life.

With the efficacy of CRT established, the question of when surgical resection could and should occur in advanced disease remained. The landmark CROSS trial cleared up some of these controversies by comparing neoadjuvant CRT plus surgery versus surgery alone [36]. After a median follow-up of 49 months, a 5-year overall survival (47 vs 34%; $p < 0.001$) and median disease-free survival (24 months in the surgery-alone arm vs not reached in the chemoradiotherapy arm) were improved in the combined modality arm, compared with the surgery-alone group. The CROSS trial solidified the role of preoperative chemoradiotherapy followed by surgery for locally advanced but resectable esophageal cancer patients, which represents most presentations in the Europe and the United States. However, the question of whether neoadjuvant chemoradiotherapy is superior to neoadjuvant chemotherapy followed by surgery remains unanswered [37]. A 2005 randomized trial from Germany compared induction chemotherapy followed by chemoradiotherapy (40 Gy) followed by surgery or the same induction chemotherapy followed by chemoradiotherapy (at least 65 Gy) without surgery finding a 2-year overall survival of 40% vs 35% (NS) and 2-year local control of 64% vs 41% favoring the non-surgery group. Perioperative mortality was also noted to be 13% vs 4% [38]. Another trial from France randomized responders of induction chemoradiation to chemoradiation alone versus chemoradiation followed by surgery in patients with locally advanced tumors, demonstrating a 2-year overall survival of 34% vs 40% that was not statistically significant $p = 0.44$, a 2-year local control 66% vs 57% ($P < 0.001$), and perioperative mortality 12% vs 0% ($P = 0.02$) [39]. Meanwhile, a Cochrane Review conducted in 2017 evaluated T3 and/or node-positive disease and found that the addition of esophagectomy to chemoradiotherapy in locally advanced esophageal squamous cell carcinoma provides little or no difference on overall survival and may be associated with higher treatment-related mortality [37]. Thus, it appears that CRT without surgical resection may yield overall survival benefit to patients with advanced disease, with the increased morbidity incurred from esophagectomies in locally advanced disease, limiting improvement in overall survival.

Newer targeted therapies are being evaluated as adjunctive agents to CRT, RT, and surgery. Drugs that target epidermal growth factor have

been investigated with disappointing results [29]. A 2014 RTOG Phase III trial evaluating cetuximab added to concurrent chemoradiation for patients undergoing non-operative management of esophageal carcinoma demonstrated no survival benefit [40]. For adenocarcinoma, the addition of drugs that target HER2 overexpression has demonstrated to improve overall survival in patients with metastatic disease [41]. Immunotherapy agents are also being investigated, for example, the ongoing KEYNOTE 590 aims to evaluate the efficacy of pembrolizumab in patients with programmed death ligand 1 (PD-L1)-positive advanced esophageal carcinoma [42]. A 2017 Cochrane review specifically investigating the roll of adjunct therapies for palliative efforts supports the use of targeted therapies for qualifying patients to improve overall survival [6].

In advanced disease, immediate concerns are related to airway obstruction, severe dysphasia, fistula formation, and tissue damage affecting function of surrounding vessels. Endoscopic ablation, radiotherapy, and brachytherapy have been explored as tools to control immediate threats and stabilize patients [23, 43, 44]. While esophageal prosthetics have been utilized since the 1960s, recent advances in endoscopically placed expandable stents have been shown to greatly improve symptoms in occlusive disease [45, 46] (Fig. 35.2).

Stenting is a well-tolerated procedure that improves the quality of life of patients who would otherwise face a potentially morbid surgical procedure or who may have limited treatment options because of comorbidities. A 2014 meta-analysis concluded that self-expanding metal stent insertion is a safe and quick tool in palliating dysphagia compared to other modalities such as intraluminal brachytherapy. However, concomitant high-dose intraluminal brachytherapy is a suitable alternative and may provide additional survival benefit with a better quality of life [43].

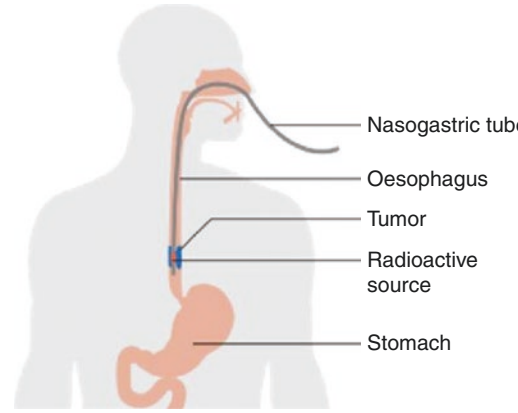

Fig. 35.2 Graphical representation of radioactive brachytherapy

Conclusion

Esophageal malignancy therapy requires a multidisciplinary approach. In the acute setting, operative and endoscopic steps can be taken to treat perforations and complete obstructions. These patients typically present with locally advanced disease. Ultimately, stenting and brachytherapy are often used as a bridge therapy to more definitive care, such as chemotherapy, radiation, and surgery. Surgery for cure, however, may not be required in these patients. Palliative radiation therapy remains the agent most used for patients with high comorbidities who cannot tolerate surgery or systemic therapies (Fig. 35.3).

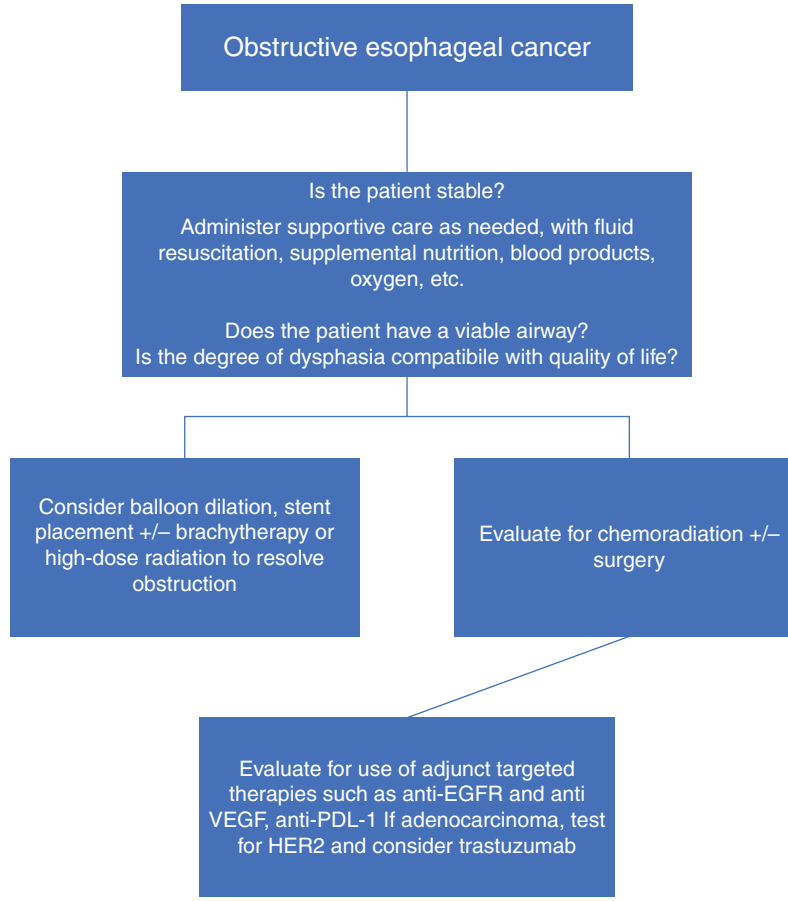

Fig. 35.3 Suggested algorithm for management of esophageal occlusion

References

1. Noone AM HN, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA, editors. Esophageal cancer, SEER cancer statistics review, 1975–2015. National Cancer Institute; 2018.
2. Siegel RL, Fedewa SA, Anderson WF, Miller KD, Ma J, Rosenberg PS, et al. Colorectal cancer incidence patterns in the United States, 1974–2013. J Natl Cancer Inst. 2017;109(8)
3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.
4. Islami F, DeSantis CE, Jemal A. Incidence Trends of Esophageal and Gastric Cancer Subtypes by Race, Ethnicity, and Age in the United States, 1997–2014. Clin Gastroenterol Hepatol. 2019;17(3):429–39.
5. Arnold M, Laversanne M, Brown LM, Devesa SS, Bray F. Predicting the future burden of esophageal cancer by histological subtype: international trends in incidence up to 2030. Am J Gastroenterol. 2017;112(8):1247–55.
6. Janmaat VT, Steyerberg EW, van der Gaast A, Mathijssen RHJ, Bruno MJ, Peppelenbosch MP, et al. Palliative chemotherapy and targeted therapies for esophageal and gastroesophageal junction cancer. Cochrane Database Syst Rev. 2017;11:CD004063.
7. Valmasoni M, Pierobon ES, Zanchettin G, Briscolini D, Moletta L, Ruol A, et al. Cervical esophageal cancer treatment strategies: a cohort study appraising the debated role of surgery. Ann Surg Oncol. 2018;25(9):2747–55.
8. Rice TW, Ishwaran H, Ferguson MK, Blackstone EH, Goldstraw P. Cancer of the esophagus and esophagogastric junction: An eighth edition staging primer. J Thorac Oncol. 2017;12(1):36–42.
9. Appelqvist P, Silvo J, Rissanen P. The results of surgery and radiotherapy in the treatment of small carcinomas of the thoracic oesophagus. Ann Clin Res. 1979;11(5):184–8.
10. Earlam R, Cunha-Melo JR. Oesophogeal squamous cell carcinoms: II. A critical view of radiotherapy. Br J Surg. 1980;67(7):457–61.

11. Newaishy GA, Read GA, Duncan W, Kerr GR. Results of radical radiotherapy of squamous cell carcinoma of the oesophagus. Clin Radiol. 1982;33(3):347–52.
12. Mantravadi RVP, Lad T, Briele H, Liebner ET. Carcinoma of the esophagus: sites of failure. Int J Radiat Oncol Biol Phys. 1982;8(11):1897–901.
13. Yang ZY, Gu XZ, Zhao S, Hong ZG, An HL, Hou FX, et al. Long term survival of radiotherapy for esophageal cancer: analysis of 1136 patients surviving for more than 5 years. Int J Radiat Oncol Biol Phys. 1983;9(12):1769–73.
14. Cooper JS, Guo MD, Herskovic A, Macdonald JS, Martenson JA Jr, Al-Sarraf M, et al. Chemoradiotherapy of locally advanced esophageal cancer: long-term follow-up of a prospective randomized trial (RTOG 85-01). Radiat Ther Oncol Group JAMA. 1999;281(17):1623–7.
15. Herskovic A, Martz K, al-Sarraf M, Leichman L, Brindle J, Vaitkevicius V, et al. Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. N Engl J Med. 1992;326(24):1593–8.
16. De-Ren S. Ten-year follow-up of esophageal cancer treated by radical radiation therapy: analysis of 869 patients. Int J Radiat Oncol Biol Phys. 1989;16(2):329–34.
17. Okawa T, Kita M, Tanaka M, Ikeda M. Results of radiotherapy for inoperable locally advanced esophageal cancer. Int J Radiat Oncol Biol Phys. 1989;17(1):49–54.
18. Sykes AJ, Burt PA, Slevin NJ, Stout R, Marrs JE. Radical radiotherapy for carcinoma of the oesophagus: an effective alternative to surgery. Radiother Oncol. 1998;48(1):15–21.
19. Petrovich Z, Langholz B, Formenti S, Luxton G, Astrahan M. Management of carcinoma of the esophagus: the role of radiotherapy. Am J Clin Oncol. 1991;14(1):80–6.
20. Shi XH, Yao W, Liu T. Late course accelerated fractionation in radiotherapy of esophageal carcinoma. Radiother Oncol. 1999;51(1):21–6.
21. al-Sarraf M, Martz K, Herskovic A, Leichman L, Brindle JS, Vaitkevicius VK, et al. Progress report of combined chemoradiotherapy versus radiotherapy alone in patients with esophageal cancer: an intergroup study. J Clin Oncol. 1997;15(1):277–84.
22. Wang JH, Lu XJ, Zhou J, Wang F. A randomized controlled trial of conventional fraction and late course accelerated hyperfraction three-dimensional conformal radiotherapy for esophageal cancer. Cell Biochem Biophys. 2012;62(1):107–12.
23. Pasquier D, Mirabel X, Adenis A, Rezvoy N, Hecquet G, Fournier C, et al. External beam radiation therapy followed by high-dose-rate brachytherapy for inoperable superficial esophageal carcinoma. Int J Radiat Oncol Biol Phys. 2006;65(5):1456–61.
24. Penniment MG, De Ieso PB, Harvey JA, Stephens S, Au H-J, O'Callaghan CJ, et al. Palliative chemoradiotherapy versus radiotherapy alone for dysphagia in advanced oesophageal cancer: a multicentre randomised controlled trial (TROG 03.01). Lancet Gastroenterol Hepatol. 2018;3(2):114–24.
25. Nigro ND, Vaitkevicius VK, Buroker T, Bradley GT, Considine B. Combined therapy for cancer of the anal canal. Dis Colon Rectum. 1981;24(2):73–5.
26. Steiger Z, Franklin R, Wilson RF, Leichman L, Asfaw I, Vaishanpayan G, et al. Complete eradication of squamous cell carcinoma of the esophagus with combined chemotherapy and radiotherapy. Am Surg. 1981;47(3):95–8.
27. John MJ, Flam MS, Mowry PA, Podolsky WJ, Xavier AM, Wittlinger PS, et al. Radiotherapy alone and chemoradiation for nonmetastatic. Cancer. 1989;63(12):2397–403.
28. Conroy T, Galais MP, Raoul JL, Bouche O, Gourgou-Bourgade S, Douillard JY, et al. Definitive chemoradiotherapy with FOLFOX versus fluorouracil and cisplatin in patients with oesophageal cancer (PRODIGE5/ACCORD17): final results of a randomised, phase 2/3 trial. Lancet Oncol. 2014;15(3):305–14.
29. Lorenzen S, Schuster T, Porschen R, Al-Batran SE, Hofheinz R, Thuss-Patience P, et al. Cetuximab plus cisplatin-5-fluorouracil versus cisplatin-5-fluorouracil alone in first-line metastatic squamous cell carcinoma of the esophagus: a randomized phase II study of the Arbeitsgemeinschaft Internistische Onkologie. Ann Oncol. 2009;20(10):1667–73.
30. Al-Batran SE, Hartmann JT, Probst S, Schmalenberg H, Hollerbach S, Hofheinz R, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol. 2008;26(9):1435–42.
31. Bouche O, Raoul JL, Bonnetain F, Giovannini M, Etienne PL, Lledo G, et al. Randomized multicenter phase II trial of a biweekly regimen of fluorouracil and leucovorin (LV5FU2), LV5FU2 plus cisplatin, or LV5FU2 plus irinotecan in patients with previously untreated metastatic gastric cancer: a Federation Francophone de Cancerologie Digestive Group Study--FFCD 9803. J Clin Oncol. 2004;22(21):4319–28.
32. Enzinger PC, Burtness BA, Niedzwiecki D, Ye X, Douglas K, Ilson DH, et al. CALGB 80403 (Alliance)/E1206: a randomized phase II study of three chemotherapy regimens plus cetuximab in metastatic esophageal and gastroesophageal junction cancers. J Clin Oncol. 2016;34(23):2736–42.
33. Minsky BD, Pajak TF, Ginsberg RJ, Pisansky TM, Martenson J, Komaki R, et al. INT 0123 (Radiation Therapy Oncology Group 94-05) phase III trial of combined-modality therapy for esophageal cancer: high-dose versus standard-dose radiation therapy. J Clin Oncol. 2002;20(5):1167–74.
34. Meerten EV, van Rij C, Tesselaar ME, Neelis K, Richel D, Hulshof M, et al. Definitive concurrent chemoradiation (CRT) with weekly paclitaxel and carboplatin for patients (pts) with irresectable esophageal cancer: a phase II study. J Clin Oncol. 2010;28(15_suppl):e14508.

35. Prasad NRV, Karthigeyan M, Vikram K, Parthasarathy R, Reddy KS. Palliative radiotherapy in esophageal cancer. Indian J Surg. 2015;77(1):34–8.
36. Shapiro J, van Lanschot JJB, Hulshof M, van Hagen P, van Berge Henegouwen MI, Wijnhoven BPL, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. Lancet Oncol. 2015;16(9):1090–8.
37. Vellayappan BA, Soon YY, Ku GY, Leong CN, Lu JJ, Tey JCS. Chemoradiotherapy versus chemoradiotherapy plus surgery for esophageal cancer. Cochrane Database Syst Rev. 2017;8:CD010511.
38. Stahl M, Stuschke M, Lehmann N, Meyer HJ, Walz MK, Seeber S, et al. Chemoradiation with and without surgery in patients with locally advanced squamous cell carcinoma of the esophagus. J Clin Oncol. 2005;23(10):2310–7.
39. Bedenne L, Michel P, Bouche O, Milan C, Mariette C, Conroy T, et al. Chemoradiation followed by surgery compared with chemoradiation alone in squamous cancer of the esophagus: FFCD 9102. J Clin Oncol. 2007;25(10):1160–8.
40. Ilson DH, Moughan J, Suntharalingam M, Dicker A, Kachnic LA, Konski AA, et al. RTOG 0436: a phase III trial evaluating the addition of cetuximab to paclitaxel, cisplatin, and radiation for patients with esophageal cancer treated without surgery. J Clin Oncol. 2014;32(15_suppl):4007.
41. Bang YJ, Van Cutsem E, Feyereislova A, Chung HC, Shen L, Sawaki A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet. 2010;376(9742):687–97.
42. Kato K, Shah M, Enzinger P, Bennouna J, Shen L, Adenis A, et al. P-052A phase 3 study of chemotherapy + pembrolizumab versus chemotherapy + placebo as first-line therapy for patients with advanced esophageal or esophagogastric junction (E/EGJ) cancer: KEYNOTE-590 – Trial in progress. Ann Oncol. 2018;29(suppl_5):mdy151.051.
43. Dai Y, Li C, Xie Y, Liu X, Zhang J, Zhou J, et al. Interventions for dysphagia in oesophageal cancer. Cochrane Database Syst Rev. 2014;10:CD005048.
44. Lettmaier S, Strnad V. Intraluminal brachytherapy in oesophageal cancer: defining its role and introducing the technique. J Contemp Brachytherapy. 2014;6(2):236–41.
45. De Palma GD, Sivero L, Galloro G, Siciliano S, Pigna F, Catanzano C. The palliation of dysphagia secondary to esophageal-cardial carcinoma with self-expandable metal prostheses. The authors' personal experience with 92 patients. Minerva Chir. 1999;54(4):213–8.
46. O'Connor T, Watson R, Lepley D Jr, Weisel W. Esophageal prosthesis for palliative intubation: further evaluation of 378 patients. Arch Surg. 1963;87(2):275–9.

Part XIII

Abdominal Surgery in Pregnant Patients

36 The Physiology of Pregnant Patients in Need of Acute Surgical Care

Candace Giles, Alan P. Gehrich, and Caela Miller

Introduction

Non-obstetric surgical disease that requires surgery occurs in 1–2% of all pregnancies [1, 2]. Gastrointestinal-related surgeries for acute appendicitis and cholecystitis are the most common non-obstetrical surgical emergencies complicating pregnancy [1, 3]. However, conditions like symptomatic cholelithiasis, ovarian cysts, ovarian torsion, adrenal tumors, splenic disorders, symptomatic hernias, complications of inflammatory bowel diseases, and other rare conditions may also require surgical intervention during pregnancy [3]. Traditionally, abdominal procedures have been approached with apprehension in the pregnant woman [4], which stems from concerns regarding surgery-related miscarriage, teratogenesis, preterm birth, and the fear of adverse fetal effects of perioperative diagnostic testing [1]. This chapter will assist the surgeon in his/her approach to non-obstetrical surgery during pregnancy, specifically in the third trimester. This chapter focuses on the physiology of pregnancy, the multidisciplinary approach for non-obstetric surgery, thromboprophylaxis, appropriate fetal heart rate monitoring, anesthetic concerns, and obstetric surgical complications.

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Physiologic Changes in Pregnancy

Physiologic changes occur soon after conception and involve most organ systems with major adaptations of the maternal physiology progressing through gestation [5]. The critical changes for surgery involve the hematopoietic, cardiovascular, respiritory, renal and gastrointestinal systems.

Hemodynamic Changes

Maternal total blood volume, plasma volume, and red blood cell mass significantly increase during pregnancy. This ensures adequate uteroplacental circulation for fetal growth and development and prepares for the blood loss associated with delivery [2, 5]. This adaption can delay the physiologic response to blood loss, as hemorrhage up to 2000 mL may occur before heart rate or blood pressure changes are exhibited [2].

Placental estrogens promote sodium retention by stimulating direct renal and hepatic production of the renin substrate-angiotensinogen [5, 6]. The renin-angiotensin system is activated leading to increased plasma levels of aldosterone with subsequent salt and water retention in the distal tubule and collecting duct [7]. This activation contributes to a total body water increase from 6.5 to 8.5 L by the end of gestation [2, 5] and helps to maintain blood pressure in pregnancy as the maternal systemic and renal arterial dilation produces an

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"underfilled" cardiovascular system [6]. Approximately 3.5 L of total body water is delegated to the fetus, placenta, and amniotic fluid. A plasma volume increase of 1200 to 1300 mL, a 20–30% increase in erythrocyte volumes of 300 to 400 mL, and the expansion of maternal blood volume by 1500–1600 mL account for the remainder of total body water [2]. The progressive increase of blood volume begins around 6–8 weeks gestation and plateaus at a maximum volume of 4700–5200 mL by 30–34 weeks' gestation [2, 5, 8]. Despite the increasing red cell mass, the physiologic anemia of pregnancy ensues as plasma volume increases more rapidly and to a greater degree than red cell mass increases, resulting in overall decreased hemoglobin concentrations during pregnancy [2, 5].

Cardiovascular Changes

The physiologic changes in the cardiovascular system do so to meet the increased metabolic stresses of pregnancy. These changes are required to facilitate delivery of oxygen to maternal tissues and allow for adequate uteroplacental circulation for fetal growth and development [2, 6]. As the gravid uterus expands, intra-abdominal pressure increases, and the diaphragm is displaced leading to cephalad and leftward lateral displacement of the heart. Both increased estrogen levels and atrial stretching lower the threshold for arrhythmias [2]. The heart endures significant remodeling secondary to increased blood volume. This remodeling is usually a global hypertrophy; however, the left atrium has the largest size increase [2, 7]. Additional transthoracic echocardiographic findings in a normal pregnancy also include transient minor mitral regurgitation, physiologic tricuspid regurgitation, and pulmonary regurgitation without aortic regurgitation [7]. Left ventricular function and ejection fraction remain unchanged as the cardiac volume and mass increase at the same pace [2].

Cardiac output is calculated as the product of stroke volume and heart rate and is a measurement of the functional capacity of the heart [5]. The cardiac output increases during pregnancy by 30–50% from 4 to 6 L/min [6, 7]. This allows increased perfusion to the uterus, maternal kidneys, extremities, breasts, and skin [2]. The increase in cardiac output is a result of a 20–50% increase in stroke volume in the setting of increased blood volume that peaks at 25–30 weeks' gestation [2, 7]. Increase in stroke volume is the result of both increased end-diastolic volume and increased ventricular wall muscle mass seen during pregnancy. While a decrease in stroke volume is noted toward term, the increased cardiac output is maintained by a rise in maternal heart rate of 10–20 bpm [6, 7].

Although the cardiac output rises, the maternal blood pressure decreases by 5–15 mm Hg with a nadir at 28 weeks' gestation secondary to decreased systemic vascular resistance [2, 7]. Progesterone and other endothelium-dependent factors, including nitric oxide, vasodilatory prostaglandins, and relaxin, cause peripheral vasodilation of blood vessels [2, 5]. Pre-pregnancy blood pressure values return during the third trimester [2].

Maternal positioning toward term has a profound effect upon the hemodynamic profile of both the mother and the fetus. When the patient is in the supine position, cardiac output is decreased secondary to compromised stroke volume. This phenomenon is called "maternal supine hypotension syndrome" in which the large gravid uterus compresses the inferior vena cava and abdominal aorta with resultant decreased return of blood to the heart and decreased flow to the uterus, respectively. Maternal symptoms may include tachycardia, hypotension, sweating, nausea, vomiting, and mental status changes. The pregnant women should therefore be placed in the left or right lateral position whenever possible. The left lateral decubitus position is preferred during surgical procedures to maintain cardiac output. This is achieved easily by placing a wedge under the patient's right hip [2].

Respiratory Changes

Increased estrogen and increased blood volume in pregnancy affect the mucosa of the nasopharynx and respiratory tract causing them to

become edematous and friable leading to hypersecretion and increased likelihood of spontaneous or manipulated epistaxis [5, 7]. Symptoms of these changes are perceived as congestion and rhinitis [2].

Structural changes of the thoracic cavity, to include relaxin-induced relaxation of ligamentous attachments of the ribcage, lead to increased ribcage subcostal angle and increased chest diameter. The enlarging uterus leads to a 4 cm elevation in the diaphragm which decreases the total lung capacity by 5%. [2, 7]. Forced expiratory volume in 1 second (FEV1) and peak expiratory flow rate (PEFR) are not affected by pregnancy [7].

The oxygen demand is significantly increased during pregnancy secondary to increased metabolic rate and increased consumption of oxygen (30–60%, 30–40 mL/min) to support the metabolic demands of maternal organs, the placenta, and the fetus. Minute ventilation, the amount of air moved in and out of the lungs in 1 min, is increased by approximately 30–50% in pregnancy as a result of increased tidal volume due to a decrease in functional residual capacity and decreased residual volume rather than increased respiratory rate. The arterial pO_2 increases and arterial pCO_2 decreases with a compensatory fall in serum bicarbonate to 18–22 mmol/L secondary to this maternal hyperventilation. Thus, a fully compensated mild respiratory alkalosis (arterial pH 7.44) is normal in pregnancy. The pregnant woman perceives this increase in minute ventilation as shortness of breath [2]. To optimize oxygen diffusion across the placenta, an oxygen saturation goal of 95% should be maintained to sustain a PaO_2 greater than 70 mm Hg [2].

There is significant maternal morbidity and mortality associated with the increased risk of gastric contents aspiration in pregnancy [2, 9]. Thus, airway protection is paramount after 20 weeks' gestation for patients who are vomiting or undergoing general anesthesia.

Gastrointestinal Changes

Unavoidable anatomic alterations to the gastrointestinal tract from the growing uterus are often associated with discomforts that pregnant women experience [10]. Moreover, displacement of intra-abdominal organs by the growing uterus and fetus may complicate the diagnosis of surgical intra-abdominal processes and can change the location of surgical incisions [2, 8].

Nausea and vomiting of pregnancy affect 50–80% of pregnant women with up to 50% of women experiencing vomiting and retching [11]. Gastrointestinal reflux affects 30–50% of pregnant women. The tone and motility of the lower esophageal sphincter, esophagus, and stomach decrease secondary to the relaxing effects of estrogen and progesterone on smooth muscle. This relaxation allows gastric contents to move up into the esophagus, which can lead to both esophageal erosion and discomfort from gastrointestinal reflux [2, 7, 8]. In addition, increased absorption of water and sodium from the intestines coupled with pressure on the sigmoid colon by expanding the uterus contributes to constipation [8]. Hormone-induced changes to the gallbladder include decreased ejection of bile and increased biliary cholesterol saturation. This increases the frequency of biliary sludge and stones [7].

Urinary Changes

Anatomic changes of the urinary system during pregnancy include cephalad displacement of the kidneys by the enlarging uterus and increase in size of the kidneys and collecting system secondary to increased vasculature and interstitial volume [2, 7]. As the renal collecting system becomes more dilated, hydronephrosis ensues, right typically greater than left, resulting in urinary stasis. This increases the risk of urinary tract infections, nephrolithiasis, and pyelonephritis [2]. Over time, bladder capacity decreases due to the outward pressure by the growing uterus leading to urinary frequency, urgency, and incontinence [8].

Adaptive changes in the renal vasculature include a 40% decrease in systemic vascular resistance. This renal arterial dilation is triggered by relaxin-induced stimulation of endothelin,

which mediates vasodilation through nitrous oxide synthesis. As a result, there is a 40–65% increase in renal plasma flow and a 50–85% increase in glomerular filtration rate compared to non-pregnant levels [7]. Physiologic decreases in serum blood urea nitrogen level, uric acid concentration, and creatinine levels are observed secondary to this hyperfiltration [7]; specifically serum creatinine decreases from average 0.8 to 0.5 mg/dL [2].

Hematological Changes

In addition to the physiologic anemia of pregnancy, there is also a progressive leukocytosis seen in pregnancy. The white blood cell count increases up to 14,000/mm^3 during pregnancy and can reach up to 30,000/mm^3 during labor and the puerperium [2, 7]. Platelet counts gradually decrease throughout the third trimester of pregnancy with thrombocytopenia being defined as platelet count less than 150,000/L [12].

Pregnancy also modifies the balance of the coagulation system in favor of clotting. This is thought to be physiologic protection against postpartum hemorrhage. Procoagulants, predominantly factors VIII, IX, and X, along with fibrinogen, rise significantly during pregnancy producing a physiologic hypercoagulable state. In addition, fibrinolysis and endogenous anticoagulants such as antithrombin and protein S decrease. Furthermore, decreased thrombolysis, increased procoagulants, and increased venous stasis secondary to compression of the inferior vena cava during pregnancy result in a five to sixfold increased risk of thromboembolic events [2, 7].

Although rare, thromboembolic events during pregnancy and the postpartum period are highly lethal events. Surgery may increase the risk of a thromboembolic event secondary to perioperative bed rest, infection, and the inflammatory syndrome. As previously stated, vena cava compression syndrome and pregnancy-induced hypercoagulability increase the intrinsic thrombotic risk of each surgery. Pneumatic compression devices placed before induction of anesthesia improve venous return and help protect against thromboembolism [5]. Additionally, the European VTE Guidelines Task Force recommends trombophylaxis with heparin until full mobility is achieved following surgery during pregnancy or the postpartum period [13].

Obstetrical Consultation and Timing of Surgery

The American College of Obstetricians and Gynecologists' Committee Obstetric Practice recognizes that non-obstetric surgery during pregnancy is a significant concern for physicians who care for women. However, due to the lack of randomized clinical trials in this populaton, there are no specific recommendations. Thus, it is imperative that surgeons obtain an obstetric consultation before performing non-obstetric surgery and other invasive procedures (e.g., cardiac catheterization or colonoscopy) as obstetricians can assess maternal physiology and anatomy that may affect intraoperative maternal-fetal well-being [14].

Classic teaching regarding non-obstetric surgery during pregnancy was that surgery during the first and third trimesters was associated with an increased risk of pregnancy loss and preterm birth, while surgery during the second trimester was associated with a reduced risk. However, a review of the medical literature proposes that these opinions are largely based on inappropriate extrapolations of poor quality data. Many studies used to formulate this opinion are decades old and do not reflect current diagnostic testing, surgical techniques, or the perioperative maternal-fetal care commonly available today. In addition, these studies compare surgical outcomes and pregnancy risks of an obstetric population to a non-obstetric population rather than assess the adverse maternal and fetal outcomes that may be associated with not performing the surgical intervention at all. Lastly, these studies underestimate the overall risk of poor outcome to the mother and fetus from the initial medical or surgical condition and instead attribute all of the risk of poor outcome to the surgical intervention [13].

Per the American College of Obstetricians and Gynecologists and the American Society of Anesthesiologists, a pregnant woman should never be denied an indicated or emergent surgery, regardless of trimester [13]. Elective surgery, however, should be postponed until after delivery [13]. Non-elective surgery should be performed, if possible, in the second trimester when preterm contractions and spontaneous abortion are least likely. Again if a non-obstetrical surgery is planned, an obstetrical care provider should be notified and involved with the care.

When deciding to perform surgery, the risks to the mother and fetus must be weighed against the dangers of inadequately treating the surgically indicated disease [4]. There is limited data regarding laparoscopic surgery in the third trimester of pregnancy with most publications reflecting either single case reports a small case series [15]. In the pregnant population, laparoscopic surgery has been shown to decrease operative time and hasten recovery and mobilization, which translates into reduced fetal exposure to anesthesia and analgesic drugs [16]. Evidence in the recent decades has suggested that laparoscopy, even in advanced gestational ages, can be performed safely and is the preferred treatment modality for many conditions [1].

Obstetric Concerns and Outcomes/ Surgical Complications

Surgeries during pregnancy have increased risks, potentially exposing the mother and the fetus to the risk of fetal loss, wound complications, pain, and preterm delivery [17]. Traditionally, surgery during the third trimester of pregnancy has been associated with increased risk of preterm labor. However, studies examining the effects of surgery on preterm labor have not used established diagnostic criteria for true preterm labor, which underminds their conclusions [1, 13].

The medical team including the surgeon, obstetrician, anesthesiologist, and neonatologist must weigh the benefits and risks of surgery for both the mother and the fetus when managing non-obstetric surgical conditions in the pregnant population [15]. Preterm delivery may occur in women having surgery in the third trimester of pregnancy. However, the severity of the underlying maternal illnesses in women requiring surgery late in pregnancy may account for the potential excess rate of preterm birth. Furthermore, maternal morbidity and mortality is increased in women whose surgery is delayed [1, 13].

The leading causes of non-obstetric acute abdomen and surgical emergency during pregnancy are acute appendicitis and symptomatic biliary disorders. The incidence of acute appendicitis is 0.13% in pregnancy, which is similar to the rate in non-pregnant woman [18]. However, pregnant patients have a greater likelihood of serious complications to include perforation with associated higher rates of fetal loss. This is thought to be the consequence of delayed diagnosis and operative intervention secondary to the conservative use of imaging modalities [19]. The rate of fetal loss in acute appendicitis is 1.5% as compared to up to 20% in perforated appendicitis and up to 37.5% with generalized peritonitis [17]. Thus, there is no role for non-operative management of uncomplicated acute appendicitis in pregnant women. Research documenting the safety of non-operative management of acute appendicitis did not include pregnant patients.

Symptomatic biliary tract disease occurs at a rate of 0.16% in pregnancy and approximately 40% of symptomatic patients require cholecystectomy. Cholecystectomy has been associated with a 5% rate of fetal loss [17]; however, increased rates of fetal demise have not been reported for laparoscopic cholecystectomy performed during the first and second trimesters [3]. Early surgical management via laparoscopic cholecystectomy is the treatment of choice in the pregnant patient with symptomatic gallbladder disease regardless of trimester. Up to 78% of patients will have recurrent gallbladder symptoms with approximately 50% of these patients requiring hospitalization and up to 23% of such patients developing acute cholecystitis, cholangitis, or gallstone pancreatitis in pregnancy [20]. With cholangitis and pancreatitis, the rate of fetal loss is up to 60% [3, 16] and preterm labor up to 20% of cases [3].

Cholecystectomy, particularly the laparoscopic approach, is recommended for symptomatic and complicated gallstone disease in the pregnant patient regardless of the trimester. Delaying treatment beyond the first 8 weeks is reasonable for symptomatic cholelithiasis in order to allow for complete fetal organogenesis.

Fetal Heart Rate Monitoring

Fetal hypoxia as a result of maternal hypoxia or hypotension during non-obstetric surgery in pregnancy is a major concern and must be considered in all surgical procedures with a potential risk of maternal hypoxia or hypotension secondary to the surgery or anesthetics used. Early reduction in uterine and fetal perfusion will occur in any maternal shock state as a result of preferential perfusion to vital maternal organs (brain, heart, and lungs) [12]. The following are the American College of Obstetricians and Gynecologists (ACOG) published general guidelines for fetal monitoring [13]:

- If the fetus is considered to be previable, before 23 weeks gestation, it is generally sufficient to ascertain the fetal heart rate by Doppler before and after the procedure.
- At a minimum, if the fetus is considered to be viable, simultaneous electronic fetal heart rate and contraction monitoring should be performed before and after the procedure to assess fetal well-being and the absence of contractions.

A fetus born after 23 weeks gestation has a greater than 50% chance of survival with neonatal intensive care [21]. This fact complicates surgical intervention as the surgeon must consider two patients while proceeding to surgery. All efforts should be directed at maintaining hemodynamic stability in the mother, which if successful, will resuscitate the fetus. Intraoperative continuous fetal monitoring has not been shown to improve the outcome of the fetus, and this decision should be made on a case-by-case basis [22]. Additionally, the decision to use fetal monitoring should be a shared decision between the anesthesia and obstetric providers, surgeons, pediatricians, nurses, and the patient to optimize maternal and fetal well-being [12]. Once the surgical intervention is completed and the mother is stabilized, further fetal monitoring is indicated. The ACOG recommends a minimum of 2–6 hours of monitoring after trauma [23]; however, no ideal duration has been established for post-operative monitoring with recommendations ranging from 4 to 48 hours.

Delivery With Maternal Demise

In the rare instance, such as trauma or septic shock where maternal death is imminent, emergent delivery of the fetus can be considered. A perimortem cesarean section is a cesarean section performed in a viable pregnancy, greater than or equal to 23 weeks gestation, in the setting of maternal cardiac arrest. It is recommended that the procedure be performed in the setting of imminent maternal death or no later than 4 min after properly performed cardiopulmonary resuscitation has failed to revive the mother [24, 25]. While this standard can seldom be met in actual practice even in ideal circumstances, prolonged resuscitation is not recommended if no maternal pulse can be obtained [18]. Rather, the uterus should be decompressed to increase the likelihood of successful maternal resuscitation. The delivery of the fetus reduces the aortocaval compression, which theoretically can increase maternal cardiac output, which may improve the maternal condition following cesarean delivery [18, 19]. Again, in this extreme instance, the obstetrician should be involved early in the management and the operating team should be prepared to perform an emergent C-section should the need arise.

Conclusion

When approaching non-obstetrical surgery, multidisciplinary management is imperative given changes in maternal physiology. The medical team must always weigh the benefits and risks of surgery regarding both the mother and the fetus when managing non-obstetrical surgical conditions in the

pregnant population. However, indicated surgery for acute conditions is safe for both the mother and the fetus, regardless of the trimester. Moreover, indicated surgery is more beneficial for both mother and fetus as complications from delayed surgery can lead to severe maternal and fetal morbidity and mortality. Specific obstetrical concerns to include preterm birth and fetal demise should be considered in addition to fetal monitoring during surgery in the third trimester of pregnancy.

References

1. Tolcher MC, Fisher WE, Clark SL. Nonobstetric surgery during pregnancy. Obstet Gynecol. 2018;132(2):395–403.
2. Hill CC, Pickinpaugh J. Physiologic changes in pregnancy. In: Obstetric and gynecology for the general surgeon: surgical clinics of North America. 2nd ed. Philadelphia: Saunders; 2008. p. 391–401.
3. Pearl JP, Price RR, Tonkin AE, Richardson WS, Stefanidis D. SAGES guidelines for the use of laparoscopy during pregnancy. Surg Endosc. 2017;31(10):3767–82.
4. Visser BC, Glasgow RE, Mulvihill KK, Mulvihill SJ. Safety and timing of nonobstetric abdominal surgery in pregnancy. Dig Surg. 2001;18(5):409–17.
5. Ouzounian JG, Elkayam U. Physiologic changes during normal pregnancy and delivery. Cardiol Clin. 2012;30(3):317–29.
6. Sanghavi M, Rutherford JD. Cardiovascular physiology of pregnancy. Circulation. 2014;130(12):1003–8.
7. Soma-Pilay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiologic changes in pregnancy. Cardiovasc J Afr. 2016;27(2):89–94.
8. Stewart MK, Terhune KP. Management of pregnant patients undergoing general surgical procedures. Surg Clin North Am. 2015;95(2):429–42.
9. Reitman E, Flood P. Anaesthetic considerations for non-obstetric surgery during pregnancy. Br J Anaesth. 2011;107(Suppl 1):i72–8.
10. Zielinski R, Searing K, Deibel M. Gastrointestinal distress in pregnancy: prevalence, assessment, and treatment of 5 common minor discomforts. J Perinat Neonatal Nurs. 2015;29(1):23–31.
11. Erick M, Cox JT, Mogensen KM. ACOG practice bulletin 189: nausea and vomiting of pregnancy. Obstet Gynecol. 2018;131(5):935.
12. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. Practice bulletin no. 166: thrombocytopenia in pregnancy. Obstet Gynecol. 2016;128(3):e43–53.
13. Ducloy-Bouthors AS, Baldini A, Abdul-Kadir R, Nizard J, ESA VTE Guidelines Task Force. European guidelines on perioperative venous thromboembolism prophylaxis: surgery during pregnancy and the immediate postpartum period. Eur J Anaesthesiol. 2018;35(2):130–3.
14. Committee on Obstetric Practice and the American Society of Anesthesiologists. Committee opinion no. 696: nonobstetric surgery during pregnancy. Obstet Gynecol. 2017;129(4):777–8.
15. Upadhyay A, Stanten S, Kazantsev G, Horoupian R, Stanten A. Laparoscopic management of a nonobstetric emergency in the third trimester of pregnancy. Surg Endosc. 2007;21(8):1344–8.
16. Nasioudis D, Tsillmigras D, Economopoulos KP. Laparoscopic cholecystectomy during pregnancy: a systematic review of 590 patients. Int J Surg. 2016;27:165–75.
17. Kwon H, Lee M, Park HS, Yoon SH, Lee CH, Roh JW. Laparoscopic management is feasible for nonobstetric surgical disease in all trimesters of pregnancy. Surg Endosc. 2018;32(6):2643–9.
18. Kocael PC, Simsek O, Saribeyoglu K, Pekmezci S, Goksoy E. Laparoscopic surgery in pregnant patients with acute abdomen. Ann Ital Chir. 2015;86(2):137–42.
19. Dizon AM, Carey ET. Minimally invasive gynecologic surgery in the pregnant patient: considerations, techniques, and postoperative management per trimester. Curr Opin Obstet Gynecol. 2018;30(4):267–71.
20. Jorge AM, Keswani RN, Veerappen A, Soper NJ, Gawron AJ. Non-operative management of symptomatic cholelithiasis in pregnancy is associated with frequent hospitalizations. J Gastrointest Surg. 2015;19(4):598–603.
21. Stensvold HJ, Klingenberg C, Stoen R, et al. Neonatal morbidity and 1-year survival of extremely preterm infants. Pediatrics. 2017;1139(3):e20161821.
22. Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal consideration. Clin Obstet Gynecol. 2009;52(4):535–45.
23. Hill CC, Pickinpaugh J. Trauma and surgical emergencies in the obstetric patient. Surg Clin North Am. 2008;88(2):421–40.
24. Jain V, Chari R, Maslovitz S, Farine D, Maternal Fetal Medicine Committee, Bujold E, Gagnon R, Basso M, Bos H, Brown R, Cooper S, Gouin K, McLeod NL, Menticoglou S, Mundle W, Pylypjuk C, Roggensack A, Sanderson F. Guidelines for the management of a pregnant trauma patient. J Obstet Gynaecol Can. 2015;37(6):553–74.
25. Mendez-Figueroa H, Dahlke JD, Vrees RA, Rouse DJ. Trauma in pregnancy: an updated systematic review. Am J Obstet Gynecol. 2013;209(1):1–10.

Radiology in the Pregnant Patient with Acute Abdominal Pain

37

Mustafa M. Alikhan

Abdominal and pelvic pain in the pregnant patient is a very common problem for patients and physicians. Such pain can be of acute or of insidious onset, and it may also be intermittent. Typically, in the pregnant patient, most abdominal pain is secondary to the gravid state. However, non-obstetric abdominal and pelvic pain during pregnancy is a relatively common indication for emergency consultation from the surgeon. The focus of this chapter will discuss intra-abdominal/non-obstetric conditions.

While diagnostic considerations to ascertain the cause of abdominal pain may be similar to that of the nonpregnant patient, limitations secondary to normal physiologic changes associated with pregnancy must be considered [7]. Confounding physiologic changes such as leukocytosis of pregnancy and increased C-reactive protein cause normal reference laboratory values to be inconclusive or equivocal at best. Progressive enlargement of the gravid uterus results in internal displacement of normal abdominal and pelvic organs and can result in a potentially challenging and confusing physical exam. Symptoms like nausea and emesis are also nonspecific and of limited value for diagnosis.

Ultimately, the etiology of the acute abdomen in pregnancy must be ascertained since it could be life-threatening to both the expectant mother and the fetus. To this end, diagnostic imaging has grown increasingly important as an adjunctive tool in order to definitively identify potential surgical pathology. Thus, a practical and successful approach for imaging the acute surgical abdomen in a pregnant patient is imperative in order to yield a clinically relevant diagnosis while mitigating any associated harmful effects of imaging upon the mother and developing fetus [27].

To understand the risk, it is essential to understand the basics of radiation and radiobiology. It is extremely important to consider the biologic effects of ionizing radiation upon the conceptus/fetus as well as a basic understanding of radiation nomenclature and basic dosimetry. The biological effects of X-rays/gamma radiation induce biological effects based upon the absorbable dose to the fetus/embryo. The doses are labeled as Gray (Gy) and millgray (mGy) or millisieverts (mSv), per convention by the American College of Radiology (ACR). Per the ACR, there are no identifiable induced developmental defects at doses under 100 mGy [37]. At doses above 100 mGy, there is a low risk for developmental deficits (i.e., gross malformations, growth retardation, mental retardation, and microcephaly), while levels in excess of 150–200 mGy have a much higher risk of developmental malformations [37].

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Within the first 2 weeks after conception, the only potential of ionizing radiation is induced termination of the pregnancy, which is an all or none event. However, usual doses of diagnostic radiation from X-rays have not been associated with such an effect. Furthermore, radiation doses from diagnostic CT or multiple pelvic radiographic examinations are also not likely to induce a termination [37]. For radiation exposure between weeks 2–15 after conception, the risk to the fetus also depends upon the body part(s) being imaged and the resultant dose. Typical studies performed for areas other than the abdomen and pelvis result in minimal scatter radiation to the fetus when the patient is shielded. Additionally, the dose of radiation from typical radiologic examinations of the abdomen and/or pelvis is usually well below any threshold that results in developmental abnormalities [37] (Table 37.1). However, a potential risk that the practitioner should be aware of is the slight increase in the risk for cancer later in life. Such a risk is very small, and there is above 99% likelihood the fetus will be unaffected by the radiation. On the other hand, CT studies of the abdomen and pelvis have significantly more radiation; but a single-phase CT scan of the abdomen/pelvis usually delivers less than 35 mGy (typically about 10–25 mGy) which is considered a low dose and would not warrant interruption of pregnancy [37].

The radiation doses of an abdominal multidetector computed tomography (MDCT) scan cause deleterious effects to embryonic/fetal DNA which increases the chance of malignancy in the future. Specifically, DNA is most sensitive to deleterious effects of radiation during the first trimester and then decreases progressively during the second and third trimesters [23]. This is due to the fact that rapidly proliferating cells are most prevalent during first trimester secondary to organogenesis that occurs from week 2–15 of development [11, 36]. Abdominal MDCT imaging of the mother for appendicitis has been reported as theoretically doubling the fetal risk for developing a childhood cancer [36]. The number of CT scans performed in pregnant females was reported to have more than doubled from the year 1997–2006 with approximately one-third being performed for the evaluation of acute appendicitis [34]; during this same time period, it was reported that the use of diagnostic imaging had increased dramatically contributing to both medical costs and to medical exposure to ionizing radiation [33]. Spontaneous abortion or fetal death may be seen in some situations.

The ACR recommends diagnostic imaging techniques that do not utilize ionizing radiation, such as ultrasound (US) and magnetic resonance

Table 37.1 Relative radiation level designations along with common example examinations for each classification

Relative radiation level[a]	Adult effective dose estimate range	Pediatrie effective dose estimate range	Example examinations
O	0 mSv	0 mSv	Ultrasound; MRI
☢	<0.1 mSv	<0.03 mSv	Chest radiographs; hand radiographs
☢☢	0.1–1 mSv	0.03–0.3 mSv	Pelvis radiographs; mammography
☢☢☢	1–10 mSv	0.3–3 mSv	Abdomen CT, nuclear medicine bone scan
☢☢☢☢	10–30 mSv	3–10 mSv	Abdomen CT without and with contrast; whole body PET
☢☢☢☢☢	30–100 mSv	10–30 mSv	CTA chest abdomen and pelvis with contrast; transjugular intrahepatic portosystemic shunt placement

https://www.acr.org/-/media/ACR/Files/Appropriateness-Criteria/RadiationDoseAssessmentIntro.pdf

[a]The RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., the region of the body exposed to ionizing radiation, the imaging guidance that is used, etc.). The RRLs for these examinations are designated as "Varies"

Table 37.2 ACR–SPR practice parameter for imaging pregnant or potentially pregnant adolescents and women with ionizing radiation – Revised 2018

Menstrual or gestational age	Conception age	<50 mGy (<5 rad)	50–100 mGy (5–10 rad)	>100 mGy (>10 rad)
0–2 weeks (0–14 days)	Prior to conception	None	None	None
3rd–4th week (15–28 days)	1st–2nd week (1–14 days)	None	Probably none	Possible spontaneous abortion
5th–10th weeks (29–70 days)	3rd–8th week (15–56 days)	None	Potential effects are scientifically uncertain and probably too subtle to be clinically detectable	Possible malformations increasing in likelihood as dose increases
11th–17th week (71–119 days)	9th–15th week (57–105 days)	None	Potential effects are scientifically uncertain and probably too subtle to be clinically detectable	Risk of diminished IQ or of mental retardation. Increasing in frequency and severity with increasing dose
18th–27th week (120–189 days)	16th–25th week (106–175 days)	None	None	IQ deficits not detectable at diagnostic doses
>27 weeks (> 189 days)	>25 weeks (>175 days)	None	None	None applicable to diagnostic medicine

https://www.acr.org/-/media/ACR/Files/Practice-Parameters/pregnant-pts.pdf

Table 37.3 Summary of imaging techniques

Imaging technique	Major advantages	Major disadvantages
Ultrasound	Cost and accessibility; safety profile	Limited assessment of alternative diagnoses; limited by body habitus; operator dependent; high rate of nonvisualized appendix
CT	High sensitivity and specificity; accessibility; ability to identify alternative diagnoses	Ionizing radiation
MRI	High sensitivity and specificity; ability to identify alternative diagnoses	Cost and accessibility; robust imaging technique required for good results; relatively long examination times

Long et al. [6]
https://www.ajronline.org/doi/10.2214/AJR.10.4323

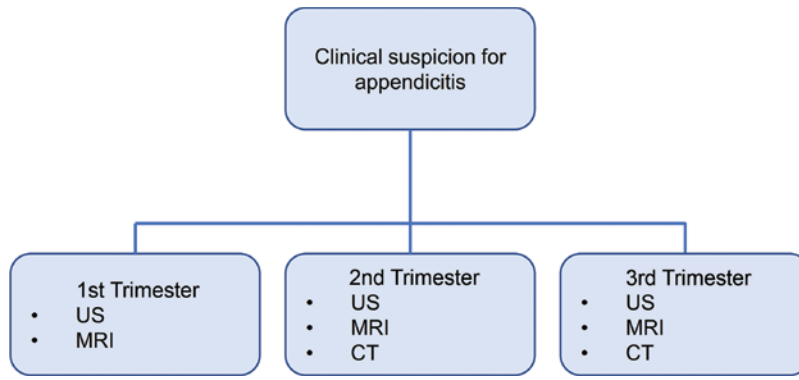

Fig. 37.1 Algorithm for imaging during pregnancy with suspected appendicitis. (Gjelsteen et al. [11])

imaging (MRI), as the first and second choices of imaging the pregnant patient with the acute abdomen (Tables 37.2 and 37.3) [25]. MDCT is thus a final option in the diagnostic imaging algorithm (Fig. 37.1).

US

US should be the initial diagnostic imaging modality for assessing the acute abdomen in the pregnant patient. US is readily available, relatively cheap,

and does not utilize ionizing radiation. However, it is important to realize that diagnostic US does have some properties that may potentially have effects on living tissues [35]. Specifically, it can result in mechanical forces that yield tissue cavitation as well as hyperthermia within an affected area. These forces can be expressed in terms of a thermal index (TI) or a mechanical index (MI) which correlate with the potential for the rise in temperature in the focal zone of the US beam as well as vibrational forces which can result in cavitation within the soft tissues, respectively [32]. It is also important to know that Doppler imaging generates higher levels of acoustic energy than does B-mode imaging since "gray scale" remote US is associated with negligible increases in TI. These forces have been shown to be significant in laboratory studies but have not been studied in mammalian fetuses. These forces are more detrimental during early gestation (i.e., the first trimester). As a result, it is incumbent on the ultrasound operator to avoid or minimize the use of Doppler imaging and utilize B-mode imaging as an alternative in the setting of ascertaining fetal cardiac activity in order to mitigate damage to the fetus. In general, though, standard US practices are thought to have a low overall possibility for fetal harm and considered to be safe [35].

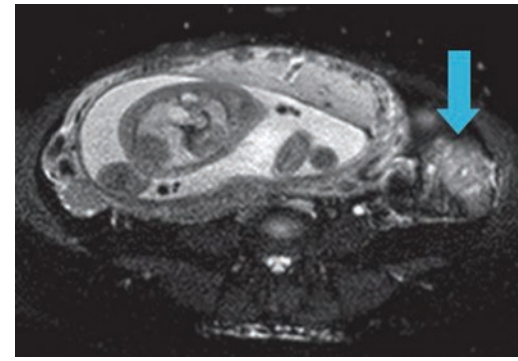

Fig. 37.2 Axial fat-suppressed fluid-sensitive image of a gravid uterus with the blue arrow pointing to the area of distal colon inflammation. https://www.consultant360.com/articles/acute-diverticulitis

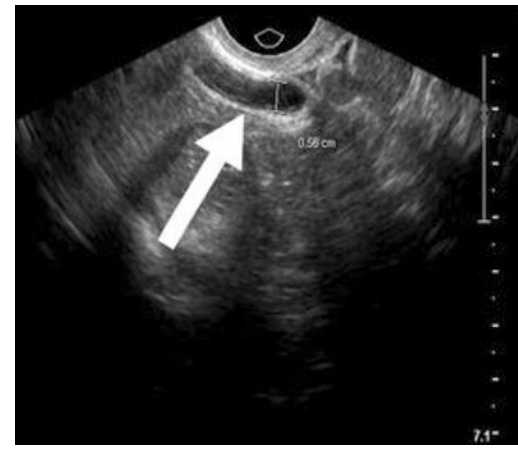

Fig. 37.3 Longitudinal view from endovaginal pelvic ultrasound shows a blind-ending tubular strucuture compatible with an appendix (arrow) in right lower quadrant that has normal thickness of 6 mm [6]

MRI

Magnetic resonance imaging (MRI) is the next best choice for evaluating the acute abdomen [30]. It can provide a larger field of view and evaluate without the use of ionizing radiation. MRI can provide high-quality images of the bowel, appendix, biliary tract, vasculature, or urinary tract without the necessity of contrast agent administration secondary to fluid-sensitive fat-suppressed imaging techniques that are currently employed (Fig. 37.2). The use of gadolinium, however, has been historically avoided because of the concern that it is a teratogen. The data is not convincing enough to wholly refute this concern.

However, unlike MDCT, which is accomplished as quickly as mere seconds, MRI requires a longer time for image acquisition. The significant benefit of the current multidetector helical CT technology is the shorter scan time for image acquisition which would result in significantly less motion artifact and potential for motion artifact as the exam may be acquitted in less than 30 seconds during a single breath-hold. Current MRI exams may take upward of 5 min and introduce the possibility of motion artifact that can degrade image quality thus yielding a sub-diagnostic exam in a patient who is in pain and cannot hold still for prolonged time. But due to radiation safety considerations, the ACR has endorsed MRI after inconclusive US examination of the gravid abdominopelvic region [25]. Thus, MRI has been increasingly used in the evaluation of the acute abdomen in pregnant patients (Fig. 37.3).

Appendicitis

There is a wide-ranging etiology of conditions that may cause acute abdominopelvic pain; and appendicitis is the most common non-obstetric surgical emergency [1–5, 7, 11]. A delay in diagnosis or nondiagnosis of acute appendicitis increases the likelihood of maternal appendiceal perforation [9]: surgical delay more than 24 hours can result in a 66% increase in the rate of appendiceal perforation [5, 6]. Furthermore, in the case of maternal appendiceal perforation, resultant fetal mortality has been reported to be as high as 37% [4, 6].

Due to the aforementioned physiological changes of pregnancy, the clinical signs and symptoms of appendicitis can demonstrate high variability which increases with the progression of the pregnancy. If there is any clinical concern for possible appendicitis in the pregnant female, US should be the initial choice of screening due to rapidity of obtaining the study. The goal of the exam is to find and demonstrate the morphology of the appendix: in the case of acute appendicitis, a blind-ending tubular structure measuring a caliber of 7 mm or greater and demonstrating hyperemia on color Doppler imaging in addition to non-compressibility would be ideal. Associated findings of a hyperechoic appendicolith and diffuse free fluid within the right lower quadrant would also be helpful secondary findings. However, non-visualization of the appendix becomes more common as the pregnancy progresses, partly due to the fact the appendix is shifted superiorly by an increasingly enlarging gravid uterus [10]. Hence, MRI can be utilized to obtain a wider view of the abdomen and pelvis and serves a role as a useful adjunct in these patients [31]. MRI has been shown to be highly effective in the exclusion of acute appendicitis: a nearly 100% negative predictive value with appendiceal visualization has been reported in several studies [2, 6, 8, 29].

Biliary Disease

Biliary pathology is a common cause of abdominal pain in pregnant women which commonly presents clinically as right upper quadrant pain. Cholelithiasis is twice as common in women than men in every demographic category [12]. Additionally, as stated in the previous chapter, the physiologic changes of pregnancy can result in biliary stasis. Elevated estrogen levels predispose to hypersecretion of biliary cholesterol in addition to decreasing gallbladder motility which can both contribute to biliary stasis and lithogenicity [12]. This is why the second most common surgical entity in pregnant women is acute cholecystitis or symptomatic cholelithiasis.

US evaluation of right upper quadrant pain is the most reliable source of diagnostic imaging which has shown to the safe and diagnostic. In the case of acute cholecystitis, gallstones are usually identified in greater than 90% of patients. Right upper quadrant US is the most common modality of identifying acute cholecystitis. A typical US indicating acute cholecystitis will show gallstones, thickening of the gallbladder wall (>3 mm), and pericholecystic fluid in addition to hyperemia. However, in the gravid patient, sonography may become less effective during the progression of the pregnancy resulting in obscuration of the gallbladder secondary to overlying bowel gas secondary and/or organ displacement.

MRI techniques can be used adjunctively for evaluation of biliary disease by acquiring fast sequence heavily fluid weighted magnetic resonance cholangiopancreatography (MRCP). Gallbladder wall thickening greater than 3 mm, gallbladder wall edema, and pericholecystic fluid can be seen in the clinical setting of acute cholecystitis on MRI. Furthermore, cholelithiasis may be apparent as signal voids on MRCP anywhere along the biliary tree: this may help in diagnosis of choledocholithiasis. Moreover, biliary stasis can be seen as diffusely fluid-filled biliary tracts.

Pancreatitis

While acute pancreatitis rarely occurs in the pregnant patient, it is most commonly associated with gallstone disease (65–100% of all cases); other less common etiologies include hypertriglyceridemia and alcohol abuse [17–19]. It is also more commonly encountered late in pregnancy (i.e., third trimester or early postpartum period)

[17, 19]. High morbidity and mortality are associated with this pathologic state manifested by preterm labor, prematurity, in utero fetal death, and a high maternal-fetal mortality [19]. Early diagnosis is paramount to decrease morbidity and mortality [19].

Intestinal Pathology

Small bowel obstruction (SBO) is another pathologic state that has potential surgical implications. The pregnant female can be predisposed to SBO secondary to a history of prior surgical interventions and concomitant adhesions, hernias, or may be seen in the setting of endometriosis. Typically, upright plain film radiography of the abdomen is the best initial study and can be used with limited deleterious effects upon the fetus, as stated earlier.

Inflammatory bowel disease (Crohn's disease and ulcerative colitis) can occur during pregnancy as many patients with this disease process are of reproductive age [13, 14]. Inflammatory bowel disease (IBD) is most common during the reproductive years. Approximately 50% of patients are less than 35 years of age at the time of diagnosis, and 25% conceive for the first time after their diagnosis of IBD. Pregnancy has not been shown to affect the course of either Crohn's disease or ulcerative colitis.

US is the primary evaluation of pregnant patients with IBD who experience symptoms suggestive of active disease. It can be used to evaluate both the large and small bowel. MRI is becoming increasingly utilized, but again, the use of gadolinium is usually avoided secondary to possible teratogenicity, especially during the first trimester.

The current use of magnetic resonance enterography (MRE), with an adapted protocol for pregnancy, has been shown to be both sensitive and specific to interrogate pregnant women with known or suspected IBD [15]. MRE is a useful modality for the evaluation of luminal inflammation [16]. Increased bowel wall signal, indicative of bowel wall edema, on fluid-sensitive fat-suppressed MRI sequences indicates active disease. Specifically, this correlates to the pathology of the disease process which results in areas of segmental bowel wall thickening. Concomitant fluid signal/edema can be evident within the surrounding fat. Associated complications visible by MRI include fistula formation, strictures, and abscess formation. Additionally, in advanced cases of disease, bowel obstruction and toxic megacolon may also be present.

Although rare, there have been cases of *diverticulitis that occur during pregnancy*. Thus, this non-obstetrical cause of abdominal pain should be kept in the differential when caring for pregnant women with a history of colonic diverticulosis and those patients with possible predisposition to this process. Plain film radiography can be used initially to evaluate for bowel obstruction or evidence of perforation manifested by dilated loops of bowel with air-fluid levels and antidependent free air on standing or decubitus radiography. MRI is a good imaging modality to evaluate the extent of suspected diverticulitis. Fat-suppressed fast-spin fluid-sensitive techniques can be employed to minimize motion artifact. Diverticula may be evident as focal outpouchings along the colonic wall that demonstrates characteristic foci of susceptibility artifact (low signal) secondary to underlying air. Again, as in IBD, colonic wall inflammatory changes also can be present. Concomitant pericolonic inflammatory changes with possible fluid collection/abscess formation can be seen in more advanced cases, while scattered foci of susceptibility artifact/signal dropout can occur in those cases with free air.

Trauma

Trauma is a common problem in today's modern world affecting 6–7% of all pregnant females and is the leading cause of non-obstetric maternal mortality [21, 22]. Etiologies of traumatic injury involve both blunt and penetrating trauma and range from accidental causes (e.g., motor vehicle accident) to assault (e.g., domestic violence). Potential abdominal injury usually is obvious in pregnant women with trauma. Furthermore, in

cases of domestic violence, the uterus and fetus may be the focal points of assault [21]. Minor trauma is much more common than major trauma; thus, minor trauma is a more common etiology of fetal morbidity and mortality [22].

After initial stabilization of the patient, US can be utilized to perform a focused abdominal sonography for trauma or FAST exam. This is an adjunct to the secondary survey physical exam, and it is used to assess for free fluid within the peritoneum as well as any gross abnormalities of the major organs in the four quadrants of the abdomen. US should also be utilized to determine fetal cardiac activity and gross anatomical exam in addition to determining the age of the fetus [20, 22].

Inasmuch as we have discussed utilizing imaging modalities that avoid the use of ionizing radiation in the other pathologic entities discussed thus far, imaging in trauma needs to be performed more expediently and accurately in order to quickly determine course of action/treatment. Specifically, both blunt and penetrating trauma can have serious detriment to both the mother and the fetus, and a delay in diagnosis could have disastrous results on both lives. Thus, conventional radiography and CT are essential in order to determine and exclude serious traumatic injuries which can result in fetal or maternal mortality. Standard trauma CT and radiography yield ionizing radiation that must be accounted for and mitigated when possible (i.e., use of judicious shielding of the gravid pelvis). Since ionizing radiation is requisite for trauma work-up, an understanding of radiation dose to the fetus is imperative.

Furthermore, it should be understood that in general fetal exposure to ionizing radiation from the radiological examinations that are routinely used in the evaluation of pregnant trauma patients still presents an overall low risk to the developing fetus [20]. As stated before, ionizing radiation has the highest teratogenic potential during organogenesis in the first trimester, with an increased risk of miscarriage before this period. After 10 weeks, radiation is more likely to produce growth restriction or CNS effects versus teratogenic changes [20]. Radiation exposure to a fetus with <18 weeks of gestation with a cumulative dose of >50–100 mGy is associated with an increased risk of fetal malformation or CNS effects. However, concern over fetal exposure to radiation should not preclude or delay any indicated radiological evaluation as this would increase both maternal and fetal morbidity and mortality rates.

Given lengthy examination times and the need to remove the patient from the acute care setting, MRI is suboptimal in the initial evaluation of post-traumatic pregnant patients. However, MRI may be used after initial stabilization for interval interrogation of specific complex clinical situations such as imaging of the neuroaxis [22]. It is for these reasons that MRI is being increasingly used as an adjunctive measure in both urgent and routine studies of pregnant females.

Conclusion

Imaging of common surgical pathology in pregnant females is very valuable because of the difficulty in diagnosing abdominal pain in this population. It is very helpful for the surgeon to have a basic understanding of the different modalities available in order to yield a diagnosis safely for both the mother and the fetus. In general, the amount of radiation exposure by even CT scanning is small. Despite this, all attempts to reduce the radiation should be made for the overall safety of the mother and the fetus.

References

1. Andersen B, Nielsen TF. Appendicitis in pregnancy: diagnosis, management and complications. Acta Obstet Gynecol Scand. 1999;78(9):758–62.
2. Israel GM, Malguria N, McCarthy S, et al. MRI vs. ultrasound for suspected appendicitis during pregnancy. J Magn Reson Imaging. 2008;28(2):428–33.
3. Mourad J, Elliott JP, Erickson L, et al. Appendicitis in pregnancy: new information that contradicts long-held clinical beliefs. Am J Obstet Gynecol. 2000;182(5):1027–9.
4. Oto A, Srinivasan PN, Ernst RD, et al. Revisiting MRI for appendix location during pregnancy. AJR Am J Roentgenol. 2006;186(3):883–7.

5. Woodfield CA, Lazarus E, Chen KC, et al. Abdominal pain in pregnancy: diagnoses and imaging unique to pregnancy–review. AJR Am J Roentgenol. 2010;194(6 Suppl):WS14–30.
6. Long SS, Long C, Lai H, et al. Imaging strategies for right lower quadrant pain in pregnancy. AJR Am J Roentgenol. 2011;196(1):4–12.
7. Tamir IL, Bongard FS, Klein SR. Acute appendicitis in the pregnant patient. Am J Surg. 1990;160(6):571–5. discussion 575–6
8. Pedrosa I, Levine D, Eyvazzadeh AD, et al. MR imaging evaluation of acute appendicitis in pregnancy. Radiology. 2006;238(3):891–9.
9. Bickell NA, Aufses AH Jr, Rojas M, Bodian C. How time affects the risk of rupture in appendicitis. J Am Coll Surg. 2006;202(3):401.
10. Oto A, Srinivasan PN, Ernst RD, Koroglu M, Cesani F, Nishino T, Chaljub G. Revisiting MRI for appendix location during pregnancy. AJR Am J Roentgenol. 2006;186(3):883.
11. Gjelsteen AC, Ching BH, Meyermann MW, et al. CT, MRI, PET, PET/CT and ultrasound in the evaluation of obstetric and gynecologic patients. Surg Clin North Am. 2008;88:361–90.
12. Ornella de Bari TY, Wang ML, et al. Cholesterol cholelithiasis in pregnant women: pathogenesis, prevention and treatment. Ann Hepatol. 2014;13(6):728–45.
13. Jana GH, Kane S. Pregnancy and inflammatory bowel disease. Gastroenterol Hepatol (NY). 2015;11(2):96–102.
14. Calderwood AH, Kane SV. IBD and pregnancy. MedGenMed. 2004;6(4):14.
15. Stern MD, Kopylov U, Ben-Horin S, Apter S, Amitai MM. Magnetic resonance enterography in pregnant women with Crohn's disease: case series and literature review. BMC Gastroenterol. 2014;14:146.
16. Naganuma M, Hisamatsu T, Kanai T, Ogata H. Magnetic resonance enterography of Crohn's disease. Expert Rev Gastroenterol Hepatol. 2015;9(1):37–45.
17. Juneja SK, Gupta S, Satpal SV, et al. Acute panreatitis in pregnany: a treatment paradigm based upon our hospital experience. Int J Appl Basic Med Res. 2013;3(2):122–5.
18. Mali P. Pancreatitis in pregnancy: etiology, diagnosis, treatment, and outcomes. Hepatobiliary Pancreat Dis Int. 2016;15(4):434–8.
19. Ducarme G, Maire F, Chatel P, et al. Acute pancreatitis during pregnancy: a review. J Perinatol. 2014;34(2):87–94.
20. Jain V, Chari R, Maslovitz S, et al. Guidelines for the management of a pregnant trauma patient. J Obstet Gynaecol Can. 2015;37(6):553–71.
21. Brown HL. Trauma in pregnancy. Obstet Gynecol. 2009;114(1):147–60.
22. Raptis CA, Mellnick VM, Raptis DA, et al. Imaging of trauma in the pregnant patient. Radiographics. 2014;34:748–63.
23. Nguyen CP, Goodman LH. Fetal risk in diagnostic radiology. Semin Ultrasound CT MRI. 2012;33:4–10.
24. Ralls PW, Balfe DM, Bree RL, et al. Evaluation of acute right lower quadrant pain. In: ACR appropriateness criteria. Reston: American College of Radiology; 1999. p. 1–8.
25. Smith MP, Katz DS, et al. ACR appropriateness criteria right lower quadrant pain – suspected appendicitis. Ultrasound Q. 2015;31(2):85–91.
26. Rosenfield AT, Newhouse JH, Bluth EI, et al. Acute onset flank pain, suspicion of stone disease. In: ACR appropriateness criteria. Reston: American College of Radiology; 1998. p. 1–3.
27. Shur J, Bottomley C, Walton K, Patel JH. Imaging of acute abdominal pain in the third trimester of pregnancy. BMJ. 2018;361:k2511.
28. Cogley JR, Ghobrial PM, et al. pulmonary embolism evaluation in the pregnant patient: a review of current imaging approaches. Semin Ultrasound CT MRI. 2011;33:11–7.
29. Vu L, Ambrose D, et al. Evaluation of MRI for the diagnosis of appendicitis during pregnancy when ultrasound is inconclusive. J Surg Res. 2009;156:145–9.
30. Khandelwal A, Fasih N, Kielar A. Imaging of acute abdomen in pregnancy. Radiol Clin N Am. 2013;51:1005–22.
31. Flexer SM, Tabib N, Peter MB. Suspected appendicitis in pregnancy. Surgeon. 2014;12:82–6.
32. Scheiner E, Abramowicz JS. A symposium on obstetric ultrasound: is all the C4 the fetus? Clin Obstet Gynecol. 2012 March;55(1):188–98.
33. Smith-Bindman R, Miglioretti DL, Larson EB. Rising use of diagnostic medical imaging in a large integrated health system. Health Aff (Millwood). 2008;27(6):1491–502.
34. Lazarus, E. Mayo-Smith W., et al. Utilization of radiological examinations in pregnant women: a ten year review – 1997–2006. RSNA annual meeting, Chicago; 2007: p. SSJ05–SSJ02.
35. Abramowicz JS. Benefits and risks of ultrasound in pregnancy. Semin Perinatol. 2013 Oct;37(5):295–300.
36. Hurwitz LM, Yoshizumi T, et al. Radiation dose to the fetus from body MDCT during early gestation. AJR Am J Roentgenol. 2006;186:871–6.
37. ACR–SPR practice parameter for imaging pregnant or potentially pregnant adolescents and women with ionizing radiation. Accessed online at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/pregnant-pts.pdf
38. ACR appropriateness criteria® radiation dose assessment introduction subcommittee on appropriateness criteria radiation exposure: Dianna D. Cody, PhD; David W. Jordan, PhD; Murray Becker, MD, PhD; Samuel Brady, PhD, MS; Karin E. Dill, MD; Richard A. Geise, PhD; Mary Ann Keenan, DMP; Tasneem Lalani, MD; Max P. Rosen, MD, MPH; Keith J. Strauss, MS (revised 2018). Accessed online at: https://www.acr.org/-/media/ACR/Files/Appropriateness-Criteria/RadiationDoseAssessmentIntro.pdf

38

Multidisciplinary Approach to Acute Care Surgical Emergencies in Pregnancy

Michael Cripps

All general surgeons should be comfortable with the management of general surgery issues in a pregnant patient. However, they must also be aware that pregnancy adds a level of complexity to patient care and embraces a multidisciplinary approach. Classic presentation of common disease processes can be masked or absent in pregnant patients due to changes in abdominal anatomy and commonplace ambiguous symptoms (nausea, vomiting, abdominal pain) that occur during normal pregnancy. In this patient population, discerning between pathologic and normal states is critical, as delay in diagnoses can have just as catastrophic effects as unnecessary interventions.

In an effort to provide a pragmatic guide for the "on-call general surgeon," this chapter will describe the diagnostic and management approach to common non-obstetric surgical issues. A focus is placed on incidence, deviations from general patient population, surgical modifications, and when to consult other specialties. Management of other less common, non-obstetric, abdominal disorders including vascular aneurysms, hepatic masses, and hepatic rupture is also included.

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General Considerations in Pregnancy

Preoperative evaluation of pregnant patients should be as thorough as with any patient, with complete physical exam and appropriate laboratory tests and imaging. Unfortunately, for the general surgeon, pathophysiologic and anatomic changes of pregnancy can obfuscate several standard indicators that are pillars of diagnoses for non-obstetric surgical issues, and radiation concerns limit routine imaging options. After 12 weeks of gestation, the uterus becomes an intra-abdominal organ and begins to distort the location of normal intra-abdominal organs, altering normal physical exam findings. In non-pregnant patients, a leukocytosis of 12–25,000/mm^3 is indicative of infection but can be a normal value in pregnancy. The diagnosis of hemorrhage and hypovolemic shock is difficult during pregnancy because of a relative anemia, resulting from a 50% decrease of plasma volume and a 20% increase in red cell mass. Tachycardia and hypotension are the sine qua non of hypovolemic shock, but because of this anemia of pregnancy, maternal hypovolemia will manifest as fetal distress before maternal tachycardia or hypotension. This situation is further complicated during late pregnancy as uterine compression of the inferior vena cava (IVC) can decrease cardiac output by 30%. Continued uterine growth results in diaphragm elevation of up to 4 cm, altering

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respiratory mechanics and leading to a predictable low CO_2 on arterial blood gas. Any near-term pregnant patient with a normal CO_2 is in respiratory distress and likely requires intubation. However, extreme care is necessary as decreased gastrointestinal motility causes increased risk of aspiration with intubation [1].

Appropriate Maternal and Fetal Preoperative and Postoperative Management

Risk stratification scoring systems exist, for preoperative use, to determine maternal risk for adverse obstetric outcomes after surgery. Ten risk factors were identified and assigned a point system (with corresponding risk) to categorize low (2.5%), intermediate (8.2%), or high risk (21.8%) of adverse outcomes (Table 38.1) [2]. Prompt diagnosis and treatment is imperative in obstetric patients as the presence of sepsis and peritonitis equates to high risk of adverse outcomes. Surgical approach is a modifiable risk factor as open surgery alone confers intermediate risk of adverse obstetric outcomes [1, 3].

Perioperative management of mother and fetus should be multidisciplinary and focus on hemodynamic stability and homeostasis for mother and baby [2]. Fetal sonogram should occur pre- and postoperatively before the 22nd week of gestation with addition of continuous fetal monitoring or cardiotocography (CTG) between 22 and 24 weeks gestation. After 24 weeks, CTG should occur during the entire perioperative time period with close co-management by obstetricians should labor begin [4].

Postoperative venous thromboembolism (DVT) prophylaxis should be initiated as soon as deemed safe by the surgical team due to the relative hypercoagulable state of pregnancy. Postoperative maternal pain control, like general population, should be a multimodal approach. Scheduled non-opioids like acetaminophen can be used during pregnancy, along with nonpharmacologic analgesics. The use of NSAIDs should be cautious and limited to non-selective COX inhibitors (ibuprofen) administered within the second trimester. NSAIDs are contraindicated if an infant with ductal-dependent cardiac disease is being breastfed. Postpartum opioid of choice is morphine, followed by tramadol, and hydrocodone due to less neonatal sedation. Hydromorphone and fentanyl are generally only considered safe in labor analgesia; codeine and oxycodone use is discouraged due to neonatal respiratory suppression. Administration of opioids via epidural decreases neonatal exposure. Methadone and buprenorphine are considered safe options for mother and fetus. The presence of uncontrolled pain despite adequate medication should prompt consultation with obstetricians to rule out obstetric complications [4–6].

Table 38.1 Risk stratification scoring system for adverse obstetric outcomes after surgery

Characteristic	Points
Pregnancy characteristic	
Cervical incompetence	16
Preterm labor during current pregnancy	15
Vaginitis or vulvovaginitis	8
Multiple gestation	6
Disease severity	
Sepsis	6
Peritonitis	5
Open surgery	5
Maternal drug abuse or dependence	3
General characteristics	
Nonwhite race/ethnicity	2
Medicaid coverage	1

Adapted from Sachs et al. [2]

Incidence and Surgical Approach

Incidence of an acute, non-obstetric, surgical abdomen in pregnancy is 1: 500–635 with more than 8000 urgent non-obstetric surgeries that occur per year, affecting 2% of pregnancies [1, 7]. When surgery is necessary, general and regional anesthesia is considered safe although volatile anesthetics may reduce risk of premature labor. Operative approach will depend on maternal body habitus, status of pregnancy, and disease process [1, 4].

Table 38.2 Guidelines for the use of laparoscopy during pregnancy

Guideline	Quality of evidence	Strength of recommendation
In the absence of access to imaging modalities, laparoscopy may be used selectively in the work-up and treatment of acute abdominal processes in pregnancy	++ (low)	Weak
Laparoscopic treatment of acute abdominal disease offers similar benefits to pregnant and non-pregnant patients compared to laparotomy	+++ (moderate)	Strong
Laparoscopy can be safely performed during any trimester of pregnancy when operation is indicated	+++ (moderate)	Strong
Gravid patients beyond the first trimester should be placed in the left lateral decubitus position or partial left lateral decubitus position to minimize compression of the vena cava	++ (low)	Strong
Initial abdominal access can be safely accomplished with an open (Hasson), Veress needle, or optical trocar technique, by surgeons experienced with these techniques, if the location is adjusted according to fundal height	++ (low)	Weak
CO_2 insufflation of 10–15 mmHg can be safely used for laparoscopy in the pregnant patient. The level of insufflation pressure should be adjusted to the patient's physiology	++ (low)	Weak
Intraoperative CO_2 monitoring by capnography should be used during laparoscopy in the pregnant patient	+++ (moderate)	Strong
Fetal heart monitoring of a fetus considered viable should occur preoperatively and postoperatively in the setting of urgent abdominal surgery during pregnancy	++ (low)	Weak
Tocolytics should not be used prophylactically in pregnant women undergoing surgery but should be considered perioperatively when signs of preterm labor are present	++++ (high)	Strong

Adapted from Pearl et al. [3]

Initially, the use of laparoscopy in pregnant patients was controversial, but it is gaining acceptance as a safe surgical approach in obstetrics. Today, the laparoscopic approach is generally considered the safe, primary surgical approach to diseases treated with laparoscopy in the non-pregnant patient. There are, however, some adversaries of laparoscopy who raise concerns that pneumoperitoneum increases intra-abdominal pressure, decreases uterine blood flow, decreases venous return with subsequent maternal hypotension and hypoxia, and causes fetal acidosis due to the absorption of carbon dioxide (CO_2) [8, 9]. In 2012, a systematic review and meta-analysis of 3415 patients showed low-grade evidence of worse fetal loss in patients undergoing laparoscopic vs. open appendectomies. It should be noted that this review was predominated by a single retrospective review where risk of fetal loss was significant in both negative and complex appendicitis, suggesting that misdiagnosis rather than surgical technique was responsible [8, 10]. In fact, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) strongly recommends laparoscopy use in any trimester when surgical intervention is indicated [3]. Other proponents of laparoscopy state the procedure is well tolerated

by the mother and fetus with minimal adverse effects in all trimesters [1, 2, 11, 12].

Should laparoscopy be pursued, SAGES published a set of guidelines to follow, some of which are shown in Table 38.2 [3]. Standard intraoperative techniques will require minor adjustments in obstetric patients. Historical evidence and SAGES guidelines recommend left lateral decubitus (LLD) or partial LLD in obstetric patients in, or beyond, the second trimester. Offloading the inferior vena cava (IVC) maintains maternal cardiac output and reduces fetal heart rate variability. A recent systematic review found that IVC compression is only significantly relieved at maternal leftward tilt ≥30° and if maternal blood pressure is appropriately supported with fluids and vasopressors. Although unlikely in general surgery, supine position can be used and may not be detrimental to the fetus [3, 13, 14]. The hypercoagulable state of pregnancy mandates the use of SCDs unless contraindicated.

Regarding port placement, an open, Hasson technique or Veress needle is used in the left upper quadrant (Palmer's point) to gain intra-abdominal access during the first trimester. During the second and third trimester, initial trocar placement should be several centimeters cephalic to uterine fundus, midline, and supra-umbilical [3, 13, 14]. Location of other ports should account for uterine fundal height. Pressure of pneumoperitoneum should be limited to 10–15 mmHg and for as short of a duration as possible [3, 8]. In the third trimester, the gravid uterus causes a loss of intra-abdominal domain and diminished laparoscopic visual field resulting in more open surgical approaches [15]. If open surgical technique is used, a common modification, beginning in the late second trimester, is to use a vertical incision or place the incision over the maximal area of tenderness [1]. If available, preoperative imaging is used to plan surgical approach. For example, an inflamed appendix sitting on the uterine dome, during the third trimester, will be just under the fascia and will be easily accessed via an open approach. In contrast, a retrocecal appendix may be better approached using laparoscopy and nontraditional appendectomy port placement.

Common Non-obstetric Surgical Problems

Appendicitis In pregnant patients, acute appendicitis is the most common cause of an acute abdomen accounting for 25% of non-obstetric operations in pregnancy [1]. Approximately 40% of cases occur in the second trimester. Interestingly, despite potential alterations in intra-abdominal anatomy, 90% of presenting patients will still endorse RLQ pain, regardless of trimester. Other abdominal symptoms are consistent with non-pregnant patients. Due to relative leukocytosis of pregnancy, the presence of granulocytosis should highlight infectious process. Delay in diagnosis should be avoided as local peritonitis often causes preterm contractions albeit preterm delivery seldom occurs (5–14% of patients) of which half are in the third trimester [1, 7].

Imaging in pregnancy is complicated by the risk of ionizing radiation exposure to the fetus. The use of computed tomography (CT) has become near ubiquitous in the assistance of diagnosing appendicitis in non-pregnant populations. In obstetric patients, concern for fetal harm secondary to CT scan radiation prompts the use of alternate imaging modalities when feasible. However, the American College of Obstetricians and Gynecologists (ACOG) imaging guidelines update in 2017 emphasize benefit of CT, to correctly and quickly diagnose acute appendicitis, may outweigh theoretical fetal risks [16]. Compression ultrasound (US) is often used to diagnose appendicitis due to high sensitivity and specificity. Diagnosis should be considered when a blind-ended, dilated to larger than 6 mm, and non-compressible tubular structure is visualized [3, 7, 17]. Should US be inconclusive, MRI may provide additional information. MRI findings diagnostic of acute appendicitis are appendix diameter >6 mm, wall thickness >2 mm, and presence of periappendiceal fat stranding [15, 17]. See previous chapter for further details of the use of radiography during pregnancy.

In non-pregnant patients with signs and symptoms of early appendicitis, there is a trend toward

intravenous antibiotics treatment and delaying operation until a more convenient time. This practice should be avoided in pregnant patients, as delay in treatment of acute appendicitis increases maternal morbidity and also increases risk to fetus should perforation occur. Incidence of appendix perforation is 66% when diagnosis is delayed over 24 hours. Fetal loss occurs 20–37% in perforated appendicitis, compared to 1.5–5% in non-perforated appendicitis [1, 7, 17].

Once the diagnosis of appendicitis is made, antibiotic administration should begin while planning for operation. Pregnancy limits antibiotic options to second-generation cephalosporins (cefuroxime), ampicillin, or metronidazole [18–20]. If an open appendectomy is performed, incision options include a muscle-splitting incision over the area of maximal tenderness or a transverse incision over the appendix (if preoperative imaging shows appendix location). For laparoscopic appendectomy, the use of an open Hasson technique avoids potential Veress needle injury to the uterus. Standard triangulation of port placement is used in the first trimester, with midline port superior to other two trocars. In the second and third trimester, ports should be clustered to the right side of the uterus [21]. Should diffuse peritonitis be encountered, copious irrigation and drain placement are indicated. Obstetricians should be notified immediately if purulent or fecal peritonitis is encountered, as there may be the need for cesarean section due to risk of fetal loss [7].

Gallbladder Disease Midepigastric pain, nausea, and vomiting are commonplace in pregnancy, and while they may be a result of pregnancy, these symptoms may be due to biliary disease. Cholelithiasis occurs in 12% pregnancies and is an incidental finding in 3.5–10% of pregnant patients. Biliary colic occurs in 0.5–1 per 1000 pregnancies [1, 2]. In pregnant patients, acute cholecystitis is the second most common non-obstetric surgical problem due to weight gain and hormonal changes facilitating sludge formation with an incidence of 31%. Estrogen increases bile lithogenicity, and progesterone impairs gallbladder emptying [1].

Manifestation of biliary symptoms is equivalent to non-pregnant patients with exception of less prevalence of a Murphy's sign. In pregnant patients, jaundice is less often due to choledocholithiasis (7%) but usually due to hepatitis (45%) or cholestasis (20%) [15]. Laboratory changes are consistent with non-pregnant patients with exception of alkaline phosphatase which doubles in pregnancy and amylase that transiently elevates. US should be used for diagnosis of biliary processes due to an accuracy of over 90% [3, 7].

Recurrent biliary colic is usually more severe than the initial episode and occurs in 92% of obstetric patients managed non-operatively in the first trimester, in 64% if presented in the second trimester, and 44% if presented in the third trimester. Half of obstetric patients with recurrent symptoms will require admission [1, 3]. Choledocholithiasis occurs in 0.1% pregnancies and requires intervention in 1:1200 pregnancies [22, 23]. Evaluation and work-up (labs, US to evaluate common bile duct, MRCP, or endoscopic US, if needed) in pregnant patients are equivalent to non-pregnant patients.

Cholangitis in pregnant patients needs prompt treatment with antibiotics, resuscitation, and ERCP if needed. Pharmacy and obstetrician consults may be beneficial to minimize fetal risk with antibiotic choice. Percutaneous transhepatic cholangiography with drainage is recommended if ERCP is not available [1]. If ERCP or intraoperative cholangiography is done, patient's lower abdomen should be shielded to decrease radiation exposure to fetus [3].

When compared to general patient populations, pregnant patients are significantly less likely to have an ERCP for acute pancreatitis, biliary stricture, abnormal liver enzymes, or jaundice [22]. However, in cases of obstructive jaundice, ERCP is thought safer than surgery [24]. The use of ERCP produces similar successful disease resolution in pregnant and non-pregnant patients. However, pregnant patients experience a significantly higher rate of post-ERCP pancreatitis (PEP), possibly due to decreased incidence of pancreatic stent placement; this rate of PEP is lower at tertiary care centers when compared to

community hospitals [22]. Post-ERCP laparoscopic cholecystectomy occurred in 0.2% of patients, and indication was the choledocholithiasis or dilated papillae [23].

Surgery in any trimester is indicated in pregnant patients with acute cholecystitis and gallstone pancreatitis. Surgery is also recommended for symptomatic cholelithiasis due to risk recurrence and risk of fetal loss as nonoperative management is associated with higher incidence spontaneous abortions, preterm labor, and preterm delivery [7]. Optimal timing of surgery is within the second trimester due to lowest risk of spontaneous abortion (5.6%), preterm labor (0%), and intra-abdominal domain as previously mentioned [25]. Intraoperative fetal monitoring can be accomplished with transvaginal US. Of note, the use of ursodeoxycholic acid may be considered for the management of bile duct debris [23].

Intestinal Obstruction Intestinal obstruction is the third most common cause of non-obstetric surgical problem and occurs in 1:4000 pregnancies. Similar to non-pregnant patients, etiology is primarily adhesions, intussusception, hernia, neoplasm, and appendicitis. Obstruction most often occurs in the second and third trimesters [15].

One major difference, in cause of obstruction in pregnancy, is that the rate of volvulus is significantly higher. Volvulus, most commonly involving theddds cecum, accounts for 25% of obstruction in pregnant patients, compared to 5% in non-pregnant patients [1]. This volvulus usually occurs when uterus size rapidly fluctuates (16–20 weeks when uterus becomes intra-abdominal, 32–36 weeks when fetus enters the pelvis, and 6 weeks postpartum). As in non-pregnant patients, cecal volvulus is primarily managed with surgery and sigmoid volvulus with colonoscopy and postpartum evaluation for definitive management.

The initial management of small bowel obstruction (SBO) in pregnant patients is similar to the general population and includes fluid resuscitation, bowel rest, and nasogastric decompression. However, in pregnant patients, liberal use of imaging and high index of suspicion should be emphasized. Serial plain abdominal X-rays can be diagnostic, and T2 MRI can identify site of bowel obstruction in 80% of cases. Historically, maternal mortality in SBO was 6–20% and fetal mortality was 20–50% [7, 17, 21]. In pregnant patients, the SBO mortality rate is 6.6–7.2%. This higher mortality rate in the obstetric population is presumed from a delay in the diagnosis with failure to discriminate symptoms of pregnancy from obstruction [26, 27]. With more aggressive incorporation of MRI and intervention, a recent study showed maternal mortality rates as low as 2% and fetal mortality 17% [28]. Obstetric patients failing to improve should prompt evaluation for laparotomy [29]. If surgery is indicated, standard operating decisions should be upheld, as with the non-pregnant population.

Pancreatitis Occurring in 1:1000–5000 of pregnancies, pancreatitis usually occurs in the late third trimester or early postpartum. Cholelithiasis increases risk of gallstone pancreatitis by 13–15% and accounts for 67–100% of pancreatitis [7, 22]. Definitive therapy should be pursued, as gallstone pancreatitis recurs up to 70% with conservative management and is associated with a maternal and fetal mortality of 15% and 10–60%, respectively [7, 18]. Presenting symptoms and laboratory results, with reliance on elevated lipase levels, are comparable to non-pregnant patients. The treatment remains largely identical to non-pregnant patients with consideration for ICU admission in those with signs of severe inflammation, resuscitation, bowel rest, electrolyte repletion, and pain control. A cholecystectomy should be doned during the same admission [1].

Diverticulitis Diverticulitis is rare in pregnancy, occurring in 1:6000 pregnancies, and evaluation is similar to appendicitis. Non-ionizing radiation imaging with MRI and US is preferred, but CT remains the imaging modality of choice for equivocal findings [15]. In cases of uncomplicated diverticulitis, antibiotic treatment regimen should include coverage of gram-negative and anaerobic bacteria. Antibiotic choice in pregnant

patients is controversial and may be discussed with obstetricians. In non-pregnant patients, diverticulitis is often treated with metronidazole and a fluoroquinolone (FQ). However, the use of FQ is controversial in pregnancy due to theoretical risk of spontaneous abortion or teratogenicity, and metronidazole has been associated with fetal facial anomalies secondary to placental transmission [18, 19]. When conservative management of diverticulitis fails, or in cases of complicated diverticulitis, an obstetric patient is managed as previously discussed in appendicitis section. Hemodynamic stability and known risks of peritonitis may prompt earlier surgical intervention with obstetricians readily available should cesarean section be needed.

Ruptured Ectopic Pregnancy The incidence of ruptured ectopic pregnancy (EP) is 1–2% but remains a main cause of maternal mortality in the first trimester, and thus, prompt diagnosis is important. Work-up should include serum human chorionic gonadotropin (ß-hCG) level and transvaginal US. A transvaginal US will demonstrate a gestational sac (GS) when ß-hCG levels are >2000 mIU/mL (sensitivity 69–99%, specificity 84–99.9%). Usually, US will show adnexal mass and pelvic free fluid. An MRI can further delineate diagnosis, showing a GS-like cystic structure, an adnexal or abdominal hematoma, tubal dilatation caused by hemosalpinx, and tubal wall enhancement [17].

Expectant medical management is possible if patient is hemodynamically stable, EP diagnosed on US, and ß-hCG is decreasing (with initial ß-hCG <1000 mIU/mL). Obstetricians should be consulted, if available. Initial high ß-hCG level (5000–10,000 mIU/mL) is associated with medical management failure rate of 14.3%. Intramuscular methotrexate, single dose (50 mg/m^2 BSA), can be offered if mild symptoms and ß-hCG <3000 mIU/mL. Serum ß-hCG levels should be rechecked on day 4 and 7; a failure of ß-hCG level to decline by 15% of baseline by day 7 should prompt additional dose (1 mg/kg). Up to four additional doses may be given (every other day with concurrent ß-hCG levels) or until ß-hCG declines by 15% [30]. Surgery, usually laparoscopic, is indicated for severe symptoms, hemodynamic instability, or high ß-hCG [17].

Rare Non-obstetric Abdominal Problems

Cesarean Section in a Hostile Abdomen Prior abdominal surgeries and resulting intra-abdominal adhesions increase risk of complications, need for multidisciplinary surgical team management, and operative times in cesarean sections (CS). In facilities that do not practice vaginal birth after a cesarean section (VBAC), reopening prior CS incision is common. Adhesion rates at second CS are 24.4–46.3%, third CS 42.8–75%, and after four or more CS 47.9–83%. Increased adhesion scores are an independent predictor of maternal and fetal mortality, increasing with each subsequent CS [31].

In elective CS, transabdominal US is occasionally used to document respiratory variation or "sliding sign" of the uterus, implying a low risk of adhesions [32]. Operative technique should include a low midline laparotomy incision, if possible, or most reasonable access away from prior surgical scars. Adhesions encountered at a prior CS incision may include the uterus, omentum, and bowel due to postpartum uterus size changes during healing. Prior incision closure method may affect the degree of adhesions. If only parietal peritoneum was closed, most adhesions are adnexal, between the uterus and bladder and occasionally between the uterus and abdominal wall. If both visceral and parietal peritoneum are closed, adhesions are less common and, when present, located between the uterus and bladder [33].

As in any repeat abdominal exploration, entry should be careful and technique should be meticulous. If any adhesions are lysed, the bowel should be carefully run prior to closing. Incision should be closed in layers and include parietal and visceral peritoneum. Postoperative care should include serial clinical assessments (serial abdominal exams, vital signs, laboratory results)

by general surgical team to monitor for potentially missed enterotomies.

Ruptured Vascular Aneurysms Visceral artery aneurysms (AA) occur in ≤0.1% of the general population and are believed to form due to the hyperdynamic condition of pregnancy. Most common site for visceral AA is the splenic artery (60%), followed by hepatic (20–50%), superior mesenteric (6%), and celiac artery (4%). Concomitant visceral AAs occur in 3.3% of patients and non-visceral AAs occur in 14.3% [34–36]. Other vascular aneurysms are rare and only discussed in case reports.

Splenic AAs are usually incidental findings, often found in middle-aged adults, and have an incidence of 0.16–10.4% in the non-pregnant population [36, 37]. Pregnancy is historically considered a leading risk factor for splenic AA as they are commonly found in multiparous women, forming due to increased portal vein blood flow and hormonal changes to arterial walls [15]. Aneurysm rupture usually occurs in when the diameter is >2 cm, and at that size, risk of aneurysm rupture in a pregnant patient is 25–50% [15, 35, 37].

Rupture of splenic AA is believed to commonly occur in the third trimester and is associated with maternal and fetal mortality rate of 75% and 95%, respectively. However, ruptured splenic AA is very rare. A large retrospective review failed to identify a ruptured splenic AA in any pregnant patient, and multiple other studies concur, noting the prevalence of a ruptured splenic AA as 0–0.004%. Due to this low prevalence, routine screening in pregnant patients is usually not performed [37]. If incidentally discovered in a pregnant patient, splenic AAs may be further imaged with US. Elective repair is ideally performed prior to pregnancy, with either an open or endovascular approach, and is indicated for asymptomatic splenic AAs >2 cm or any symptomatic visceral AA, regardless of size [38].

As ruptured splenic AAs are rare in pregnancy, these patients should be managed as the general patient population, beginning with resuscitation. Splenectomy has traditionally been the procedure of choice, but interventional radiology (IR) and splenic preservation are also implemented. In the general population, IR embolization of ruptured splenic AAs has successfully coiled the aneurysm, and several patients survived [36, 37]. Spleen preservation may be possible, especially in saccular splenic AAs located in the proximal or mid-artery, with resection of aneurysm or reconstruction with end-to-end anastomosis. Less commonly reported interventions are partial aneurysmectomy, aneurysmorrhaphy, or endovascular stent placements [36, 38].

Hepatic Masses While often discovered incidentally, hepatic masses are also found in obstetric patients during work-up of persistent acute right upper abdominal or epigastric pain. Discovery of a liver mass in an obstetric patient should raise concern for the potential rupture or hemorrhage of the mass and prompt further imaging. Ultrasound is preferred, but MRI is useful to further distinguish lesions [15]. While able to provide additional information regarding liver mass diagnosis and resectability, angiography is usually deferred during pregnancy due to radiation exposure, and percutaneous liver biopsy is avoided due to concern for hemorrhage [39]. Due to potential high maternal and fetal mortality in ruptured liver masses, resection is considered on an individual basis.

Focal nodular hyperplasia (FNH) occurs in 3% of adults in the general population, and a majority (80–90%) are females in reproductive years. Imaging with MRI demonstrates a central scar. Hormone sensitivity of FNH is controversial, but FNHs are commonly thought to be unaffected by pregnancy. These lesions are usually asymptomatic with rare case reports of transient peripartum growth of FNH but uneventful pregnancy and delivery [40–42]. Thus, conservative management of FNH in pregnancy is preferred unless the lesion is symptomatic or larger than 8 cm, and then resection is considered [43].

Hepatic hemangiomas are the most common benign liver lesion in general population (2–20%). Pregnancy is not considered to pose higher risk of hemangiomas, hemorrhage, or rup-

ture, when compared to the non-pregnant patient. On US, hemangiomas are well circumscribed and will appear hyperechoic compared to the surrounding normal liver. MRI shows peripheral nodular enhancement. Observation is indicated for hemangiomas smaller than 5 cm [42]. Some lesions may be amenable to angioembolization, but generally, surgical resection is indicated for increasing symptoms, rapid lesion growth, lesions larger than 10 cm, thrombocytopenia, rupture with intraperitoneal hemorrhage, and malignant appearance [39, 43].

Hepatic adenomas are rare lesions with estimated occurrence in the general public of 30–40 per million patients. Usually occurring in young females with long-term oral contraceptive use, hepatic adenomas are highly vascular. US will show a nondescript mass while MRI will show a hypervascular lesion with peripheral vessels. In non-pregnant patients, hepatic adenomas should be electively resected when >5 cm or future fertility is desired, due to concern for hemorrhage that could potentially be exacerbated during pregnancy [42, 44]. In pregnancy, the presence of adenoma confers maternal mortality risk of 44% and fetal mortality risk of 38%. Rare cases of spontaneous rupture caused by adenoma in pregnancy have been described [39]. If the adenoma size, patient hemodynamics, and hemoglobin/hematocrit are stable, expectant monitoring should occur in an obstetric patient. In cases of adenoma growth or bleeding, intervention is indicated and preferred during the second trimester. Peripheral liver lesions can be resected in the first or second trimester with either laparoscopic or open techniques. Radiofrequency ablation and transcatheter arterial embolization can be used for treatment or to decrease lesion size and hemorrhage, if in amenable location [43, 45].

Hepatic Rupture In addition to the hepatic masses previously discussed that are a risk for rupture in the pregnant patient, intrahepatic cholestasis of pregnancy, acute fatty liver of pregnancy (AFLP), or HELLP syndrome (severe eclampsia and preeclampsia with hemolysis, elevated liver enzymes, and low platelet levels) also pose risk of spontaneous liver rupture. Maternal and fetal mortality is 40–60% due to hemorrhagic shock, metabolic derangements, and coagulopathy. Rupture usually occurs in the late third trimester, and patients present with hypertension, quickly progressing to shock. Obstetrician consultation must occur to assess need of pregnancy termination. If rupture occurs, damage control procedures should be performed expeditiously for hemorrhage control of the liver including packing, Pringle maneuver, and ligation of bleeding vessels [7].

Conclusion

While acute care surgeons are not specifically trained in obstetrics, they are often readily available and should possess the confidence, sound clinical judgment, and safe surgical skills for general surgery diseases that can be carefully adapted to obstetric patients. As in the general population, prompt recognition of surgical emergencies and thoughtful planning of non-emergent surgeries cannot be overemphasized. Surgeons should have a low threshold for consulting obstetricians especially if there is gross purulence in the abdomen or if there is a bleeding catastrophe because these instances increase mortality in both the mother and the fetus. In not deviating from ingrained, prudent surgical practices, acute care surgeons may safely treat pregnant patients with common non-obstetric surgical complaints.

References

1. Skubic JJ, Salim A. Emergency general surgery in pregnancy. Trauma Surg Acute Care Open. 2017;2(1):e000125.
2. Sachs A, et al. Risk factors and risk stratification for adverse obstetrical outcomes after appendectomy or cholecystectomy during pregnancy. JAMA Surg. 2017;152(5):436–41.
3. Pearl JP, Price R, Tonkin AE, Richardson WS, Stefanidis D. SAGES guidelines for the use of laparoscopy during pregnancy. 2017 May 2017 [cited 2018 26 Jul]; May 2017:[SAGES Guidelines May 2017]. Available from: sages.org/publications/guidelines/guidelines-for-diagnosis-treatment-and-use-of-laparoscopy-for-surgical-problems-during-pregnancy.

4. Ninke T, et al. Anesthesia and pain management during pregnancyAnaesthesist. 2015;64(5):347–56.
5. Lamvu G, Feranec J, Blanton E. Perioperative pain management: an update for obstetrician-gynecologists. Am J Obstet Gynecol. 2018;218(2):193–9.
6. Coluzzi F, et al. Chronic pain management in pregnancy and lactation. Minerva Anestesiol. 2014;80(2):211–24.
7. Augustin G, Majerovic M. Non-obstetrical acute abdomen during pregnancy. Eur J Obstet Gynecol Reprod Biol. 2007;131(1):4–12.
8. Wilasrusmee C, et al. Systematic review and meta-analysis of safety of laparoscopic versus open appendicectomy for suspected appendicitis in pregnancy. Br J Surg. 2012;99(11):1470–8.
9. Fatum M, Rojansky N. Laparoscopic surgery during pregnancy. Obstet Gynecol Surv. 2001;56(1):50–9.
10. McGory ML, et al. Negative appendectomy in pregnant women is associated with a substantial risk of fetal loss. J Am Coll Surg. 2007;205(4):534–40.
11. Weiner E, et al. Laparoscopic surgery performed in advanced pregnancy compared to early pregnancy. Arch Gynecol Obstet. 2015;292(5):1063–8.
12. Walker HG, et al. Laparoscopic appendicectomy in pregnancy: a systematic review of the published evidence. Int J Surg. 2014;12(11):1235–41.
13. Humphries A, et al. The effect of supine positioning on maternal hemodynamics during late pregnancy. J Matern Fetal Neonatal Med. 2018:1–8.
14. Lee AJ, Landau R. Aortocaval compression syndrome: time to revisit certain dogmas. Anesth Analg. 2017;125(6):1975–85.
15. Evans SR, et al. Surgery in pregnancy. Curr Probl Surg. 2012;49(6):333–88.
16. Practice, m.C.o.O.a.G.C.o.O. Guidelines for diagnostic imaging during pregnancy and lactation. [cited 2018 29 Aug 2018]; Number 723, October 2017: Available from: https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Guidelines-for-Diagnostic-Imaging-During-Pregnancy-and-Lactation
17. Masselli G, et al. Evaluating the acute abdomen in the pregnant patient. Radiol Clin N Am. 2015;53(6):1309–25.
18. Mikami DJ, Henry JC, Ellison EC. Surgery in the pregnant patient. In: Sabiston textbook of surgery. Philadelphia: Elsevier; 2017. p. 2053–67.
19. Longo SA, et al. Gastrointestinal conditions during pregnancy. Clin Colon Rectal Surg. 2010;23(2):80–9.
20. Koss CA, Baras DC, Lane SD, Aubry R, Marcus M, Markowitz LE, Koumans EH. Investigation of metronidazole use during pregnancy and adverse birth outcomes. Antimicrob Agents Chemother. 2012;56(9):4800–5. PMID: 22751543.
21. Miloudi N, et al. Acute appendicitis in pregnancy: specific features of diagnosis and treatment. J Visc Surg. 2012;149(4):e275–9.
22. Inamdar S, et al. Pregnancy is a risk factor for pancreatitis after endoscopic retrograde cholangiopancreatography in a national cohort study. Clin Gastroenterol Hepatol. 2016;14(1):107–14.
23. Tham T. Safety of ERCP during pregnancy. Am J Gastroenterol. 2003;98(2):308–11.
24. Friedel D, et al. Gastrointestinal endoscopy in the pregnant woman. World J Gastrointest Endosc. 2014;6(5):156–67.
25. Boregowda G, Shehata HA. Gastrointestinal and liver disease in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2013;27(6):835–53.
26. Meier RP, et al. Clinical outcome in acute small bowel obstruction after surgical or conservative management. World J Surg. 2014;38(12):3082–8.
27. Peacock O, Bassett M, Kuryba A, Walker K, Davies E, Anderson I, Vohra RS, National Emergency Laparotomy Audit (NELA) Project Team. Thirty-day mortality in patients undergoing laparotomy for small bowel obstruction. Br J Surg. 2018;105(8):1006–13.
28. Webster PJ, et al. Small bowel obstruction in pregnancy is a complex surgical problem with a high risk of fetal loss. Ann R Coll Surg Engl. 2015;97(5):339–44.
29. Zachariah SK, Fenn MG. Acute intestinal obstruction complicating pregnancy: diagnosis and surgical management. BMJ Case Rep. 2014;2014:pii: bcr2013203235.
30. Ectopic pregnancy. In Cunningham F, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS, editors. Williams obstetrics. New York: McGraw-Hill; 2013.
31. Arlier S, et al. Incidence of adhesions and maternal and neonatal morbidity after repeat cesarean section. Arch Gynecol Obstet. 2017;295(2):303–11.
32. Baron J, et al. Sonographic evaluation of intra-abdominal adhesions during the third trimester of pregnancy: a novel technique in women undergoing repeated cesarean section. Ultrasound Obstet Gynecol. 2018;52:662.
33. Seyam E, et al. Laparoscopic management of adhesions developed after peritoneal nonclosure in primary cesarean section delivery. Obstet Gynecol Int. 2018;2018:6901764.
34. Lee W-J, Kao Y. Acute abdomen during pregnancy. Tzu Chi Med J. 2013;25(4):256–7.
35. Juntermanns B, et al. Visceral artery aneurysms. Gefasschirurgie. 2018;23(Suppl 1):19–22.
36. van Rijn MJ, et al. Visceral aneurysms: old paradigms, new insights? Best Pract Res Clin Gastroenterol. 2017;31(1):97–104.
37. Nanez L, et al. Ruptured splenic artery aneurysms are exceedingly rare in pregnant women. J Vasc Surg. 2014;60(6):1520–3.
38. Pulli R, et al. Surgical treatment of visceral artery aneurysms: a 25-year experience. J Vasc Surg. 2008;48(2):334–42.

39. Athanassiou AM, Craigo SD. Liver masses in pregnancy. Semin Perinatol. 1998;22(2):166–77.
40. Kim MJ, et al. A case of focal nodular hyperplasia with growth progression during pregnancy. Clin Mol Hepatol. 2014;20(4):392–7.
41. Roncalli M, Sciarra A, Tommaso LD. Benign hepatocellular nodules of healthy liver: focal nodular hyperplasia and hepatocellular adenoma. Clin Mol Hepatol. 2016;22(2):199–211.
42. Milburn J, et al. Diagnosis and management of liver masses in pregnancy. Obstet Gynaecol. 2016;18(1):43–51.
43. Fodor M, et al. Indications for liver surgery in benign tumours. Eur Surg. 2018;50(3):125–31.
44. Klompenhouwer AJ, et al. Management and outcome of hepatocellular adenoma with massive bleeding at presentation. World J Gastroenterol. 2017;23(25):4579–86.
45. Noels JE, et al. Management of hepatocellular adenoma during pregnancy. J Hepatol. 2011;54(3):553–8.

Part XIV

Ruptured Liver Tumors

39 Management of Ruptured Hepatic Tumors

Jillian Piaggione and Richard Smith

Introduction

Liver tumors are becoming more prevalent in developed countries due to better and increased imaging, widespread medication use, and rise in cirrhosis secondary to hepatitis C and nonalcoholic steatosis. Identification of a benign or malignant tumor and an understanding of its unique risks will guide treatment options. Spontaneous hepatic tumor rupture is rare, with an overall prevalence of 1% in Western countries [1]. The presentation of hepatic tumor rupture ranges from the undramatic with nonspecific symptoms to the spectacular, life-threatening with hemoperitoneum and shock [2]. While there is some risk of rupture with any liver lesion, the most likely benign and malignant liver tumors to spontaneously rupture and bleed are hepatic adenomas (HA) and hepatocellular carcinoma (HCC), respectively.

Benign Tumors

Hepatic hemangiomas are common, rarely symptomatic, and are generally associated with an excellent prognosis with no malignant potential. They have a female predominance (3:1) [3]. Hepatic hemangiomas are congenital vascular malformations. They have a prevalence in autopsy studies ranging between 3% and 20% [4]. They are categorized as capillary hemangiomas (usually peripheral and small) or cavernous hemangiomas (larger). Giant hepatic hemangiomas (GHHs) are cavernous hemangiomas greater than 4 cm in diameter. GHHs are more likely to be symptomatic [5]. Clinical manifestations include rupture, intramural bleeding, Kasabach-Merritt syndrome (consumptive coagulopathy and congestive heart failure), and compression of nearby organs or vessels. Rupture is thought to be a rare event occurring in 1–4% of cases [6]. Clinical manifestations of rupture most commonly consist of sudden abdominal pain and anemia secondary to a hemoperitoneum. Disseminated intravascular coagulopathy has been described in cases of rupture [7, 8]. Hypovolemic shock occurs in about one third of cases [9]. The global mortality of rupture is approximately 35%, and it seems to be related to the size of the lesions. The rate of rupture seems to be associated with the increasing size of the hemangioma, particularly for superficial lesions [6, 9, 10].

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Data on outcomes is limited to case reports and small series, but there is a described mortality rate ranging from 60% to 75% for spontaneous rupture with an operative mortality rate from this complication of 36.4% [11, 12]. Surgical hemostatic methods such as packing, hepatic artery ligation, and hepatic suture have been used to contain the bleeding in cases of ruptured hemangioma [9]. Surgical resection and enucleation are considered the treatments of choice. The size and location of a lesion are decisive when the surgeon has to determine whether to perform either a formal segmental resection or an enucleation [6]. Recent studies have emphasized the use of transcatheter hepatic arterial embolization (TAE) in the effective treatment of larger symptomatic hemangiomas, for those at risk of bleeding, and before exploratory laparotomy to treat patients with a hemorrhagic hemangioma [6, 11–13]. The data is not controlled, but TAE appears to have significantly improved outcomes with ruptured hemangiomas more recently [6, 13].

Hepatic adenoma Hepatocellular adenoma (HCA) is a rare benign liver tumor that occurs most frequently on women of reproductive age. There is an association with the estrogen-containing oral contraceptive pills (OCPs) [14–16]. Hepatic adenoma has an estimated annual incidence of 30–40 per million among users of OCPs for greater than 2 years compared to 1 per million in nonusers or women with less than 2 years of OCP use [14]. Hepatocellular adenoma (HCA) carries a risk of malignant transformation and spontaneous bleeding [16–20]. HCAs are highly vascular tumors, and hemorrhage is a relatively common complication, occurring in approximately 25% of the patients with HCA [17]. Bleeding has been associated with OCP use, tumor size of >5 cm, and exophytic growth of the tumor [17, 18]. Hemorrhage can be classified as intratumoral (grade I), intrahepatic (grade II), or intraperitoneal (grade III) hemorrhage [18]. Fortunately, most hemorrhages are intratumoral. However, rupture of the HCA can occur, resulting in intraparenchymal, subcapsular, or free rupture and hemoperitoneum [15].

HCA can also be subtyped based on immunohistochemistry or typical MRI features. The subtypes are inflammatory HCA (40–50%, IHCA), HNF1A-mutated HCA (30–40%, H-HCA), β-catenin-activated HCA (10–15% b-HCA), and unclassified HCA (10–25%, UHCA) [21–23]. Some studies have shown that the risk for hemorrhage is the greatest for the inflammatory subtype [15, 18]. However, the increased risk with the inflammatory subtype is not a universal finding [24, 25]. β-catenin (exon 3)-mutated HCA (b-HCA) tumors carry a higher risk of malignant transformation, independent of tumor size [24].

The most common recommendation for management for non-ruptured tumors sized <5 cm is to follow with serial imaging [20]. Discontinuation of oral contraceptives has been shown in some studies to lead to regression of tumor size or even resolution of smaller HAs [20, 26–29]. Some authors advocate a trial of stopping OCPs even for lesions larger than 5 cm and continued nonoperative management for those that shrink to less than 5 cm within 6 months [15, 18, 30, 31]. Others have argued for resection of all HAs greater than 4 cm in all patients fit to undergo operation [32]. Bieze et al. examined 45 patients with HCAs prospectively and found that bleeding was associated with lesions >35 mm and exophytic lesions [33]. Denve et al. examined a prospective surgical database from 5 institutions that found 124 patients and showed that tumor size >7 cm and the use of hormones within the last 6 months were significantly associated with bleeding [32]. This study also identified a total of five patients (4%) that had evidence of hepatocellular carcinoma (HCC) within an adenoma on final pathology, and the smallest tumor with histologic evidence of malignancy was 8 cm in diameter [32].

The standard treatment for ruptured HA had been an emergency laparotomy with gauze packing or partial liver resection to achieve adequate hemostasis. However, there was significant morbidity and a mortality rate of 5–10% with this approach [15, 30, 34]. This compares to a <1% mortality with elective resection of HA [35]. The development and widespread availability of selective arterial embolization (SAE) in the last decade have offered a less invasive method for controlling bleeding and potentially avoiding

resection altogether [15, 20, 30, 36]. In multiple studies TAE has been shown to lead to hemodynamic stabilization in selected patients with acceptable morbidity and often a decrease in size of the HA [37–39, 92]. Karkar et al. treated 100 HCAs in 52 patients with resection, TAE, or observation. Thirty-seven HAs were treated with TAE. Twenty percent of the embolizations were done for hemorrhage. Of thirty-seven HAs embolized, three persistent lesions required second interventions. All other lesions disappeared (5 adenomas), decreased in size (22 adenomas), or remained stable (7 adenomas) after a single embolization. This was in comparison to 2 recurrences in the 43 patients with HA who underwent resection [35]. Similarly, Dheodar et al. performed embolizations in eight patients with HAs of which seven out of eight were for bleeding or high risk of bleeding. Regression of the HAs was noted in all embolized HCAs following treatment [40]. Erdogan et al. described four patients with ruptured HAs treated with TAE. Embolization was successful in all patients without complication. The HA regressed in two of these patients [41].

The pregnant patient with hepatic adenoma presents unique challenges. First, the rise in estrogen hormones can induce adenoma growth, which then increases the risk for spontaneous rupture and hemorrhage. Second, the stakes are higher for a ruptured HA in the pregnant patient as the maternal and fetal mortality rates have been reported as 44% and 38%, respectively [42]. Third, while the symptoms of a growing and/or bleeding HA may mimic other pathologies such as gallbladder disease, appendicitis, biliary pancreatitis, or PE, in the pregnant patient, obstetric-specific causes of abdominal pain, such as preeclampsia and hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, are also added to the differential, possibly adding to diagnostic delay [43]. Lastly, pregnancy can limit diagnostic and treatment options, given the increased risk of radiation exposure to the fetus, especially before 26 weeks. Thus, the use of arterial embolization in the pregnant patient should be limited to emergency situations where benefits outweigh the risks of radiation exposure and other treatment options unfavorable [43]. In the past, some have advocated to recommend that women with HA avoid pregnancy, due to the potential for rupture and the high associated maternal and fetal mortality. However, given the limited available literature and data on management of HA during pregnancy, it is difficult to determine the precise risk factors for complications, and therefore there are no standard guidelines. A 2004 retrospective case review study recommended an aggressive approach toward HA resection, especially when >5 cm, due to the high mortality rate associated with rupture. Admittedly in the same study, the smallest tumor that ruptured was 6.5 cm [42]. A more recent 2011 case series of 12 women and 17 pregnancies showed no ruptures even with large tumors. They and other authors have advocated a more conservative approach, recommending close monitoring, especially when <5 cm, and conclude that it is safe to allow pregnancy [43].

Treatment of HCA during pregnancy may be indicated when the lesion shows signs of growth or bleeding. The choice of follow-up, surgery, radiofrequency ablation (RFA), or TAE for the treatment of HCAs in pregnancy is often a matter of debate and dependent on the clinical condition of the patient. Surgery of lesions located at the periphery of the liver can be performed safely within the first or second trimester. Consideration for a minimally invasive approach should be given [44]. Radiation exposure during RFA or TAE should be weighed carefully during the early phase of pregnancy. Whenever an HCA is discovered during pregnancy, the second trimester is the optimal moment for invasive treatment, if indicated, as anesthesia is well tolerated at this stage and the effects of the fetus on operative exposure are still minimal [31].

With a ruptured HA during pregnancy, an initial conservative management and hemodynamic stabilization are justified. In case of active bleeding with persistent hemodynamic instability or hemoperitoneum, intervention may be considered. TAE can be a solution for unstable patients and patients with persistent bleeding. As the risk of rebleeding is very low after TAE and cessation of OCP and most HCAs regress spontaneously,

secondary interventions, such as tumor resection, SAE, or RFA, can often be avoided in patients with HCA >5 cm after follow-up.

FNH is the second most common benign hepatic tumor after hemangioma. FNHs are usually incidentally discovered, with only 20% of patients reporting pain and symptoms secondary to a liver mass [45]. Due to the fact that they are not known to be aggressive or display malignant potential, there is generally no need for surveillance. However, there are several case reports of hemorrhage from ruptured FNH. Nine out of the ten reported cases were in women, there was one fatality in a patient in late pregnancy, and maximum tumor diameter ranged from 1 to 10 cm, with a median of 7 cm [45–54]. Due to limited data and experience, there are no guidelines for ruptured FNH. However, TAE followed by consideration for delayed resection is a reasonable approach based on other pathology results.

Malignant Tumors

The most common malignant liver tumors include HCC; fibrolamellar HCC, a unique variant of HCC that usually develops in younger patients without cirrhosis; intrahepatic cholangiocarcinoma, which is frequently associated with viral hepatitis and cirrhosis; and metastatic disease, most commonly, colorectal metastasis.

Hepatocellular Carcinoma

The incidence of ruptured HCC varies significantly by region. It represents less than 3% of HCC cases in the Western hemisphere but up to 26% of cases in the Eastern hemisphere [2, 55, 56]. A sudden onset of abdominal pain is the most common presenting symptom and present in 66–100% of cases [2, 57–61]. The rupture of HCC is associated with shock in 33–90% of patients [2, 57–60]. Patient factors associated with rupture include age, systemic hypertension, and greater degree of liver dysfunction. [59, 62–64] Tumor factors associated with rupture of an HCC are size (>5 cm) and peripheral location of tumors [59, 62–65]. Zhu et al. compared 200 patients with ruptured HCCs to a similarly matched group of 202 patients with non-ruptured HCCs and found, on multivariate logistic regression analysis, systemic hypertension, liver cirrhosis, tumor size >5 cm, tumor protrusion from the liver surface, vascular thrombus, and extrahepatic invasion were predictive for spontaneous rupture of HCC [59].

The mechanism of spontaneous rupture is unknown but there are several theories. One hypothesis for the mechanism of rupture of HCC suggests that rupture occurs when a combination of tumor occlusion of venous outflow and rapid expansion of the tumor secondary to bleeding from within its substance leads a high intratumoral pressure resulting in splitting of the overlying hepatic parenchyma and rupture [2, 59, 65–67]. Zhu et al. suggested that spontaneous rupture of HCC may be related directly to the vasculature in the tumor. There is degeneration of elastin and degradation of type IV collagen, rendering the blood vessels stiff and weak and causing them to fracture more easily when the vascular wall tension increases from hypertension or minor trauma [59, 68]. A long history of hypertension (which is associated with rupture) can lead to injury of the blood vessels, making them more friable. In addition, patients with liver cirrhosis always have underlying coagulopathy. The combination can lead to hemorrhage within the tumor and then initiate tumor rupture [66]. This may occur in small tumors in confined anatomic spaces such as the sharp angles of segments 2, 3, and 6 leading to rupture [66].

The treatment of ruptured hepatocellular carcinoma has the primary goal of achieving hemostasis, but in contrast to benign entities, the treatment of ruptured HCC must also consider the stage of the malignancy and the preservation of functional liver. Initial treatment options to control bleeding include resection, transarterial bland embolization (TAE)/chemoembolization (TACE), and conservative or noninterventional management. Surgical hemostatic procedures can include plication, suturing, packing, hepatic artery ligation, and resection. Conservative treatment corresponded to correction of coagulopathy,

continuing resuscitation with blood products, support of hemodynamics, and close monitoring. Unfortunately, studies looking at the success of these varied modalities and the populations for which they are deployed are varied and with mixed results. Additionally, the long-term oncologic outcomes also show heterogeneity between studies, and optimal timing and candidate selection for definitive treatment remain unclear.

Overall survival for patients with ruptured HCC is poor. Moris et al. recently performed a comprehensive systematic review of available literature on ruptured HCC and examined 35 studies and found an overall aggregate inhospital, 1-, and 6-month survival of 57%, 66.9%, and 53%, respectively [63]. Conservative or noninterventional therapy itself has been shown to have particularly poor outcome with 1-year survival of 0–1% [63, 69]. This should be reserved for patients with a prohibitively poor prognosis [63].

Historically, open surgical control was used for treatment of ruptured hepatocellular carcinoma. Studies show a fairly high success rate in controlling bleeding at 70–95% but at a high mortality rate of 34–75% (Table 39.1). Suture plication is generally limited by the friable tumor tissue and applicable only when the bleeding site is small and superficial [71]. Packing of a bleeding tumor can be effective in tamponade of the bleeding. It is most effective where there is an opposing surface such as the diaphragm. Based on data from packing of traumatic injury of the liver, the packing should not be left in more than 72 hours or risk sepsis [72, 73]. Rebleeding may occur with removal of the packing [74]. Just as in the trauma patient, perihepatic packing role is in the hemodynamically unstable patients who require a damage control laparotomy for rapid control so that further resuscitation and correction of acidosis, hypothermia, and coagulopathy can be achieved. Hepatic artery ligation (HAL) takes advantage of the livers' dual blood supply from the hepatic artery and the portal vein. The portal vein supplies 70% of the total hepatic perfusion in the normal liver. In contrast, the HCC derives almost all of its blood supply from the hepatic artery. In theory this allows control of the hemorrhage from the tumor while maintaining the majority of flow to the remaining liver in that distribution. Indeed, HAL has a success rate of 69.1–100% [57, 65, 70]. In theory the more selective the HAL, the lower the risk of postprocedure liver failure, but there is some evidence to suggest a higher rebleed rate when SHAL is compared to HAL [65]. Being more selective also allows for future treatment of the HCC with resection or embolization.

Primary resection of the ruptured HCC has the advantage of controlling the bleeding and offering the only potentially curable option for the malignancy. However, liver resection for control of bleeding has generally had poor outcomes [33, 65, 75]. The acute setting and clinical condition of the patient also make accurate staging and assessment of liver function to identify appropriate candidates for resectional treatment [65]. Despite these limitations, some authors have shown success in treating patients with a ruptured HCC in a one-stage fashion. Vergara et al. looked at six patients treated with a one-stage

Table 39.1 Results of open surgical control of bleeding

Source	Patients	Methods	Success rate	Rebleed rate	Liver Failure rate	Mortality rate
Chearanai et al. [70]	37	Packing, plication, HAL, HR	70.30%			62.20%
Chen et al. [56]	27	Packing, suturing, HAL, HR				28%
Lai et al. [60]	56	Plication, CHAL, SHAL, HR	69.60%	30.40%	28.50%	75%
Xu and Yan [33]	19	Packing, HAL, HR	94.70%	5.30%	15.80%	47%
Liu et al. [2]	35	Plication, CHAL, SHAL, HR, packing	82.90%			34%
Ong et al. [57]	42	Resection, HAL, packing, suturing				54%

hepatectomy for ruptured HCC with a 16.5% inhospital mortality and a 33% 5-year overall survival [55]. Hai et al. looked at 36 patients, the majority of which were CTP class A, all of which were hemodynamically stable and with peripheral lesions. Postoperative mortality rate was 5.8% (2/36). The estimated 1-, 3-, and 5- year survivals for patients who underwent liver resection were 88%, 54%, and 51% respectively [76]. It should be recognized that these are highly selected patients in whom these results were achieved, and one-stage emergency liver resection should be reserved for patients with a small and easily accessible tumor and a normally functioning liver.

TAE has become the first-line treatment in many centers for ruptured HCC [2, 58, 64]. TAE can be considered in all patients with relatively well-preserved liver function and without complete portal vein thrombosis. Partial portal vein thromboses can be a relative contraindication but have been used successfully in a small number of partial occlusions [65]. TAE of HCC may still be safe even in the setting of portal vein occlusion if collateral circulation is present and hepatic reserve is sufficient. This requires precise identification of the site of bleeding, allowing TAE to be as selective as possible [61]. Computed tomography prior to TAE is important because it can identify patency of the portal vein and localize the tumor prior to angiogram as extravasation of contrast from the tumor is only seen in 13.2–35.7% of patients [38, 77, 78]. Kang et al. in one of the largest series on TAE for ruptured HCC found that that the site of active contrast leakage was far more readily recognized on CT scans than on hepatic arteriogram [61]. Transarterial embolization for hemostasis has a high success rate of 53–100% [2, 38, 61, 77, 79, 80]. The major life-threatening complication is liver failure (11.8–33.3%). [2, 38, 77, 79–82] Retrospective studies showed that TAE appears to have very poor outcomes with significantly elevated bilirubin (>2.7 md/dL) [38, 61, 77, 80, 82]. TAE can be used as a temporary/bridging measure for hemostasis in patients with resectable ruptured HCCs but with equivocal clinical and laboratory parameters for hepatectomy or questionable expected post-hepatectomy liver function [69]. Another indication is resectable ruptured HCCs where a large ruptured tumor is walled off by a hematoma and/or adhesion and dissection during resection risks re-rupture and significant hemorrhage. TAE (even if spontaneous hemostasis is achieved) might mitigate some of the danger of the subsequent resection [64].

Patients with ruptured HCC who undergo resection for cure generally have worse long-term survival when compared to patients without rupture [2, 59, 62]. Despite the overall poorer survival for ruptured HCC, prolonged survival has been observed in selected patients with one-stage and two-stage curative hepatic resection [2] (Table 39.2).

Ruptured HCC is defined by the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) as a T4 lesion and is staged similar to tumors with vascular or bile duct invasion [85]. Ruptured HCC is associated with larger-sized tumors, higher incidence of vascular invasion, vascular thrombus, and extrahepatic invasion than non-

Table 39.2 Results of surgery with intent to cure

Study	Patients	Median time	Median overall survival (OS)	1-year OS	3-year OS	5-year OS
Liu et al. [2]	33	16.5 days	25.7 months			
Zhu et al. [67]	105	15 days	12 months	57.10%	19%	7.60%
Li et al. [66]	89		12 months	66%	23.40%	10.10%
Chen et al. [56]	23			60%	40.50%	26.50%
Yeh et al. [83]	60			54.20%	35%	21.20%
Tanaka et al. [84]	58	40 days	40 months		48%	37%
Yang et al. [39]	143			66.20%	25.10%	16.80%
Chan et al. [64]	84			66%	37%	22.30%
Zhong [69]	106			59.40%		

ruptured HCC [39, 59, 64]. These factors are the same factors that lead to worse survival in non-ruptured HCC. Aoki et al. in a review of 1106 ruptured HCCs found that although rupture itself had an additional negative impact on patient survival, the impact was equivalent to an additional 0.5–1.5 stages added to the baseline TNM stage. This impact had a greater impact in cases that otherwise would have been staged low [62]. Some studies that used propensity score analysis to account for confounding variables reported that rupture itself had no impact in overall survival (OS) [64, 84]. This data would suggest that assigning a T4 stage to all ruptured HCCs risks overstaging some patients and not accurately reflect prognosis [63].

Management of spontaneous rupture of HCC remains a challenge, with an overall mortality rate in excess of 40%. The treatment of ruptured HCC should first establish a hemodynamically stable patient. If the patient remains hemodynamically stable, conservative management with resuscitation and correction of coagulation defects should continue. When the patient is not hemodynamically stable or bleeding continues, intervention should be offered. This intervention should take into account the patient's clinical condition, HCC stage, and location of the HCC. The primary concern of the intervention is to stop the bleeding and preserve as much liver as possible. One-stage resection for a ruptured HCC is possible but should probably be limited to patients with relative hemodynamic stability, preserved liver, and small peripheral tumors. For all other patients, control of the bleeding should be the major concern. This can be very successfully accomplished by TAE. One of the main complications of TAE in ruptured HCC has been liver failure so this should be as selective as possible. Patients with initial control of bleeding can be evaluated for extent of disease, liver function, and suitability for hepatectomy to be performed on a semi-elective basis once physiologic condition has completely normalized. Outcome has historically been worse for ruptured HCC, but much of this effect may be the tumor characteristics and not the rupture itself, and so long-term survival with resection is possible.

Conclusion

A ruptured liver tumor is a rare, but potentially spectacular event with potential for significant mortality. The management must consider the underlying etiology, condition of the patient, and outcomes for the various modalities available for control of hemostasis and definitive management. Transarterial embolization offers a minimally invasive option for control of bleeding and may be definitive long term for benign entities. Resection, usually staged, offers the best option for long-term survival in patients with malignancy.

References

1. Battula N, Tsapralis D, Takhar A, Coldham C, Mayer D, Isaac J, Bramhall SR. Aetio-pathogenesis and the management of spontaneous liver bleeding in the West: a 16-year single-centre experience. HPB (Oxford). 2012;14(6):382–9.
2. Liu CL, Fan ST, Lo CM, et al. Management of spontaneous rupture of hepatocellular carcinoma: single center experience. J Clin Oncol. 2001;19:3725–2730.
3. Sicklick JK, D'Angelica M, Fong Y. The liver. In: Townsend CM, Beauchamp RD, Evers BM, Mattox KL, editors. Sabiston textbook of surgery: the biological basis of modern surgical practice. 19th ed; 2012. p. 1411–75.
4. Choi BY, Nguyen MH. The diagnosis and management of benign hepatic tumors. J Clin Gastroenterol. 2005;39:401–12.
5. Beatty J, Mitchell J, Holsten S, Ferdinand C. Traumatic rupture of a previously undiagnosed Giant hepatic hemangioma. Ann Surg. 2013;79:e314–5.
6. Ribeiro MA Jr, Papaiordanou F, JM G, et al. Spontaneous rupture of hepatic hemangiomas: a review of the literature. World J Hepatol. 2010;2:428–33.
7. Güngör T, Aytan H, Tapisiz OL, Zergeroğlu S. An unusual case of incidental rupture of liver hemangioma during labor. Chin Med J (Engl). 2004;117:311–3.
8. Costa SRP, Speranzini MB, Horta SH, Miotto MJ, Myake A, Henriques AC. Surgical treatment of painful hepatic hemangioma. Einstein. 2009;7:88–90.
9. Vokaer B, Kothonidis K, Delatte P, De Cooman S, Pector JC, Liberale G. Should ruptured liver haemangioma be treated by surgery or by conservative means? A case report. Acta Chir Belg. 2008;108:761–4.
10. Aiura K, Ohshima R, Matsumoto K, Ishii S, Arisawa Y, Nakagawa M, Nakagawa M, Noga K. Spontaneous rupture of liver hemangioma: risk factors for rupture. J Hepato-Biliary-Pancreat Surg. 1996;3:308–12.

11. Corigliano N, Mercantini P, Amodio PM, et al. Hemoperitoneum from a spontaneous rupture of a giant hemangioma of the liver: report of a case. Surg Today. 2003;33:459–63.
12. Jain V, Ramachandran V, Garg R, Pal S, Gamanagatti SR, Srivastava DN. Spontaneous rupture of a giant hepatic hemangioma- sequential management with transcatheter arterial embolization and resection. Saudi J Gastroenterol. 2010;16:116–9.
13. Yamamoto T, Kawarada Y, Yano T, Noguchi T, Mizumoto R. Spontaneous rupture of hemangioma of the liver: treatment with transcatheter hepatic arterial embolization. Am J Gastroenterol. 1991;86:1645–9.
14. Rooks JB, Ory HW, Ishak KG, Strauss LT, Greenspan JR, Hill AP, et al. Epidemiology of hepatocellular adenoma. The role of oral contraceptive use. JAMA. 1979;242:644–8.
15. Klompenhouwer AJ, de Man RA, Thomeer MGJ, Ijzermans JNM. Management and outcome of hepatocellular adenoma with massive bleeding at presentation. World J Gastroenterol. 2017;23(25):4579–86.
16. Stoot JH, Coelen RJ, De Jong MC, Dejong CH. Malignant transformation of hepatocellular adenomas into hepatocellular carcinomas: a systematic review including more than 1600 adenoma cases. HPB (Oxford). 2010;12:509–22.
17. van Aalten SM, de Man RA, IJzermans JN, Terkivatan T. Systematic review of hemorrhage and rupture of hepatocellular adenomas. Br J Surg. 2012;99:911–6.
18. Bieze M, Phoa SS, Verheij J, van Lienden KP, van Gulik TM. Risk factors for bleeding in hepatocellular adenoma. Br J Surg. 2014;101:847–55.
19. Stoot JH, van der Linden E, Terpstra OT, Schaapherder AF. Lifesaving therapy for hemorrhaging liver adenomas using selective arterial embolization. Br J Surg. 2007;94:1249–53.
20. Terkivatan T, de Wilt JH, de Man RA, van Rijn RR, Tilanus HW, IJzermans JN. Treatment of ruptured hepatocellular adenoma. Br J Surg. 2001;88:207–9.
21. van Aalten SM, Thomeer MG, Terkivatan T, Dwarkasing RS, Verheij J, de Man RA, Ijzermans JN. Hepatocellular adenomas: correlation of MR imaging findings with pathologic subtype classification. Radiology. 2011;261:172–81.
22. Ronot M, Bahrami S, Calderaro J, Valla DC, Bedossa P, Belghiti J, Vilgrain V, Paradis V. Hepatocellular adenomas: accuracy of magnetic resonance imaging and liver biopsy in subtype classification. Hepatology. 2011;53:1182–91.
23. Laumonier H, Bioulac-Sage P, Laurent C, Zucman-Rossi J, Balabaud C, Trillaud H. Hepatocellular adenomas: magnetic resonance imaging features as a function of molecular pathological classification. Hepatology. 2008;48:808–18.
24. Bioulac-Sage P, Laumonier H, Couchy G, Le Bail B, Sa Cunha A, Rullier A, et al. Hepatocellular adenoma management and phenotypic classification: the Bordeaux experience. Hepatology. 2009;50:481–9.
25. van Aalten SM, Verheij J, Terkivatan T, Dwarkasing RS, de Man RA, Ijzermans JN. Validation of a liver adenoma classification system in a tertiary referral centre: implications for clinical practice. J Hepatol. 2011;55(1):120–5.
26. Ault GT, Wren SM, Ralls PW, Reynolds TB, Stain SC. Selective management of hepatic adenomas. Am Surg. 1996;62:825–9.
27. Edmondson HA, Reynolds TB, Henderson B, Benton B. Regression of liver cell adenomas associated with oral contraceptives. Ann Intern Med. 1977;86:180–2.
28. Ramseur WL, Cooper MR. Asymptomatic liver cell adenomas. Another case of resolution after discontinuation of oral contraceptive use. JAMA. 1978;239:1647–8.
29. Steinbrecher UP, Lisbona R, Huang SN, Mishkin S. Complete regression of hepatocellular adenoma after withdrawal of oral contraceptives. Dig Dis Sci. 1981;26:1045–50.
30. Huurman V, Schaapherder A. Management of ruptured hepatic adenoma. Dig Surg. 2010;27:56–60.
31. Thomeer M, Broker M, Verheij J, Doukas M, Terkivata T, Bijdevaate D, De Man R, Moelker A, IJzermans J. Hepatocellular adenoma: when and how to treat? Update of current evidence. Ther Adv Gastroenterol. 2016;9:898–912.
32. Deneve JL, Pawlik TM, Cunningham S, Clary B, Reddy S, Scoggins CR, Martin RC, D'Angelica M, Staley CA, Choti MA, Jarnagin WR, Schulick RD, Kooby DA. Liver cell adenoma: a multicenter analysis of risk factors for rupture and malignancy. Ann Surg Oncol. 2009;16:640–8.
33. Xu HS, Yan JB. Conservative management of spontaneous ruptured hepatocellular carcinoma. Am Surg. 1994;60:629–33.
34. Shortell CK, Schwartz SI. Hepatic adenoma and focal nodular hyperplasia. Surg Gynecol Obstet. 1991;173:426–31.
35. Karkar A, Tang L, Kashikar N, Gonen M, Solomon S, Dematteo R, et al. Management of hepatocellular adenoma: comparison of resection, embolization and observation. HPB (Oxford). 2013;15:235–43.
36. Parizel PM, Makkat S, Van Miert E, Van Goethem JW, van den Hauwe L, De Schepper AM. Intracranial hemorrhage: principles of CT and MRI interpretation. Eur Radiol. 2001;11:1770–83.
37. Toso C, Majno P, Andres A, Rubbia-Brandt L, Berney T, Buhler L, Morel P, Mentha G. Management of hepatocellular adenoma: solitary-uncomplicated, multiple and ruptured tumors. World J Gastroenterol. 2005;11:5691–5.
38. Okazaki M, Higashihara H, Koganemaru F, et al. Intraperitoneal hemorrhage from hepatocellular carcinoma: emergency chemoembolization or embolization. Radiology. 1991;180:647–51.
39. Yang T, Sun YF, Zhang J, Lau WY, Lai EC, Lu JH, Shen F, Wu MC. Partial hepatectomy for ruptured hepatocellular carcinoma. Br J Surg. 2013;100:1071–9.
40. Deodhar A, Brody L, Covey A, Brown K, Getrajdman G. Bland embolization in the treatment of hepatic adenomas: preliminary experience. J Vasc Interv Radiol. 2011;22:795–9.

41. Erdogan D, van Delden O, Busch O, Gouma D, van Gulik T. Selective transcatheter arterial embolization for treatment of bleeding complications or reduction of tumor mass of hepatocellular ad. Cardiovasc Intervent Radiol. 2007;30:1252–8.
42. Cobey FC, Salem RR. A review of liver masses in pregnancy and a proposed algorithm for their diagnosis and management. Am J Surg. 2004;187:181–91.
43. Noels JE, van Aalten SM, van der Windt DJ, Kok N, de Man RA, Terkivatan T, IJzermans J. Management of Hepatocellular adenoma during pregnancy. J Hepatol. 2011;54:553–8.
44. Parangi S, levine D, Henry A, Isakovich N, Pories S. Surgical gastrointestinal disorders during pregnancy. Am J Surg. 2007;193:223–32.
45. Kinoshita M, Takemura S, Tanaka S, Hamano G, Ito T, Aota T, Koda M, Ohsawa M, Kubo S. Ruptured focal nodular hyperplasia observed during follow-up: a case report. Surg Case Rep. 2017;3:44.
46. Becker YT, Raiford DS, Webb L, Wright JK, Chapman WC, Pinson CW. Rupture and hemorrhage of hepatic focal nodular hyperplasia. Am Surg. 1995;61:210–4. [PubMed]
47. Mays ET, Christopherson WM, Barrows GH. Focal nodular hyperplasia of the liver. Possible relationship to oral contraceptives. Am J Clin Pathol. 1974;61:735–46.
48. Hardwigsen J, Pons J, Veit V, Garcia S, Le Treut YP. A life-threatening complication of focal nodular hyperplasia. J Hepatol. 2001;35:310–2.
49. Bathe OF, Mies C, Franceschi D, Casillas J, Livingstone AS. Massive hemorrhage and infarction complicating focal nodular hyperplasia of the liver. HPB. 2003;5:123–6.
50. Chang SK, Chung YF, Thng CH, Loo HW. Focal nodular hyperplasia presenting as acute abdomen. Singap Med J. 2005;46:90–2.
51. Rahili A, Cai J, Trastour C, Juwid A, Benchimol D, Zheng M, et al. Spontaneous rupture and hemorrhage of hepatic focal nodular hyperplasia in lobus caudatus. J Hepato-Biliary-Pancreat Surg. 2005;12:138–42. https://doi.org/10.1007/s00534-004-0936-1.
52. Demarco MP, Shen P, Bradley RF, Levine EA. Intraperitoneal hemorrhage in a patient with hepatic focal nodular hyperplasia. Am Surg. 2006;72:555–9.
53. Li T, Qin LX, Ji Y, Sun HC, Ye QH, Wang L, et al. Atypical hepatic focal nodular hyperplasia presenting as acute abdomen and misdiagnosed as hepatocellular carcinoma. Hepatol Res. 2007;37:1100–5.
54. Yajima D, Kondo F, Nakatani Y, Saitoh H, Hayakawa M, Sato Y, et al. A fatal case of subcapsular liver hemorrhage in late pregnancy: a review of hemorrhages caused by hepatocellular hyperplastic nodules. J Forensic Sci. 2013;58:S253–7.
55. Vergara V, Muratore A, Bouzari H, Polastri R, Ferrero A, Galatola G, Capussotti L. Spontaneous rupture of hepatocellular carcinoma: surgical resection and long-term survival. Eur J Surg Oncol. 2000;26:770–2.
56. Chen CY, Lin XZ, Shin JS, et al. Spontaneous rupture of hepatocellular carcinoma. A review of 141 Taiwanese cases and comparison with nonrupture cases. J Clin Gastroenterol. 1995;21:238–42.
57. Ong GB, Taw JL. Spontaneous rupture of hepatocellular carcinoma. BMJ. 1972;4:146–9.
58. Scwartz L, Bubenheim M, Zemour J, Herrero A, Muscari F, Ayav A, Riboud R, et al. Bleeding recurrence and mortality following interventional management of spontaneous HCC rupture: results of a multicenter European study. World J Surg. 2018;42:225–3.
59. Zhu Q, Jing L, Yan J, Huang L, Wu M, Yan Y. Predictors and clinical outcomes for spontaneous rupture of hepatocellular carcinoma. World J Gastroenterol. 2012;18:7302–7.
60. Lai E, Wu K, Choi T, Fan S, Wong J. Spontaneous ruptured hepatocellular carcinoma: an appraisal of surgical treatment. Ann Surg. 1989;210:24–8.
61. Kung C, Liu B, Ng S, Lee T, Cheng Y, Chen M, Ko S. Transcatheter arterial embolization in the emergency department for hemodynamic instability due to ruptured hepatocellular carcinoma: analysis of 167 cases. Am J Roentgenol. 2008;19:W231–9.
62. Aoki T, Kokudo N, Matsuyama Y, et al. Prognostic impact of spontaneous tumor rupture in patients with hepatocellular carcinoma: an analysis of 1160 cases from a nationwide survey. Ann Surg. 2014;259:532–42.
63. Moris D, Chakedis J, Sun S, Spolverato G, Tsilimigras D, Ntanasis-Stathopoulos I, Spartalis E, Pawlik T. Management, outcomes, and prognostic factors of ruptured hepatocellular carcinoma: a systematic review. J Surg Oncol. 2018;117:341–53.
64. Chan AC, Dai JW, Chok KS, Cheung TT, Lo CM. Prognostic influence of spontaneous tumor rupture on hepatocellular carcinoma after interval hepatectomy. Surgery. 2016;159:409–17.
65. Lai ECH, Lau WY. Spontaneous rupture of hepatocellular carcinoma: a systematic review. Arch Surg. 2006;141:191–8.
66. Li J, Huang L, Liu C, Cai J, Yan J, Xu F, Wu M, Yan Y. Risk factors and surgical outcomes for spontaneous rupture of BCLC stages A and B hepatocellular carcinoma: a case control study. World J Gastroenterol. 2014;20:9121–7.
67. Zhu LX, Wang GS, Fan ST. Spontaneous rupture of hepatocellular carcinoma. Br J Surg. 1996;83:602–7.
68. Zhu LX, Liu Y, Fan ST. Ultrastructural study of the vascular endothelium of patients with spontaneous rupture of hepatocellular carcinoma. Asian J Surg. 2002;25:157–62.
69. Zhong F, Cheng XS, He K, et al. Treatment outcomes of spontaneous rupture of hepatocellular carcinoma with hemorrhagic shock: a multicenter study. Springerplus. 2016;5:1101.
70. Chearanai O, Plengvanit U, Asavanich C, Damrongsak D, Sindhvananda K, Boonyapisit S. Spontaneous rupture of primary hepatoma: report of 63 cases with particular reference to the pathogenesis and ratio-

nale of treatment by hepatic artery ligation. Cancer. 1983;51:1532–6.
71. Balasegaram M. Spontaneous intraperitoneal rupture of primary liver-cell carcinoma. Aust N Z J Surg. 1968;37:332–7.
72. Saifi J, Fortune JB, Graca L, Shah DM. Benefits of intra-abdominal pack placement for the management of nonmechanical hemorrhage. Arch Surg. 1990;125:119–22.
73. Abikhaled JA, Granchi TS, Wall MJ, Hirshberg A, Mattox KL. Prolonged abdominal packing for trauma is associated with increased morbidity and mortality. Am Surg. 1997;63:1109–12.
74. Caruso DM, Battistella FD, Owings JT, Lee SL, Samaco RC. Perihepatic packing of major liver injuries: complications and mortality. Arch Surg. 1999;134:958–62.
75. Leung KL, Lau WY, Lai PBS, Yiu RYC, Meng WCS, Leow CK. Spontaneous rupture of hepatocellular carcinoma. Arch Surg. 1999;134:1103–7.
76. Hai L, Yong-Hong P, Yong F, Ren-Feng L. One-stage liver resection for spontaneous rupture of hepatocellular carcinoma. World J Surg. 2005;29:1316–8.
77. Ngan H, Tso WK, Lai CL, Fan ST. The role of hepatic arterial embolization in the treatment of spontaneous rupture of hepatocellular carcinoma. Clin Radiol. 1998;53:338–41.
78. Hirai K, Kawazoe Y, Yamashita K, et al. Transcatheter arterial embolization for spontaneous rupture of hepatocellular carcinoma. Am J Gastroenterol. 1986;81:275–9.
79. Hsieh JS, Huang CJ, Huang YS, Sheen PC, Huang TJ. Intraperitoneal hemorrhage due to spontaneous rupture of hepatocellular carcinoma: treatment by hepatic artery embolization. AJR Am J Roentgenol. 1987;149:715–7.
80. Leung CS, Tang CN, Fung KH, Li MKW. A retrospective review of transcatheter hepatic arterial embolization for ruptured hepatocellular carcinoma. J R Coll Surg Edinb. 2002;47:685–8.
81. Sato Y, Fujiwara K, Furui S, et al. Benefit of transcatheter arterial embolization for ruptured hepatocellular carcinoma complicating liver cirrhosis. Gastroenterology. 1985;89:157–9.
82. Corr P, Chan M, Lau WY, Metreweli C. The role of hepatic arterial embolization in the management of ruptured hepatocellular carcinoma. Clin Radiol. 1993;48:163–5.
83. Yeh C, Lee W, Jeng L, Chen M, Yu M. Spontaneous tumor rupture and prognosis in patients hepatocellular carcinoma. Br J Surg. 2002;89:1125–9.
84. Tanaka S, Kaibori M, Ueno M, et al. Surgical outcomes for the ruptured hepatocellular carcinoma: multicenter analysis with a case-controlled study. J Gastrointest Surg. 2016;20:2021–34.
85. American Joint Committee on Cancer. Cancer staging manual. New York: Springer; 2009.

Part XV

GI Bleeding from Stomach and Duodenal Disease

40 Surgery: When to Operate and When to Resuscitate and What Kind of Operation?

Deepika Koganti and Alec Beekley

While significant advances have been made in the management of upper gastrointestinal (UGI) bleeding, the mortality rate still remains shockingly high at 13.8%. In fact, some literature supports that the mortality for non-variceal UGI bleeding has not changed over the past several years [1]. Moreover, the incidence of UGI bleed with shock has increased over the past decade [2]. Therefore, it is crucial that medical professionals expeditiously diagnose and expertly manage this potentially lethal problem.

An UGI bleed is defined as a source of bleeding proximal to the ligament of Treitz. UGI bleeds can often be distinguished from lower GI bleeds based on symptoms such as hematemesis and melena. Once the diagnosis is made, the etiology must be discerned to guide further management. Gastric or duodenal ulcers (28–59%) are the most common cause of UGI bleeds [3, 4]. Other gastric sources include Mallory-Weiss tears at the gastroesophageal junction, angiodysplasias, stress gastritis, gastroesophageal varices, portal hypertensive gastropathy, gastric antral vascular ectasia (GAVE), Cameron lesions, Dieulafoy's lesions, and malignancy. Duodenal sources include duodenitis, malignancy, vascular malformations, and, rare but potentially fatal, aortoenteric fistulas [5].

Initial assessment of the patient will guide the next steps in management. If any concerning vital signs such as tachycardia or hypotension are present, large bore intravenous lines should be placed with initiation of crystalloid resuscitation, a urinary catheter inserted, laboratory analysis, and blood products mobilized prior to further evaluation [6]. Laboratory evaluation should include complete blood count, comprehensive metabolic panel including liver function tests, standard coagulation parameters, arterial blood gas with lactate, and type and crossmatch to prepare packed red blood cells, platelets, and plasma. Intensive care unit (ICU) admission is warranted in such instances or if a patient's comorbidities are of such severity that they have little physiologic reserve to tolerate blood loss. The European Society for Gastrointestinal Endoscopy (ESGE) recommends a restrictive red blood cell transfusion strategy that aims for a target hemoglobin between 7 and 9 g/dL with a higher target hemoglobin considered in patients with significant comorbidities [4]. A randomized controlled trial found that among patients with severe acute upper gastrointestinal bleeding, outcomes were significantly improved with a restrictive transfusion strategy, in which the hemoglobin threshold

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was 7 g/dL, as compared with a liberal transfusion strategy, in which the hemoglobin threshold was 9 g/dL [7]. The data remains controversial regarding coagulopathy in UGI bleeds. An observational study found patients with coagulopathy (INR > 1.5) had more than a fivefold increased risk of inhospital mortality compared to patients without coagulopathy [8]. However, no clear guidelines exist on how to manage coagulopathy. The International Consensus Recommendations on the Management of Patients With Nonvariceal Upper Gastrointestinal Bleeding states that coagulopathy should be corrected in patients receiving anticoagulation; however, reversal should not delay endoscopy [9]. The Registry on Non-variceal Upper Gastrointestinal Bleeding and Endoscopy Canadian cohort study found that neither INR nor platelet count predicted rebleeding [1]. However, unlike platelet count, an INR of 1.5 or higher was associated with increased mortality rate [8]. Although tranexamic acid (TXA) has been used in massive traumas, the role of TXA remains inconclusive as no randomized trials have been completed [10, 11].

Risk scores have been developed to help triage patients and determine further treatments. While one study found relative inability of any group of physicians to accurately predict the presence of high-risk lesions requiring endoscopic therapy [12], another one found clinical judgment to be more accurate [13]. While no single risk calculator exists for all outcomes, the Glasgow-Blatchford score is able to predict the need for transfusion or further intervention. The point-based system takes into consideration the patient's systolic blood pressure, blood urea nitrogen, hemoglobin based on gender, tachycardia, melena, syncope, liver disease, and heart failure [14]. On the other hand, the Rockall system can be used to predict mortality based on age, shock, comorbidity, diagnosis, major stigmata of recent hemorrhage, and rebleeding [15].

Once an UGI bleed has been diagnosed and the patient appropriately resuscitated, the initiation of a proton-pump inhibitor (PPI) should be started. The National Institute for Health and Clinical Excellence (NICE) guidelines recommend only giving a PPI if the patient [4] has a non-variceal UGI bleed and signs of recent bleeding on endoscopy [16]. However, other guidelines recommend a high-dose intravenous bolus PPI followed by continuous infusion (80 mg then 8 mg/hour) as long as it does not delay endoscopy [4, 9]. This recommendation is based on a Cochrane review of randomized controlled trials that found PPI treatment before endoscopy significantly decreases need for endoscopic therapy; however, there was no change in mortality, rebleeding, or need for surgery [17].

As the patient is being resuscitated, the endoscopy, interventional radiology, and surgical teams should be notified of the patient. Upper endoscopy within 24 hours of presentation for non-variceal UGI bleed is considered standard of care and even a quality of care indicator as it has been shown to reduce mortality in high-risk patients [9, 18, 19]. Endoscopy should be done more urgently, ideally in less than 12 hours, in patients with hemodynamic instability despite resuscitation, hematemesis or bloody nasogastric tube output, or inability to reverse anticoagulation [4]. The Forrest classification is often used to guide endoscopic management as it prognosticates risk for rebleeding, need for surgery, and mortality. The classification is as follows: IA, active spurting; IB, active oozing; IIA, non-bleeding visible vessel; IIB, adherent clot; IIC, flat pigmented spot; and III, clean ulcer base [20, 21]. Recommendations from the American College of Gastroenterology (ACG) are class IA, IB, and IIA should undergo endoscopic treatments. IIB lesions are per clinician judgment, and class III lesions do not need intervention. Current endoscopic therapies include epinephrine injections, thermal therapy, injection of sclerosing agents, and clips. There are strong recommendations for the use of sclerosants and thermal therapy as they have been shown to decrease rebleeding, need for surgery, and mortality. Epinephrine has been shown to have favorable outcomes but only when combined with a second therapy, while clips are more effective than epinephrine alone but no different than other modalities [20, 22, 23]. While second-look endoscopy had been done in the past, guidelines now recommend against repeat endoscopy in 24 hours unless the patient is bleeding again [9, 20]. Repeat

endoscopy is standard treatment for recurrent bleeding as it has been shown to decrease the need for surgery and has less complications [24]. If repeat endoscopy fails to control the bleed, interventional radiology or surgery should be the next steps in management [20].

Although there are no randomized trials comparing embolization to surgery, transcatheter embolization is considered the next step after two failed endoscopies with clinical success rates reported as high as 63–97% [4, 25–27]. Embolization can be localized, proximal, or segmental in nature. Localized or super-selective embolization is ideal to prevent bowel ischemia [27]. If the patient is hemodynamically stable, pre-embolization CT angiography can be useful in localizing the bleeding vessel [25]. Hemostatic options with embolization include coils, polyvinyl alcohol (PVA), gelatin sponge with coils, and N-butyl cyanoacrylate [27]. Metallic coils alone have been shown to have a higher risk of rebleeding and should be used in combination with Gelfoam or PVA [28]. If transcatheter embolization is unsuccessful, the patient should be taken to surgery. However, repeat endoscopic therapy can be considered if the patient becomes hemodynamically stable or if the patient has a partial response to resuscitation. At this point, despite the failure of transcatheter intervention, the surgeon can still use the information gained from the angiographic images to attempt to localize the bleed and guide operative planning.

Surgical Treatment

Surgery to treat upper gastrointestinal hemorrhage is reserved for those patients who fail endoscopy and/or interventional radiologic attempts to control hemorrhage; patients who cannot be rendered hemodynamically stable despite ongoing resuscitation; patients with recurrent hemorrhage and shock; patients who suffer complications of other interventions to control hemorrhage (perforation, ischemia); and patients who, because of age or comorbidities, may be deemed not fit to tolerate prolonged resuscitation or multiple endoscopic or interventional attempts at hemorrhage control. The provider team may also elect for earlier surgery than otherwise would be contemplated in patients who refuse blood transfusions for religious reasons, have difficult blood crossmatches, or have severe medical comorbidities or prior anatomic changes that limit therapeutic options (e.g., prior Roux-en-Y operation).

Involvement of the surgeon early in the course of the severe UGI bleed patient can allow for coordination between specialists and exchange of data that set the surgeon and patient up for success in the operating room. If possible, presence of the surgeon at repeat endoscopy or interventional radiology procedures allows the surgeon to have a clear idea where the source of the bleeding is, allows the surgeon to see variations in anatomy, and provides reminders for colleagues from other disciplines to think of the worst case scenario (e.g., endoscopist tattoos bleeding site for easier surgical identification if the patient requires operation).

Preparation for Surgery

The surgeon should request that a flexible endoscope, self-retaining retractor system, and blood products be available in the operating room at the start of the case. The patient should be placed supine on the operating table. By the time most UGI patients requiring surgery arrive in the operating room, large bore or central venous access, arterial lines, and urinary drainage have been established. If these “safety net” interventions have not been established because of the patient’s critical condition, they should be accomplished in parallel by the anesthesia team or other members of the surgical team while the primary surgeon prepares for operation. Surgical skin preparation should extend from nipples to groin.

Surgical Technique

The superior abdominal midline incision is the utility incision for surgical treatment of UGI bleeds. It should be used in any unstable

patient, in patients in whom the bleeding source has not been clearly localized, and in patients in whom extensive scarring is known or suspected because of prior operations. Minimally invasive techniques (laparoscopy and combined endoscopy and laparoscopy) are feasible but should be reserved for stabilized patients and those with recurrent, non-massive hemorrhages.

Treatment of Bleeding Duodenal Ulcer

Once upper abdominal exposure is gained, the hepatic flexure of the colon should be mobilized by incising the white line of Toldt and a generous Kocher maneuver should be performed. The pylorus is identified and a stay suture placed superiorly and inferiorly in preparation for a longitudinal incision through the pylorus. The incision is then taken distally onto the duodenum until the bleeding is identified, usually on the posterior wall of the duodenal bulb. The bleeding site, frequently the gastroduodenal artery, is often described as running cephalad to caudad with a medial transverse pancreatic branch arising close to the site of bleed. Hence, classic surgical teaching is there are three points of ligation that must be placed to adequately control hemorrhage (superior, inferior, and medial). In reality, surgeons often place once or two figure of eight sutures (whatever is necessary for hemorrhage control), but the three point of ligation should be attempted to prevent rebleeding (Fig. 40.1). Completion of the treatment should be truncal vagotomy and Heineke-Mikulicz or Finney pyloroplasty to close the duodenotomy, although hemodynamically unstable patients without prior history of ulcers and without prior antacid treatment could simply have pyloroplasty for closure.

A fibrotic duodenal bulb or pylorus can provide a particular challenge in the setting of surgery for duodenal ulcer bleeding. Classic closure techniques such as the Nissen-Bsteh, stump duodenostomy with gastrojejunostomy, and Bancroft closures [29] may not perform as well as a duodenojejunostomy [30].

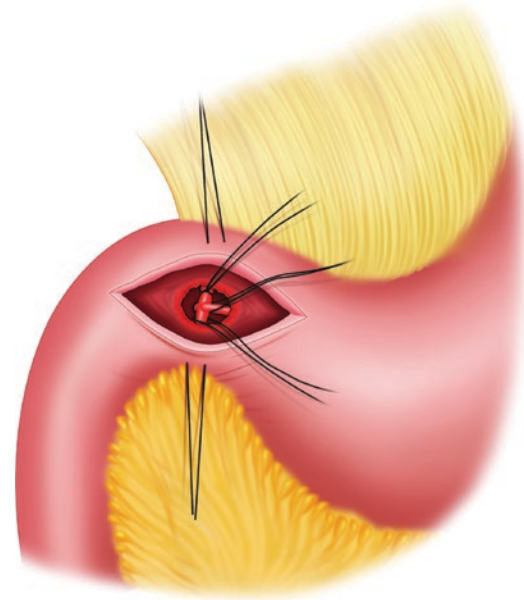

Fig. 40.1 Diagram demonstrating classic stitch placement to control duodenal artery hemorrhage

Surgical Treatment of Gastric Ulcers and Other Gastric Lesions

The majority of gastric lesions requiring operation can be managed with direct oversewing of bleeding site(s) or limited wedge resection; however, more extensive operations such as devascularization procedures or subtotal or total resection are sometimes required. If possible, operations that both control hemorrhage and definitively treat the source of the hemorrhage should be attempted (partial gastrectomy with Billroth I or II reconstruction), although anatomic and physiologic considerations may render this inadvisable. In almost all instances of non-resectional treatment, it is recommended that circumferential biopsies of the lesion are performed to evaluate for malignancy. Preoperative localization with endoscopic tattoo or angiographic localization substantially increases precision and speed of operation. In selected, stabilized patients, laparo-

scopic approaches to these interventions have been utilized, and combined endoscopic/laparoscopic operations can allow real-time localization of lesions for limited resection and provide nearly instantaneous confirmation of successful bleeding control and/or adequate gross resection margins. Resection alone is associated with bleeding recurrence in up to 20% of patients, so if patient stability permits, resection should be combined with truncal vagotomy and drainage [31].

A challenging surgical problem is the bleeding type IV or high-lying gastric ulcer near the GE junction. Ulcer size, associated inflammation and adherence to local blood supply and other structures, and proximity to the GE junction can preclude safe wedge resection. Historically, such lesions were treated with distal gastrectomy and resection of the ulcer up to portions of the GE junction and esophagus with (1) Roux-en-Y esophago-gastrojejunostomy (Csendes procedure); (2) total or near-total gastrectomy with Roux-en-Y gastrojejunostomy or esophagojejunostomy; or (3) antrectomy with truncal vagotomy with the ulcer oversewn through an anterior gastrotomy and left in situ (often combined with left gastric artery ligation) [32]. The first two procedures have the disadvantage of high morbidity and mortality, particularly in unstable patients; the last procedure has the disadvantage of potentially leaving malignant tissue in situ. The last procedure, nevertheless, should be considered a damage control maneuver to control hemorrhage and obtain tissue, if possible, for diagnosis.

In the current era, the challenging clinical entity described above can now be managed by temporizing or controlling hemorrhage with endoscopy and/or interventional radiology embolization of the left gastric artery, allowing resuscitation and stabilization of the patient (Figs. 40.2 and 40.3). This approach may be followed by a combined endoscopic and laparoscopic approach to see if ulcer resection can be achieved without compromising the GE junction. Alternatively, the hemorrhage can be temporized long enough with minimally invasive means to allow tissue diagnosis and definitive surgical planning if malignancy is diagnosed.

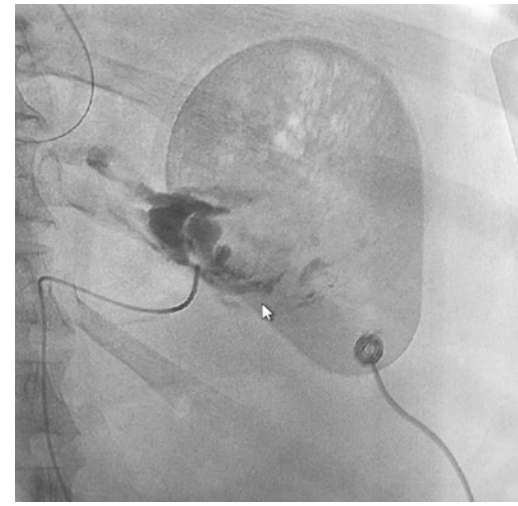

Fig. 40.2 63-year-old patient who began hemorrhaging from upper stomach 2 weeks after salvage chemotherapy for recurrent gastric lymphoma. Endoscopy revealed multiple mucosal erosions and bleeding sites which could not be endoscopically controlled

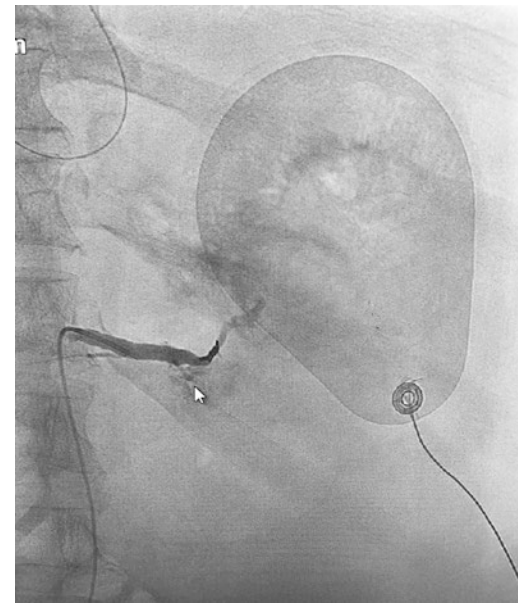

Fig. 40.3 Patient from Fig. 40.2 status post-successful embolization of left gastric artery. Gastroenterology and surgery teams prepared to repeat endoscopy or intervene surgically if bleeding resumed (which it did not)

Conclusion

Modern treatment of upper gastrointestinal bleeding involves a multidisciplinary approach, and many centers have teams of providers and care algorithms in place to respond to crisis patients. Because surgical intervention for UGI bleed has become such a relatively uncommon event, surgeons must keep abreast of all the tools available to them in the multidisciplinary armamentarium.

Bibliography

1. Barkun A, Sabbah S, Enns R, 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. https://doi.org/10.1111/j.1572-0241.2004.30272.x.
2. Siddiqui NS, Paul S, Khan Z, et al. Rising events and improved outcomes of gastrointestinal bleed with shock in USA: a 12-year national analysis. J Clin Gastroenterol. 2018; https://doi.org/10.1097/MCG.0000000000000995.
3. Targownik LE, Nabalamba A. Trends in management and outcomes of acute nonvariceal upper gastrointestinal bleeding: 1993–2003. Clin Gastroenterol Hepatol. 2006;4:1459–66. https://doi.org/10.1016/j.cgh.2006.08.018.
4. Gralnek IM, Dumonceau J-M, Kuipers EJ, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy. 2015;47:a1–46. https://doi.org/10.1055/s-0034-1393172.
5. Feinman M, Haut ER. Upper gastrointestinal bleeding. Surg Clin North Am. 2014;94:43–53. https://doi.org/10.1016/j.suc.2013.10.004.
6. Lau JYW, Barkun A, Fan D, et al. Challenges in the management of acute peptic ulcer bleeding. Lancet. 2013;381:2033–43. https://doi.org/10.1016/S0140-6736(13)60596-6.
7. Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013;368:11–21. https://doi.org/10.1056/NEJMoa1211801.
8. Jairath V, Kahan BC, Stanworth SJ, et al. Prevalence, management, and outcomes of patients with coagulopathy after acute nonvariceal upper gastrointestinal bleeding in the United Kingdom. Transfusion. 2013;53:1069–76. https://doi.org/10.1111/j.1537-2995.2012.03849.x.
9. Barkun AN, Bardou M, Kuipers EJ, et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2010;152:101–13. https://doi.org/10.7326/0003-4819-152-2-201001190-00009.
10. Bennett C, Klingenberg SL, Langholz E, Gluud LL. Tranexamic acid for upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2014:CD006640. https://doi.org/10.1002/14651858.CD006640.pub3.
11. Redeen S. The trend of tranexamic use in upper gastrointestinal bleeding ulcers. Gastroenterology Res. 2017;10:159–65. https://doi.org/10.14740/gr836w.
12. de Melo SW, Bhore R, Rockey DC. Clinical judgment does not circumvent the need for diagnostic endoscopy in upper gastrointestinal hemorrhage. J Investig Med. 2013;61:1146–51. https://doi.org/10.2310/JIM.0000000000000011.
13. Farooq FT, Lee MH, Das A, et al. Clinical triage decision vs risk scores in predicting the need for endotherapy in upper gastrointestinal bleeding. Am J Emerg Med. 2012;30:129–34. https://doi.org/10.1016/j.ajem.2010.11.007.
14. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet. 2000;356:1318–21. https://doi.org/10.1016/S0140-6736(00)02816-6.
15. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. Gut. 1996;38:316–21.
16. Dworzynski K, Pollit V, Kelsey A, et al. Management of acute upper gastrointestinal bleeding: summary of NICE guidance. BMJ. 2012;344:e3412. https://doi.org/10.1136/bmj.e3412.
17. Sreedharan A, Martin J, Leontiadis GI, et al. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2010:CD005415. https://doi.org/10.1002/14651858.CD005415.pub3.
18. Kanwal F, Barkun A, Gralnek IM, et al. Measuring quality of care in patients with nonvariceal upper gastrointestinal hemorrhage: development of an explicit quality indicator set. Am J Gastroenterol. 2010;105:1710–8. https://doi.org/10.1038/ajg.2010.180.
19. Lim LG, Ho KY, Chan YH, et al. Urgent endoscopy is associated with lower mortality in high-risk but not low-risk nonvariceal upper gastrointestinal bleeding. Endoscopy. 2011;43:300–6. https://doi.org/10.1055/s-0030-1256110.
20. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107:345–60. quiz 361. https://doi.org/10.1038/ajg.2011.480.
21. Forrest JA, Finlayson ND, Shearman DJ. Endoscopy in gastrointestinal bleeding. Lancet. 1974;2:394–7.
22. Laine L, McQuaid KR. Endoscopic therapy for bleeding ulcers: an evidence-based approach based on meta-analyses of randomized controlled trials. Clin Gastroenterol Hepatol. 2009;7:33–47. quiz 1. https://doi.org/10.1016/j.cgh.2008.08.016.

23. Vergara M, Bennett C, Calvet X, Gisbert JP. Epinephrine injection versus epinephrine injection and a second endoscopic method in high-risk bleeding ulcers. Cochrane Database Syst Rev. 2014:CD005584. https://doi.org/10.1002/14651858.CD005584.pub3.
24. Lau JY, Sung JJ, Lam YH, et al. Endoscopic retreatment compared with surgery in patients with recurrent bleeding after initial endoscopic control of bleeding ulcers. N Engl J Med. 1999;340:751–6. https://doi.org/10.1056/NEJM199903113401002.
25. Loffroy R, Rao P, Ota S, et al. Embolization of acute nonvariceal upper gastrointestinal hemorrhage resistant to endoscopic treatment: results and predictors of recurrent bleeding. Cardiovasc Intervent Radiol. 2010;33:1088–100. https://doi.org/10.1007/s00270-010-9829-7.
26. Miller M, Smith TP. Angiographic diagnosis and endovascular management of nonvariceal gastrointestinal hemorrhage. Gastroenterol Clin N Am. 2005;34:735–52. https://doi.org/10.1016/j.gtc.2005.09.001.
27. Shin JH. Recent update of embolization of upper gastrointestinal tract bleeding. Korean J Radiol. 2012;13(Suppl 1):S31–9. https://doi.org/10.3348/kjr.2012.13.S1.S31.
28. Aina R, Oliva VL, Therasse É, et al. Arterial embolotherapy for upper gastrointestinal hemorrhage: outcome assessment. J Vasc Interv Radiol. 2001;12:195–200. https://doi.org/10.1016/S1051-0443(07)61825-9.
29. Bennett JM. Modified Bancroft procedure for the difficult duodenal stump. Arch Surg. 1972;104(2):219–22.
30. Vashist YK, Yekebas EF, Gebauer F, et al. Management of the difficult duodenal stump in penetrating duodenal ulcer disease: a comparative analysis of duodenojejunostomy with "classical" stump closure (Nissen–Bsteh). Arch Surg. 2012;397(8):1243–9.
31. Jordan PH Jr. Surgery for peptic ulcer disease. Curr Probl Surg. 1991;28:265.
32. Conter RL, Kauffman GL. Benign gastric ulcer and stress gastritis. In: Cameron JL, editor. Current surgical therapy. 7th ed. St. Louis: Mosby; 2001. p. 77–80.

41 Endoscopic Management of Non-variceal Acute Gastrointestinal Bleeding

Franklin Goldwire

Introduction

Acute upper gastrointestinal bleeding is defined as bleeding from the esophagus to the ligament of Treitz and accounts for approximately 400,000 hospital admissions per year [1] with an annual cost of approximately $8 billion dollars a year. Peptic ulcers, including duodenal ulcers, account for approximately 60% of all admissions for upper gastrointestinal bleeding, with Mallory-Weiss tears and arteriovenous malformations making up another 15% [2]. In this chapter our primary focus will be on the initial medical and endoscopic managements of overt gastrointestinal bleeding due to peptic ulcer disease.

Ulcers are breaks in the mucosal surface that extend beyond the muscularis mucosa in the submucosa leading to bleeding. Nonsteroidal anti-inflammatory medications and *Helicobacter pylori* infections are the leading causes of ulcer formation. Patients with upper gastrointestinal bleeding usually present with hematemesis, melena, or hematochezia. Hematemesis suggests bleeding that is proximal to the ligament of Treitz and can be described as both coffee-ground material or frank blood. Melena is described as black, tarry, foul-smelling stools, and it can occur with bleeding as little as 50 mL [3]. Though typically seen with lower gastrointestinal bleeding, hematochezia can be seen with upper gastrointestinal blood loss. This is usually due to a brisk upper gastrointestinal bleeding and is often associated with hypotension and tachycardia [4].

Initial Assessment

Once the diagnosis of upper gastrointestinal bleeding is suspected, the hemodynamic stability of the patient should be addressed. Two large-bore (18 g) intravenous (IV) lines should be placed, and early aggressive resuscitation with IV fluids should be started, with at least 500 mL of normal saline or lactated ringers [5]. A complete blood count should be obtained along with type and crossmatching of the blood. If needed, blood transfusion should be given. The transfusion goal should be set to maintain hemoglobin of >7 g/dL [6]. Setting higher transfusion goals was associated with increased mortality and increased rate of rebleeding. Patients with comorbidities such as cirrhosis or coronary artery disease should have a slightly higher transfusion goal of 10 g/dL (see Fig. 41.1).

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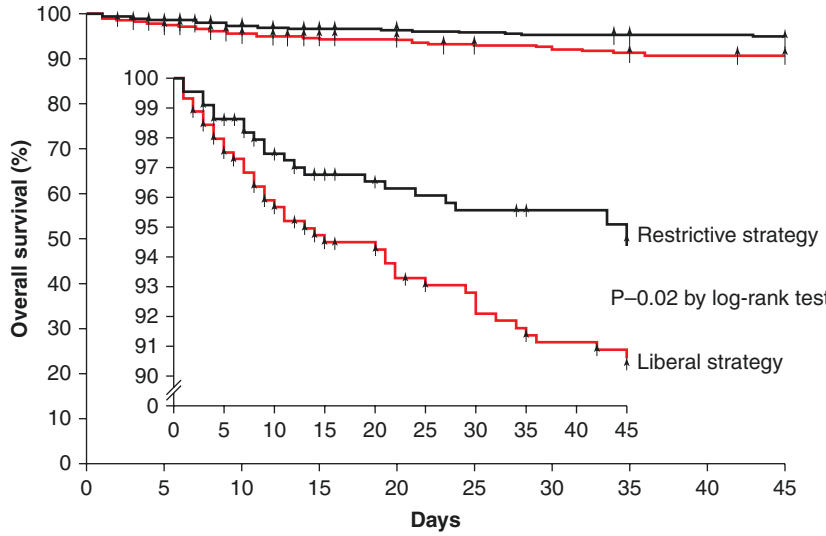

Fig. 41.1 Survival according to transfusion strategy

In patients with large volume hematemesis, intubation should be considered to help protect the patient's airway. Several predictive scoring systems have been developed to help risk-stratify patients at increased risk of mortality and rebleeding. The Glasgow-Blatchford bleeding score uses hemoglobin (>13.0 g/dL for men and >12.0 g/dL for women), blood urea nitrogen (<18.2 mg/dL), initial systolic blood pressure (>110 mm Hg), sex, heart rate (<100 beats/min), melena, syncope, liver disease, and cardiac failure to determine likelihood of need for inpatient endoscopic therapy [7]. Comparison of the Glasgow-Blatchford and Rockall scores showed the Glasgow-Blatchford score to be superior in predicting the need for inpatient endoscopy versus outpatient management [7]. Patients with a Glasgow-Blatchford score of 0 have a low risk of having a lesion that requires endoscopic intervention.

Initial Therapy

Since their introduction in 1989, proton-pump inhibitors have been the mainstay of initial management of non-variceal upper gastrointestinal bleeding. Lau et al. in 2007 performed a study looking at proton-pump inhibitor infusion prior to endoscopic therapy. They randomized patients with non-variceal upper gastrointestinal bleeding to an 80 mg bolus followed by 8 mg/hour infusion of omeprazole and placebo. Patients who received omeprazole had lesions, which had greater resolution in stigmata of bleeding and active bleeding when compared to placebo group [8]. The patients also had a decreased hospitalization stay, need for endoscopic therapy, and need for repeat endoscopy. However, there was no difference in the need for blood transfusion, recurrent bleeding, need for surgery, and death. A meta-analysis, however, showed that early

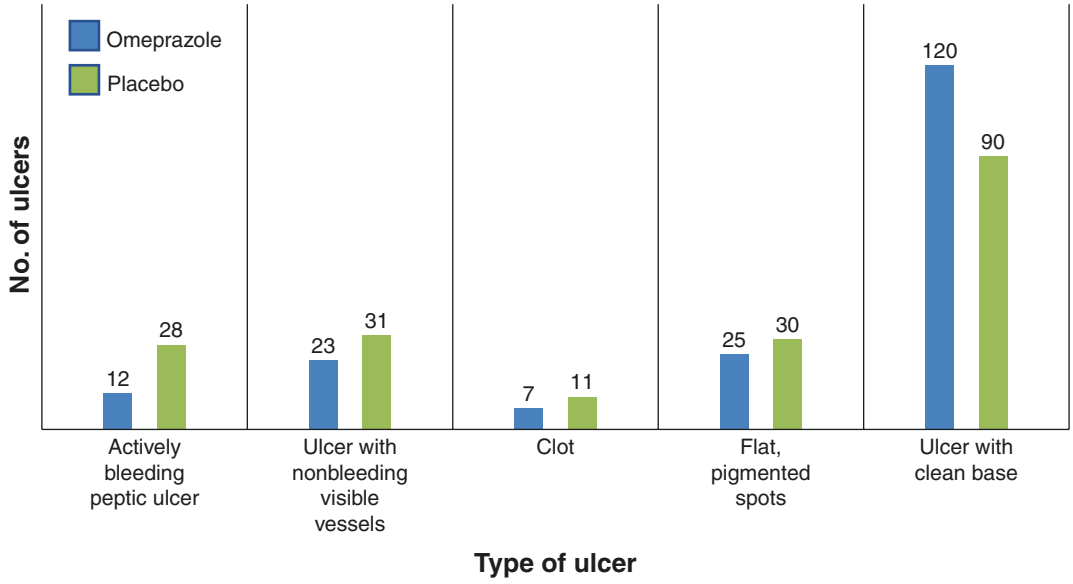

Fig. 41.2 Forrest Classification of Ulcer At Time of Endoscopy for Omeprazole vs. Placebo

proton-pump inhibitor therapy showed decreased rebleeding and need for surgery [9]. It also demonstrated improved outcomes in patients where endoscopy was delayed or not even provided (see Fig. 41.2).

Endoscopic Therapy

Patients with upper gastrointestinal bleeding should be evaluated with upper endoscopy in order to determine etiology of bleeding, determine risk of rebleeding, and provide therapeutic intervention if needed. Timing of the endoscopy has always been a topic of debate, and several studies have sought to answer this question. If the endoscopy is performed too soon, this may result in negative outcome due to under-resuscitation; and if endoscopy is performed too late, this may result in increased mortality due to persistent bleeding. Studies have shown that performing endoscopy within 24 hours decreases length of hospital stay, reduces rebleeding, and reduces mortality [9].

Cooper et al. performed a retrospective study in which they looked at 909 admissions for non-variceal upper gastrointestinal bleeding across 13 hospitals. Patients were divided into groups who received endoscopy within 24 and those who underwent delayed endoscopy. In patients who underwent early endoscopy, there was a reduction in recurrent bleeding, the need for surgery, and inhospital length of stay [10]. In another study, Tai et al. looked at patients who had endoscopy done within 8 hours and those done between 8 and 24 hours after admission. Their study demonstrated that there was no difference in mortality, rebleeding, or length of stay [11]. Based on these studies, endoscopy within the first 24 hours allows for adequate resuscitation without affecting outcome.

Once the source of bleeding is determined, the next step is to assess the risk of rebleeding to determine if endoscopic therapy is needed. Patients with active bleeding at time of endoscopy have a 55% risk of rebleeding and an 11% mortality [12]. Patients with a visible vessel have a rebleeding risk of 43% with an 11% mortality, [12] while flat pigmented spots and clean-based ulcers have a lower risk of rebleeding at 10% and 5%, respectively [12]. The mortality of these lesions with rebleeding are 2% and 3%, respectively [12]. When it comes to ulcers with an adherent clot, rebleeding is approximately 20% with a 7% mortality [12]. It is current practice that lesions with higher rebleeding risk such as

active bleeding or visible vessel receive endoscopic therapy, while clean-based ulcers and flat pigmented spots do not. At this time, it is controversial whether or not to treat lesions with an adherent clot. A meta-analysis of randomized controlled trials showed no difference in rebleeding in patients with an adherent clot who received endoscopy therapy versus patients who did not received therapy [13]. However there are randomized controlled trials and another meta-analysis that show a decrease in rebleeding with endoscopic therapy but no difference in the hospital length of stay, need for surgery, need for transfusion, and mortality [14, 15]. This is thought to be due to the etiology of ulcers. As a result, treatment of adherent clot remains largely practitioner dependent. Table 41.1 summarizes the risk of rebleeding and mortality based on the appearance of the ulcer.

Once it has been determined that endoscopic therapy is necessary, the next decision determines the treatment modality. Approved modalities include thermal therapy (which includes both the heater probes and bipolar surgical energy), injection therapy, clips, and glue. Laine et al. performed a meta-analysis to determine the efficacy of these different treatment modalities. Epinephrine is the primary agent used in injection therapy. It is good at providing initial hemostasis; however, the effects are short-lived. Epinephrine generally is applied to an actively bleeding ulcer or ulcer with a visible vessel; it is usually in a concentration of 1:10,000 or 1:20,000 in 0.5 mL up to 2 mL allocations in the center and in four quadrants around the ulcer until bleeding slows or stops. There is no proven minimum volume of epinephrine needed to obtain hemostasis, but volumes of greater than 45 mL have been proven to be almost as effective as other monotherapy. Epinephrine was shown to provide initial hemostasis but did not reduce risk of rebleeding (RR, 0.50; 95% CI, 0.23–1.07) or reduction in need for surgery (RR, 0.29; 95% CI, 0.07–1.21) specifically in patients with active bleeding or other high-risk stigmata [13].

Table 4.1 Forrest Classification System

Stigmata	Further bleeding ($N = 2994$)	Surgery for bleeding ($N = 1499$)	Mortality ($N = 1387$)
Active bleeding	55% (17–100%)	35% (20–69%)	11% (0–23%)
Non-bleeding visible vessel	43% (0–81%)	34% (0–56%)	11% (0–21%)
Adherent clot	22% (14–36%)	10% (5–12%)	7% (0–10%)
Flat pigmented spot	10% (0–13%)	6% (0–10%)	3% (0–10%)
Clean ulcer base	5% (0–10%)	0.5% (0–3%)	2% (0–3%)

Epinephrine was also compared to other modalities in producing a durable hemostasis with monotherapy. When compared to a heater probe, bipolar surgical energy, fibrin glue, and clipping, there was significant rebleeding with epinephrine alone [13]. Epinephrine only approached the same efficacy as other modalities if a second treatment of epinephrine was implemented [13].

Thermal therapy is a misnomer, as it includes the heater probe that cauterizes or applies direct heat to the vessel and bipolar electrosurgical energy, which uses electric current to cause cellular elements to vibrate, which generates heat. The heat generated is enough to denature the cellular proteins to form a coagulum and cause hemostasis [16]. These options were also evaluated as primary modalities for achieving durable hemostasis. Both showed significant reduction in rebleeding, need for surgery, and overall mortality when compared to no therapy [13]. There is no significant difference in the two different modalities. A meta-analysis of thermal therapy alone versus injection with epinephrine followed by thermal therapy was conducted. They showed that there was a slight benefit to combination therapy over thermal therapy alone [13]. Other agents like thrombin were looked at to see if they provided additional benefit. Results showed that thrombin did not provide any benefit over thermal therapy alone [13]. When compared to sclerosing agents, both modes of thermal therapy were superior with less rebleeding and a decreased need for surgery [13].

Mechanical therapy using clips is another modality for achieving hemostasis. Clips as monotherapy are superior to epinephrine alone. When compared to other modalities including thermal therapy with and without epinephrine and sclerosing agents with and without epinephrine, the results showed that clips as monotherapy trended toward being less effective in achieving initial hemostasis [18]. This is thought to be due to the types of clips used, when these studies were conducted, and the variability among endoscopists.

Ultimately the goal when treating bleeding is to stop the bleeding and reduce risk or rebleeding. Thrombin and fibrin glue will not be discussed because they are not currently available in the United States, though they are believed to be coming to the market soon. It is recommended that dual therapy with epinephrine and another modality being either thermal therapy, bipolar surgical energy, or clipping be used.

When applying thermal therapy, you should have the scope as close as possible to the ulcer without obscuring visibility. The heater probe should be advanced through the scope and applied to the area of bleeding or visible vessel. Thermal therapy should be applied for at least 8–10 seconds while simultaneously applying pressure to the treatment area. This should be repeated until bleeding stops, the vessel flattens, and the ulcer whitens. Setting of 15 W is recommended for the bipolar surgical energy and 30 J for the heater probe. A 10 Fr or 3.2 mm probe is recommended for the stomach, and the small 7 Fr or 2.3 mm probe is recommended for the small bowel. Clips should be applied over the vessel or area of bleeding. Multiple clips can be placed until the bleeding stops.

Novel Therapies

There are some new modalities that are being used for treatment of bleeding. These instruments show promise but will need continued studies. In 2017 Brandler et al. published a study that showed that over the scope clips were successful in reducing risk of bleeding as primary therapy in patients with upper gastrointestinal bleeding [17]. Monopolar surgical energy forceps are primarily used with endoscopic mucosal dissection to help control bleeding. Nunoue et al. published data showing that monopolar energy forceps are superior to heater probe [18]. Hemostatic spray is a topical coagulant. Studies show that initially hemostasis is achieved approximately 92–95% of the time, but there is a significant rebleed rate of approximately 25% [19]. Thus, this is used in a setting with perfuse bleeding that is unable to be controlled with standard therapy. Once you obtained hemostasis, repeat endoscopy will be needed to fully evaluate the underlying etiology of bleeding. Hemospray shows a particular utility in malignant bleeding [20].

In addition to endoscopic therapy for active upper gastrointestinal bleeding, continued infusion of PPI for 72 hours is recommended as it reduces risk of rebleeding. Those patients with increased risk of bleeding include ones with hemodynamic instability, comorbid illnesses, active bleeding at time of endoscopy, an ulcer size greater than 2 cm, a posterior duodenal ulcer, and a lesser curvature ulcer.

Anticoagulation

Antiplatelet platelet agents are a very common form of anticoagulation. The most common antiplatelet agents are nonsteroidal anti-inflammatory medications and thienopyridines. These medications should be held at the time of presentation, and for episodes of severe bleeding, platelet transfusion can be considered. Once hemostasis has been achieved, it is general safe to resume antiplatelet therapy without increased risk of rebleeding. A randomized controlled trial of patients presenting with acute peptic ulcer bleeding on daily aspirin for secondary prophylaxis of cardiovascular or cerebrovascular disease that required regular antiplatelet therapy did not show any increase in rebleeding and showed a decrease in 30-day mortality compared to patients who had medication held [21].

For those patients who are receiving warfarin, an elevated international normalized ratio (INR)

greater than 1.5 on admission has been associated with increased mortality [22]. At the time of presentation, the benefits of stopping anticoagulation should be weighted with the risk of embolism due to the underlying etiology. Patients with moderately elevated INRs (1.5–2.5) do not need to have their IRN normalized prior to endoscopy. After the patient has been adequately resuscitated, upper endoscopy can be safely performed. In a randomized controlled trial looking at patients on warfarin who presented with upper gastrointestinal bleeding and a moderately elevated INR, there was no difference in rate of rebleeding or mortality with a control group [23]. Subsequent studies have confirmed this [24], so therapeutic endoscopy up to an INR of 2.5 is safe.

Novel anticoagulants such as dabigatran, rivaroxaban, apixaban, and edoxaban are becoming more popular. Like other anticoagulants it is associated with increased risk of bleeding. As with coumadin the benefits of holding the mediation has to be weighed against the thrombotic risk. These medications have short half-lives of 5–15 hours. Initial management should consist of adequate resuscitation followed therapeutic endoscopy. If there is significant bleeding, then transfusion of clotting factors should be considered.

Conclusion

Non-variceal upper gastrointestinal bleeding particularly due to peptic ulcer disease contributes to a significant number of hospitalizations. However, the emergence of proton-pump inhibitors and advances in endoscopic therapy have led to a decrease in morbidity and mortality as well as a need for surgery. Once a patient is identified as having an upper gastrointestinal bleeding, it is recommended that they be started on a proton-pump inhibitor and adequately resuscitated. Within 24 hours, a diagnostic endoscopic evaluation to determine the underlying etiology is recommended. For patients who are hemodynamically abnormal or who have only a partial response to fluid resuscitation, one should consider endoscopic intervention earlier. If repeat endoscopic therapy is needed based on stigmata of recent bleeding, combination therapy with epinephrine is superior to monotherapy. If bleeding persists, then angiography and or surgical modalities should be considered for definitive treatment.

References

1. Kanwal F, Barkun A, Gralnek IM, et al. Measuring quality of care in patients with nonvariceal upper gastrointestinal hemorrhage: development of an explicit quality indicator set. Am J Gastroenterol. 2010;105(8):1710–8.
2. Longstreth GF. Epidemiology of hospitalization for acute upper gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1995;90(2):206–10.
3. Doherty G, editor. Current diagnosis and treatment: surgery. 13th ed. New York: McGraw-Hill Companies; 2010. p. 493.
4. Jensen DM, Machicado GA. Diagnosis and treatment of severe hematochezia. The role of urgent colonoscopy after purge. Gastroenterology. 1988;95:1569.
5. Baradarian R, Ramdhaney S, Chapalamadugu R, et al. Early intensive resuscitation of patients with upper gastrointestinal bleeding decreases mortality. Am J Gastroenterol. 2004;99:619.
6. Villaneuva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013;368(1):11–21.
7. Pang SH, Ching JYL, Lau JYW, et al. Comparing the Blatchford and pre-endoscopic Rockall score in predicting the need for endoscopic therapy in patients with upper GI hemorrhage. Gastrointest Endosc. 2010;71:1134–40.
8. Lau JY, Leung WK, Wu JCY, et al. Omeprazole before endoscopy in patients with gastrointestinal bleeding. N Engl J Med. 2007;356:1631–40.
9. Zhang YS, Li Q, He BS, Liu R, Li ZJ. Proton pump inhibitors therapy vs H2 receptor antagonists therapy for upper gastrointestinal bleeding after endoscopy: a meta-analysis. World J Gastroenterol. 2015;21(20):6341–51.
10. Cooper GS, Chak A, Way LE, et al. Early endoscopy in upper gastrointestinal hemorrhage: associations with recurrent bleeding, surgery, and length of hospital stay. Gastrointest Endosc. 1999;49:145–52.
11. Tai CM, Huang SP, Wang HP, et al. High-risk ED patients with nonvariceal upper gastrointestinal hemorrhage undergoing emergency or urgent endoscopy: a retrospective analysis. Am J Emerg Med. 2007;25:273–8.
12. Laine L, Peterson WL. Bleeding peptic ulcer. N Engl J Med. 1994;331:717–27.
13. Laine L, McQuaid KR. Endoscopic therapy for bleeding ulcers: an evidence-based approach based on

meta-analyses of randomized controlled trials. Clin Gastroenterol Hepatol. 2009;7:33–47.
14. Bleau B, Gostout C, Sherman K, et al. Recurrent bleeding from peptic ulcer associated with adherent clot: a randomized study comparing endoscopic treatment with medical therapy. Gastrointest Endosc. 2002;56:1–6.
15. Kahi CJ, Jensen DM, Sung JJ, et al. Endoscopic therapy versus medical therapy for bleeding peptic ulcer with adherent clot: a meta-analysis. Gastroenterology. 2005;129(3):855–62.
16. Jones DB, Brunt LM, Feldman LS, Mikami DJ, Robinson TN, Jones SB. Safe energy use in the operating room. Curr Probl Surg. 2015;52(11):447–68.
17. Brandler J, Baruah A, Zeb M, et al. Efficacy of over-the-scope clips in management of high-risk gastrointestinal bleeding. Clin Gastroenterol Hepatol. 2018;16(5):690–696.e1.
18. Nunoue T, Takenaka R, Hori K, et al. A randomized trial of monopolar soft-mode coagulation versus heater probe thermocoagulation for peptic ulcer bleeding. J Clin Gastroenterol. 2015;49(6):472–6.
19. Chen YI, Barkun A, Nolan S. Hemostatic powder TC-325 in the management of upper and lower gastrointestinal bleeding: a two-year experience at a single institution. Endoscopy. 2015;47(2):167–71.
20. Arena M, Masci E, Eusebi LH, et al. Hemospray for treatment of acute bleeding due to upper gastrointestinal tumors. Dig Liver Dis. 2017;49(5):514–7.
21. Sung JJ, Lau JY, Ching JY, et al. Continuation of low-dose aspirin therapy in peptic ulcer bleeding: a randomized trial. Ann Intern Med. 2010;152:1–9.
22. Saltzman JR, Tabak YP, Hyett BH, et al. A simple risk score accurately predicts in-hospital mortality, length of stay, and cost in acute upper GI bleeding. Gastrointest Endosc. 2011;74:1215–24.
23. Choudari CP, Rajgopal C, Palmer KR. Acute gastrointestinal haemorrhage in anticoagulated patients: diagnoses and response to endo- scopic treatment. Gut. 1994;35:464–6.
24. Wolf AT, Wasan SK, Saltzman JR. Impact of anticoagulation on rebleeding following endoscopic therapy for nonvariceal upper gastrointestinal hemorrhage. Am J Gastroenterol. 2007;102:290–6.

Interventional Radiology in GI Hemorrhage

42

Christopher Nicholas

Introduction

Both upper and lower gastrointestinal hemorrhage are frequently encountered in the acute care setting and typically require ongoing collaboration between emergency medicine, internal medicine, surgery, and radiology throughout the various phases of a patient's care. This chapter will focus on the assessment and treatment of adult patients with acute upper or lower gastrointestinal (GI) hemorrhage, under the presumption that the patient is presenting acutely and requires urgent or emergent inpatient intervention. We will explore the topic through a multidisciplinary lens with a specific focus on minimally invasive image-guided endovascular therapy performed by interventional radiology (IR), a subspecialty of radiology that many students and physicians alike consider unfamiliar or esoteric.

Gastrointestinal hemorrhage disproportionately affects males (male:female, 2:1) and the elderly [1]. One can expect that as our population continues to age and more individuals are living longer, GI hemorrhage will only become a more commonly encountered clinical scenario. Considering the fact that upper GI bleeds alone account for an estimated 20,000 deaths in the United States annually [2], knowledge of treatment paradigms and the role of each discipline involved in a patient's often complex hospital course is paramount.

GI hemorrhage can be divided into two categories: upper and lower. An upper GI bleed (UGIB) is typically defined as any source of hemorrhage that originates proximal to the ligament of Treitz (i.e., esophagus, stomach, duodenum), while a lower GI bleed (LGIB) is considered anything originating distal to this (i.e., jejunum, ileum, colon, rectum, anus). As the GI tract includes many different structures, the origin of bleeding can vary quite considerably. While not exhaustive, common etiologies for acute upper and lower GI hemorrhage can be found in Fig. 42.1. In addition to categorizing bleeding sources into upper versus lower, it is helpful to further categorize the origin into variceal versus non-variceal, as this will radically alter the approach for endovascular therapies.

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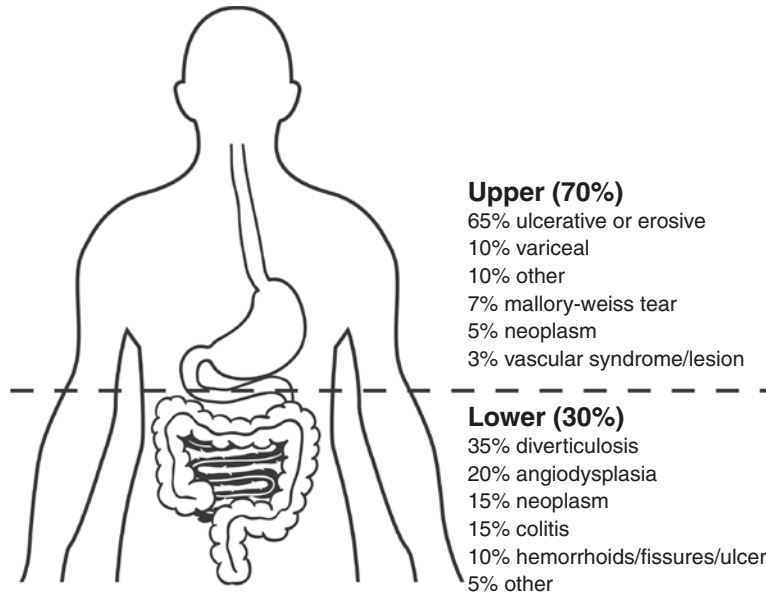

Fig. 42.1 Common etiologies of GI hemorrhage. (Adapted from Lee and Laberge [1])

Treatment Approach

As with many areas of medicine, treatment strategies usually follow a "least invasive to most invasive" paradigm, provided the patient is hemodynamically stable (see Fig. 42.2). Initially, the patient should be medically optimized which includes correcting underlying coagulation parameters to ensure the success of future hemostatic endeavors. While every institution differs, the first-line intervention after medical optimization is typically endoscopy. In the clinical setting suggestive of UGIBs, endoscopy can be both diagnostic (differentiating variceal vs non-variceal) and therapeutic. Common endoscopic therapies include injection (e.g., sclerosant, epinephrine), thermal (i.e., coagulation), and mechanical (e.g., banding, clips) [3]. These are discussed in further detail in the previous chapter.

In LGIBs, either upper or lower endoscopy can be entertained initially, since brisk UGIBs can masquerade as a LGIB [1]. Many suggest placing an NG tube and aspirate to look for blood products. Presence of blood products would prompt one to start with upper endoscopy first [4]. A caveat to the above is that many times, patients end up undergoing cross-sectional imag-

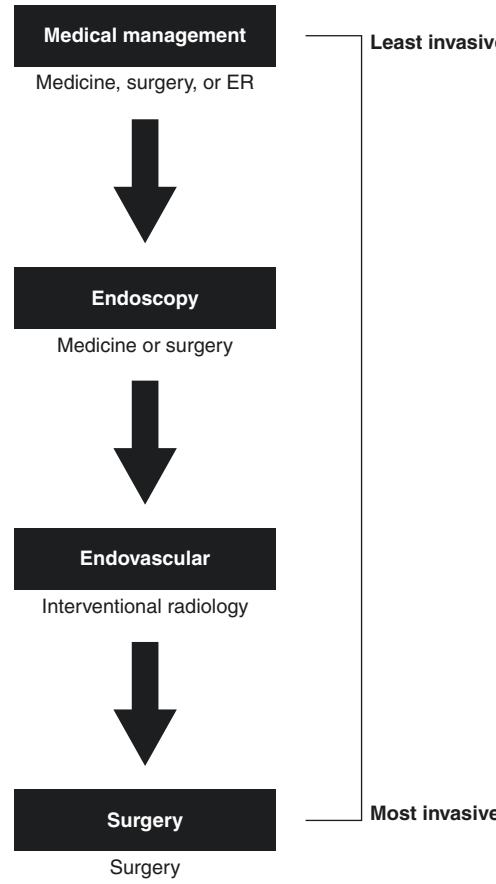

Fig. 42.2 GI bleed interventions and the services responsible, ordered from least invasive to most invasive

ing on presentation which can oftentimes determine the site of pathology and hence direct therapy accordingly, whether it be endoscopic, endovascular, or surgical.

In the event endoscopy identifies the source of bleeding but fails to stop the bleeding for technical reasons, endovascular therapy by interventional radiology can be considered. Sometimes endoscopy may not identify the source of bleeding. In both of these cases (provided that the patient is stable enough), the author recommends a multiphase CT scan for procedural planning and diagnostic troubleshooting, respectively. In the event that endovascular therapy by IR fails to stop the hemorrhage or fails to identify the source, surgical exploration can be considered. An example treatment algorithm at our institution can be seen in Fig. 42.3.

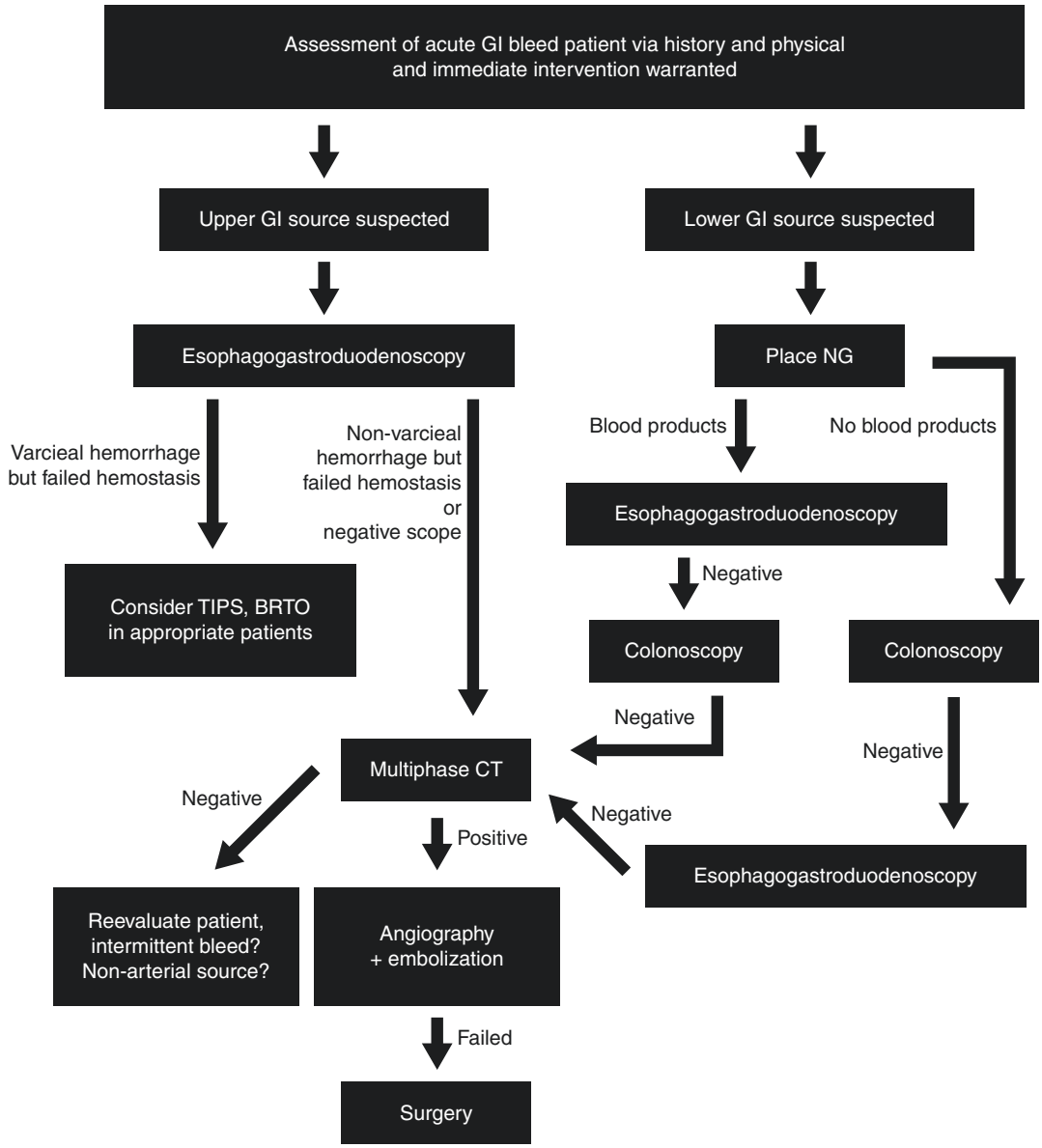

Fig. 42.3 Treatment algorithm for acute GI hemorrhage based on our institution

An exception to the "endoscopy first" guideline may be encountered in patients who are massively bleeding and are hemodynamically unstable. Specifically, for LGIB patients the absence of bowel preparation can severely limit the utility of colonoscopy [5]. If bowel preparation is administered in anticipation for colonoscopy, this can delay treatment, which oftentimes is not acceptable in the unstable patient. In this scenario, interventional radiology or surgery is often consulted prior to endoscopy. Clinical judgment must always be used and there are always exceptions to algorithms. Furthermore, clear, expeditious communication among all the services mentioned is of the utmost importance in scenarios where time is precious.

Interventional Radiology

When an interventional radiologist is consulted for an upper GI bleeding case, they must differentiate variceal from non-variceal hemorrhage, as they are treated radically differently. While this often can be accomplished with multiphase CT, endoscopy typically has already been performed and has made this distinction. Treatment has often already been attempted via endoscopy as well. From an IR standpoint, variceal hemorrhage can be treated via placement of a transjugular intrahepatic portosystemic shunt (TIPS) to lower portal pressure with or without balloon-occluded retrograde transvenous obliteration (BRTO) of the bleeding varix itself. These therapies are discussed in further detail in other chapters, and we will focus on embolization as a treatment for arterial hemorrhage in this chapter. With respect to arterial hemorrhage, vasopressin infusion has been waning in popularity in recent years in favor of embolization [6]. It should be noted that venous sources of bleeding are not treated with arterial embolization, emphasizing the point that embolization via IR cannot be viewed as a catchall therapy for every GI hemorrhage case.

We have established that in most treatment algorithms, endoscopy is the universally accepted initial intervention. With failed endoscopy, embolization is usually next pursued, with conventional surgery used as a bailout [1]. In comparison, endovascular therapy by IR for non-variceal UGIB has been shown to have similar or slightly higher chances of re-bleeding than surgery but is less invasive, although no studies have demonstrated a significant mortality difference. Some have pointed out that patients selected for IR procedures tend to have more comorbidities (i.e., they are worse conventional surgical candidates), which may confound this lack of difference in mortality. Nonetheless, embolization has been well established as an alternative to surgery with similar outcomes in difficult patients [7]. In the case of failed embolization, decision for IR to attempt embolization again versus taking the patient to surgery depends on multiple factors, particularly how stable the patient is. In our experience, repeat CT angiography is helpful in these situations for troubleshooting.

Embolization

Embolization is the purposeful obstruction of a blood vessel, in this case to achieve hemostasis. Embolization by IR can be performed for arterial UGIBs as well as LGIBs, with similar technique for both. The difference lies only in where the treatment is rendered with respect to the target vessel. Prior to embolization of a bleeding artery, an interventional radiologist must first identify and subsequently navigate a catheter to the offending artery from inside the arterial system. This is accomplished angiographically and begins by first gaining arterial access by entering the lumen of an artery with a needle, usually via an ultrasound-guided puncture of a common femoral artery or the left radial artery. A floppy tip wire is placed through the needle as a placeholder of sorts, the needle is removed, and a hollow vascular sheath is placed as an access port. Various permutations of this "needle-wire-catheter" technique for vascular access have been in use since the mid-twentieth century [8]. With multiple wires and catheters available, the opera-

tor can navigate to the aorta and into various visceral vessels under fluoroscopy. The vessels' courses are inferred, as they cannot be seen directly under x-ray. Dense iodinated contrast can be injected through the catheter in use to opacify the vessels on imaging, which not only provides a road map of the arterial anatomy but can also demonstrate extravasation of contrast. Contrast extravasation is indicative of active hemorrhage and hence where embolization efforts should be directed. There are a variety of embolization techniques that can be utilized, including but not limited to metallic coil placement, cyanoacrylate ("glue") injection, particle/microsphere injection, and absorbable gelatin sponge (common trade names include Gelfoam by Pfizer or Surgifoam by Ethicon). The choice of embolic agent is beyond the scope of this passage. Examples of upper and lower GI bleed embolization cases can be seen in Figs. 42.4 and 42.5, respectively.

Use of Computed Tomography (CT)

In recent years many institutions have incorporated CT angiography (CTA) into management pathways [5]. At our institution when time/patient stability permits, we will routinely perform a multiphase CT prior to attempting embolization. Our CT protocol includes a non-contrast phase to assess for preexisting hyperdense material/structures that may be confused for extravasated contrast media on subsequent post-contrast phases, an arterial phase to look for active arterial extravasation/hemorrhage, and a portal venous phase looking for pooling of blood. Oral contrast should not be administered as this will impede detection of IV contrast extravasation.

Multiphase CT prior to embolization has multiple justifications. First, CT can detect bleeding occurring at rates as low as 0.3 ml/min, compared to conventional angiography at 0.5 ml/min [9]. Therefore, if active bleeding cannot be seen on CTA, logically it will not be seen on conventional angiography which, if performed, would subject the patient to the risks of an invasive procedure without the benefit of identifying the embolization target. Intermittent arterial bleeding can, however, cause a diagnostic dilemma [10]. While "catching" an active bleed on CTA may be fraught with the same pitfalls as trying to catch it on endoscopy or conventional angiography, CTA is generally easier to obtain and less invasive than both of the aforementioned. Another indispensable use of CTA is for preprocedure planning. CT angiography will provide a road map of the vascular anatomy as well as the site of active hemorrhage beforehand, allowing the interventional radiologist to formulate an efficient, targeted treatment plan ahead of time. This has been shown to translate into reduced angiographic procedure times [11]. Anecdotally, we feel that hasty intraprocedural decision-making is mitigated, potentially minimizing operator error. Finally, CT can provide a diagnosis for many of the common causes of bleeding including but not limited to diverticulosis, angiodysplasia, colitis, and neoplasm [5].

Patients with GI hemorrhage are often medically complex, volume depleted, and in turn prone to renal failure. On this note, one must keep in mind that conventional angiography and CTA both require the administration of iodinated intravascular contrast, which is associated with contrast-induced nephropathy (CIN). From a multidisciplinary standpoint, nephrology is often involved for these reasons. While the best treatment for CIN is prevention (i.e., not administering unnecessary contrast media) [12], in the hemorrhaging patient, hemostasis generally takes precedence over potential for renal failure. In patients with poor renal function, the decision to perform CTA versus going straight to conventional angiography is controversial. It is the author's opinion that CT angiography will yield much more information, including exactly which vessel is bleeding, and therefore allow the interventionalist to formulate a highly targeted treatment plan (arterial access, go straight to bleeding vessel, embolize, close), saving both time and contrast media. Operator preferences may differ and the decision must be made on a case-by-case basis.

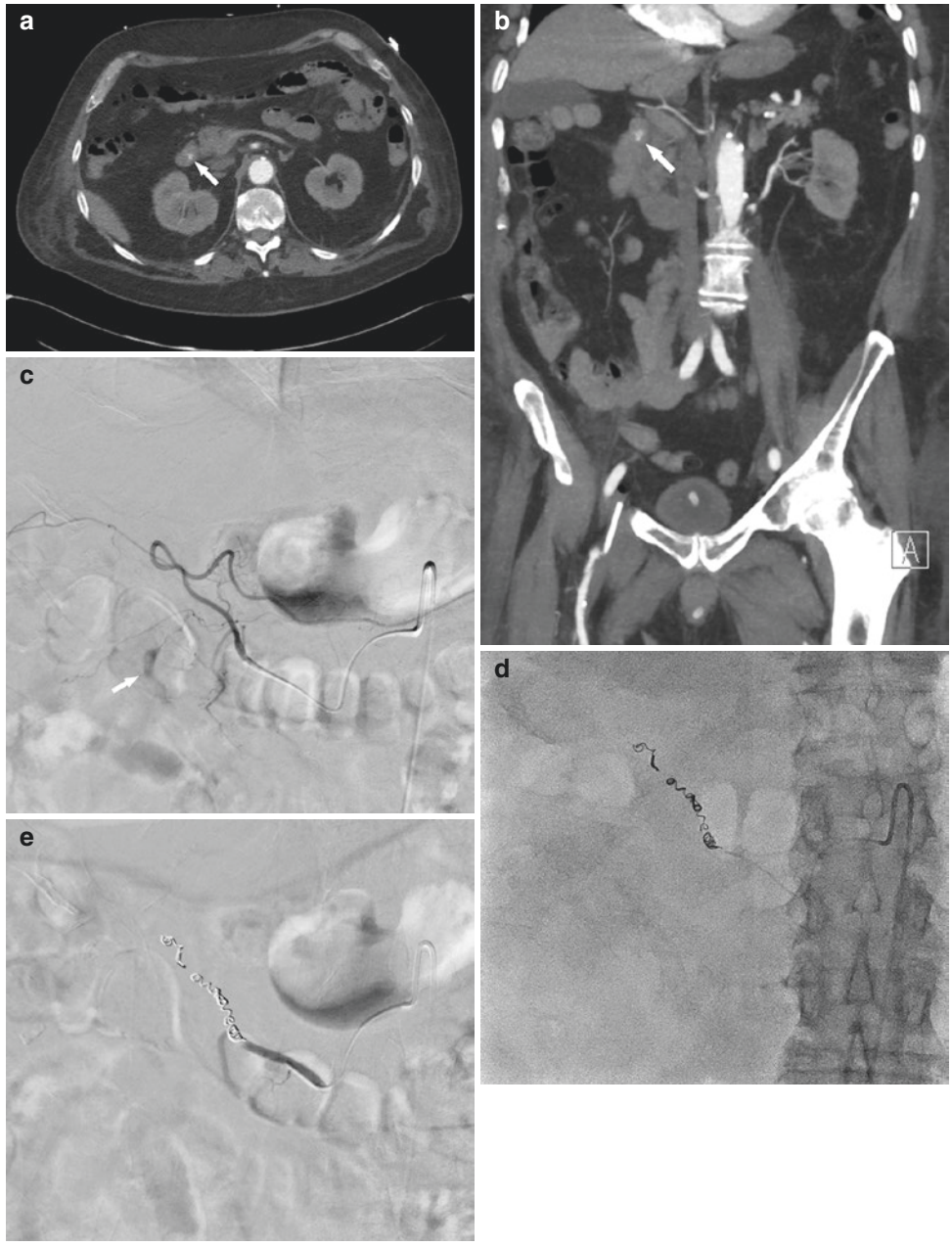

Fig. 42.4 Example of upper GI bleed from inferior pancreaticoduodenal artery with subsequent coil embolization. Axial (**a**) and coronal (**b**) CT images of the abdomen and pelvis show extravasation of contrast into the duodenum (arrows). The patient was taken to the angiography suite for angiography and embolization. Right common femoral artery access was achieved, the SMA was selected with reverse curve base catheter, and microcatheter (placed through the base catheter) was used to super select the inferior pancreaticoduodenal artery. Digital subtraction angiography (DSA) from the inferior pancreaticoduodenal artery (**c**) shows active contrast extravasation from a small branch (arrow), correlating with CT findings. Fluoroscopic image (**d**) shows coils deployed in the inferior pancreaticoduodenal artery. Final DSA image (**e**) demonstrates successful occlusion of the vessel and cessation of hemorrhage. Images courtesy of Dr. Jonathan Marshall, DO

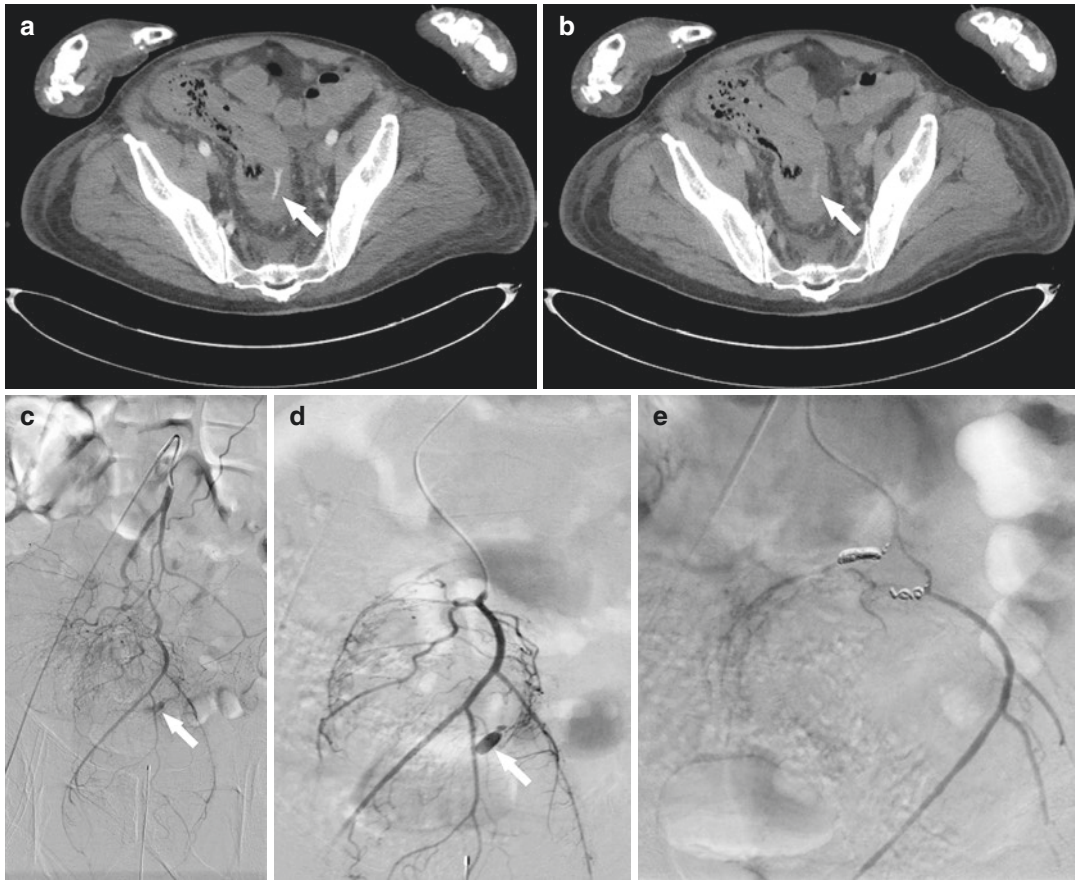

Fig. 42.5 Example of lower GI bleed from superior rectal artery with subsequent coil embolization. Axial arterial (**a**) and venous (**b**) phase CT images of the pelvis show contrast extravasation into the rectum (arrows). Note how the contrast pools on the more delayed venous phase image, appearing less dense than the earlier arterial phase image. Patient was brought to the angiography suite and right common femoral artery access achieved. Reverse curve base catheter used to select the inferior mesenteric artery (IMA). DSA from the IMA (**c**) shows active extravasation of contrast from a branch of the superior rectal artery (arrow). A microcatheter was used to super select the superior rectal artery. DSA with catheter in closer proximity to the site of hemorrhage (**d**) yields better detail, showing bleeding pseudoaneurysm (arrow). Interrogation of multiple branches with microcatheter determined supply was via two branches which were both coil embolized. Final DSA image shows successful occlusion of offending vessels and cessation of active hemorrhage (**e**)

Summary

Managing acute upper and lower GI hemorrhage is a common situation that requires collaboration and input from multiple disciplines including emergency medicine, internal medicine, radiology, and surgery. Conventional medical school rotations generally lack core rotations in IR, and therefore many students (and physicians even) may have limited understanding of IR's role. This chapter reviews that topic, with specific emphasis on embolization for arterial hemorrhage. After optimal medical management, endoscopy is usually the first-line intervention for both upper and lower GI bleeds. Arterial embolization is a minimally invasive alternative to surgery generally performed in the setting of failed endoscopy. It is not a treatment for venous/variceal hemorrhage. Multiphase CT to establish source of bleeding is becoming an accepted diagnostic step prior to

embolization. Conventional surgery should be considered in the setting of failed embolization(s) and continued hemorrhage in an unstable patient.

References

1. Lee EW, Laberge JM. Differential diagnosis of gastrointestinal bleeding. Tech Vasc Interv Radiol. 2005;7:112–22.
2. El-Tawil AM. Trends on gastrointestinal bleeding and mortality: where are we standing? World J Gastroenterol. 2012;18(11):1154–8.
3. Kim JS, Park SM, Kim BW. Endoscopic management of peptic ulcer bleeding. Clin Endosc. 2015;48:106–11.
4. ASGE Standards of Practice Committee. The role of endoscopy in the patient with lower GI bleeding. Gastrointest Endosc. 2014;79(6):875–85.
5. Reis FRS, Cardia PP, D'Ippolito G. Computed tomography angiography in patients with active gastrointestinal bleeding. Radiol Bras. 2015;48(6):381–90.
6. Funaki B. On-call treatment of acute gastrointestinal hemorrhage. Semin Intervent Radiol. 2006;23(3):215–22. https://doi.org/10.1055/s-2006-948758.
7. Mirsadraee S, Tirukonda P, Nicholson A, Everett SM, McPherson SJ. Embolization for non-variceal upper gastrointestinal tract haemorrhage: a systematic review. Clin Radiol. 2011;66:500–9.
8. Seldinger SI. Catheter replacement of the needle in percutaneous arteriography: a new technique. Acta Radiol. 1953. Reprinted in American Journal of Roentgenology. 1984;142:5–7. https://doi.org/10.2214/ajr.142.1.5.
9. Wu LM, Xu JR, Yin Y, Qu XH. Usefulness of CT angiography in diagnosing acute gastrointestinal bleeding: a meta-analysis. World J Gastroenterol. 2010;16(31):3957–63.
10. Geffroy Y, Rodallec MH, Boulay-Coletta I, Jullès MC, Ridereau-Zins C, Zins M. Multidetector CT angiography in acute gastrointestinal bleeding: why, when, and how. Radiographics. 2011;31(3):E35–46.
11. Storace M, Martin JG, Shah J, Bercu Z. CTA as an adjuvant tool for acute intra-abdominal or gastrointestinal bleeding. Tech Vasc Intervent Radiol. 2017;20:248–57.
12. Mohammed NMA, Mahfouz A, Achkar K, Rafie IM, Hajar R. Contrastinduced nephropathy. Heart Views. 2013;14(3):106–16.

Part XVI

Empyema

Empyema: Incidence and Medical Management

43

Kinsley Hubel and Jessica Bunin

Incidence and Epidemiology

Pleural effusions result when fluid accumulates between the visceral and parietal pleura. The fluid accumulation develops due to dilated capillary beds allowing neutrophils and monocytes into the pleural space. The presence of neutrophils and monocytes leads to an increase in inflammatory cytokines which increases the vascular permeability further drawing fluid into the pleural space, called an uncomplicated parapneumonic effusion [1–5]. If the parapneumonic effusion becomes infected as a result of microbial migration, it becomes a complicated parapneumonic effusion [4]. If pleural fluid cultures are positive or there is frankly purulent fluid aspirated from pleural space, it is defined as an empyema [4]. There are approximately 80,000 cases of empyema annually combined between the United States and the United Kingdom [1]. Up to 57% of patients with bacterial pneumonia will develop a pleural effusion, and 20–40% will develop an empyema [1–4] (see Fig. 43.1).

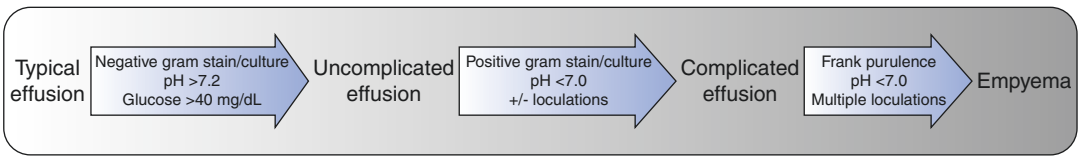

Fig. 43.1 Transition of parapneumonic effusion to empyema

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Risk Factors

Common risk factors for developing empyema include [1, 3, 5–7]:

- Chronic lung disease (i.e., chronic obstructive pulmonary disease)
- Immunosuppression (human immunodeficiency virus, diabetes mellitus, chronic excessive alcohol intake, chronic steroid use, smoking, immunoglobulin deficiency)
- Intravenous drug use
- Malnutrition
- Aspiration
- Post thoracic surgery
- Thoracic trauma (blunt trauma, esophageal perforation)

Clinical Presentation

Patients with empyema will initially present with features consistent with pneumonia including shortness of breath, productive cough, fever, night sweats, and dull or pleuritic chest pain [1, 3, 7, 8]. Older patients may present primarily with weight loss, cough, or anemia. Empyema should be considered in patients who have pneumonia that has failed to respond to antibiotics. If they have pneumonia with a persistent fever, leukocytosis, or C-reactive protein (CRP) elevation, they should also be considered [4, 9].

Table 43.1 Differential diagnosis for empyema [7, 8]

Uncomplicated parapneumonic effusion
Hemothorax
Hepatic hydrothorax
Malignancy (lung, breast, ovarian, lymphoma)
Pulmonary embolism
Esophageal rupture
Uremia
Nephrotic syndrome
Heart failure
Benign asbestos pleural effusion
Autoimmune pleural effusion (systemic lupus or rheumatoid arthritis)

Patients will likely be hypoxic, tachypneic, and febrile and may be hemodynamically unstable [7, 9, 10]. Exam findings consistent with a pleural effusion will be present including decreased breath sounds on the affected side, pleural friction rub, decreased tactile fremitus, decreased vocal resonance, dullness to percussion, and asymmetric chest expansion. Obstructive shock physiology may develop in the setting of a large empyema. There are many case reports of patients developing pericardial tamponade physiology in the setting of large empyemas due to external compression from the empyema (Table 43.1).

Diagnostic Evaluation

The initial diagnostic evaluation begins with a posterior-anterior (PA) chest x-ray [1, 7, 8] (see Fig. 43.2). The next step traditionally has been obtaining a lateral decubitus x-ray; however, bedside ultrasound has become more common over the past 15 years due to improved sensitivity and specificity in evaluating the possible effusion [9, 11–13]. The authors recommend proceeding directly to bedside ultrasound once there is suspicion for a pleural effusion. Ultrasound provides more information about the quality and nature of the effusion, if it is free-flowing or loculated and if there is a collection of fluid that would be amenable to a diagnostic or therapeutic thoracentesis [1, 8, 11, 12, 14].

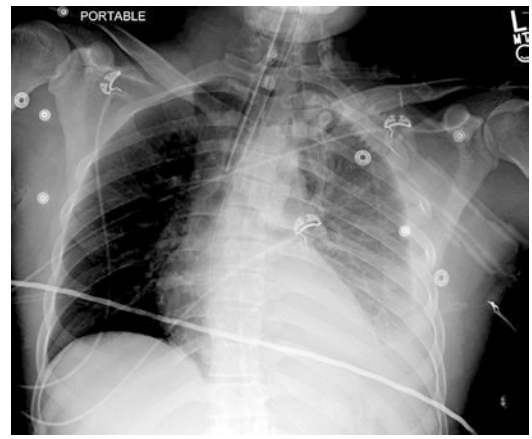

Fig. 43.2 Portable anterior-posterior view of chest x-ray in a patient with empyema

Computed tomography (CT) of the chest is better able to distinguish lung parenchyma that is compressed due to empyema [8, 11–13]. Thickened pleura is noted in 86–100% of patients with empyema. A CT chest with IV contrast is useful when patients present with loculated effusions [15]. It may also help differentiate between malignant effusion, empyema, and lung abscess [15, 16] (see Fig. 43.3).

Thoracentesis should be performed to evaluate the effusion to determine if an infectious organism is present. Table 43.2 contains the indicated tests to perform on the pleural fluid.

Blood cultures should also be obtained [1, 10]. Leukocytosis and CRP levels may be used to monitor response to treatment [1, 9]. Serum labs should also be collected at the same time as the pleural fluid. The recommended serum labs include total protein, lactate dehydrogenase (LDH), and glucose. Light's criteria are used to differentiate between transudative and exudative effusions [17]. The most common cause of a transudative pleural effusion is heart failure. Exudative effusions are usually due to infection, malignancy, or pulmonary embolisms. Light's criteria are calculated based upon differences between the amount of protein and LDH in the serum and pleural fluid samples [17]. Using Light's criteria the effusion will be exudative if it is an empyema and should appear purulent on aspiration. Table 43.3 summarizes Light's criteria [17].

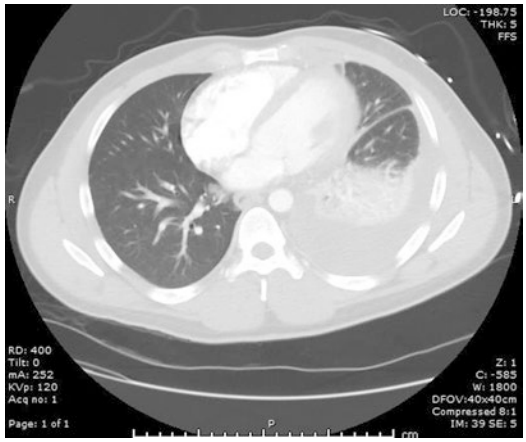

Fig. 43.3 Computed tomography of the chest without contrast in a patient with an empyema

Table 43.2 Pleural fluid testing

Cell count with differential	Total protein
Glucose	Lactate dehydrogenase
pH (on point of care testing)	Gram stain and culture[a]
Cytology	Fungal cultures (if suspected)
Acid-fast bacilli cultures (if suspected)	Adenosine deaminase (if indicated)

[a]Using blood culture bottles increases the culture yield

Table 43.3 Light's criteria

Exudative effusion if more than one of the following is present:
Ratio of pleural fluid to serum protein >0.5
Ratio of pleural fluid to serum LDH >0.6
Pleural fluid LDH ≥200 units

Pathogens

It is important to note that approximately 40% of pleural cultures yield no organisms despite a purulent effusion [1, 2, 9]. This may be explained by infections due to anaerobes, which are fastidious, difficult to culture organisms.

Community Acquired The most common pathogens are *Streptococcus pneumoniae* and other *Streptococcus* species, which account for 50% of empyemas with positive cultures [18, 19]. Other etiologies include methicillin-sensitive *Staphylococcus aureus* (MSSA), gram-negative organisms such as *E. coli* or *Enterobacteriaceae*, and anaerobes including *Bacteroides*, *Fusobacterium*, and *Peptostreptococcus* [1, 9, 19].

Hospital Acquired Methicillin-resistant *Staphylococcus aureus* (MRSA) accounts for one quarter of hospital-acquired empyemas [18, 19]. The combination of MSSA and gram-negative organisms such as *Pseudomonas aeruginosa*, *Klebsiella*, and *E. coli* accounts for another quarter of the hospital-acquired empyema pathogens [1, 10, 19].

Table 43.4 Light's classification of parapneumonic effusions and empyema [4]

Class	Type	Features
I	Nonsignificant parapneumonic effusion	<10 mm on decubitus x-ray
II	Typical parapneumonic effusion	>10 mm on decubitus x-ray Glucose >40 mg/dL pH >7.2 Negative gram stain/ culture
III	Borderline complicated parapneumonic effusion	pH 7.0–7.2 and/or LDH >1000 units/L Glucose >40 mg/dL Negative gram stain/ culture
IV	Simple complicated parapneumonic effusion	pH <7 Glucose <40 mg/dL Positive gram stain/ culture No loculations or purulence
V	Complex complicated parapneumonic effusion	pH <7 Glucose <40 mg/dL Positive gram stain/ culture Multiloculated
VI	Simple empyema	pH <7 Frank purulence Single locule or free-flowing
VII	Complex empyema	pH <7 Frank purulence Multiple loculations

Management

The management of parapneumonic effusions and empyemas varies based on character of the pleural fluid. Light divided parapneumonic effusions into seven categories based upon lab evaluation, the appearance of the pleural fluid, and the presence of loculations (Table 43.4) [4].

Antibiotics

Antibiotics are important in the management of all parapneumonic effusions and empyemas. They may be used as an isolated intervention in class I, nonsignificant pleural effusions, and class II, typical parapneumonic effusions [1, 4, 20]. For any complicated parapneumonic effusion or empyema, antibiotics should be used in conjunction with drainage of the effusion either through thoracentesis, tube thoracostomy, or surgical intervention such as through video-assisted thoracoscopic surgery (VATS) or open thoracotomy [4, 9, 10, 21].

Table 43.5 Empiric antibiotic regimens

Community acquired	Hospital acquired or severe disease
Beta-lactam + beta-lactamase inhibitor	Vancomycin or linezolid + piperacillin/tazobactam
Beta-lactam + metronidazole	Vancomycin or linezolid + cefepime + metronidazole
	Vancomycin or linezolid + meropenem

Antibiotics are chosen based on the local antibiogram and the culture results. Empiric therapy should be initiated based on the likely organisms. Anaerobic coverage is needed if there has been trauma or aspiration. Table 43.5 includes empiric antibiotic regimens [1, 9, 10]. There is no formal consensus on the duration of antibiotics. Three weeks of antibiotic therapy is often recommended after drainage of the empyema, however, and the decision to discontinue therapy depends on the degree of clinical improvement, resolution of leukocytosis, and CRP normalization [1, 10, 22].

Drainage

Drainage of the effusion is indicated if the pH is <7.2, the glucose is <40 (2.2 mmol/L), the gram stain is positive, purulent fluid is aspirated, or if the patient is clinically deteriorating [1, 7, 9, 20]. This can be accomplished through several methods. Serial thoracentesis may be used if the fluid is not frankly purulent and if the pH is between 7.0 and 7.2 with a normal glucose [1, 9, 23]. Tube thoracostomy should be used if there are few to no loculations within the fluid collection [1, 8, 20, 21]. While there is no proven clinical benefit to a specific chest tube size, 10–14 French chest tubes are most commonly used as smaller chest tubes are less painful [24, 25]. Small- and moderate-sized chest tubes should be flushed regularly to prevent clogging. Surgical drainage

is often required if the patient has persistent features of sepsis despite antibiotics and chest tube placement [26, 27]. Early surgical intervention should be considered when there are multiple loculations with evidence of trapped lung [26, 27]. The British Thoracic Society Guidelines consider surgical intervention as second line for management of empyemas [1]. The surgical options include VATS or a thoracotomy [20, 27]. VATS should be considered if there are multiple loculations in the empyema. Open surgery is generally reserved for patients who have failed all other treatment modalities. The optimal time for surgical consultation is difficult to pinpoint as there are several factors that contribute to this determination. The clinical response to treatment, the radiographic evidence of complications, and underlying cause of the effusion all contribute to the likelihood that surgical intervention will be necessary. In general, however, one should consider consultation if there is clinical worsening in the days following drainage or if there is radiographic evidence that drainage was not successful. Surgical treatment options will be discussed further in the next chapter.

Serial Thoracentesis

Serial thoracentesis involves repeated thoracentesis with drainage of the pleural effusion. The indication for drainage is reaccumulation of the pleural fluid on imaging usually in conjunction with symptoms of the effusion [1, 23]. This method of drainage is only indicated for class III, borderline complicated, effusions [23]. A borderline complicated effusion has no loculations or purulence, and labs demonstrate a slightly reduced pH (7.0–7.2), with normal glucose and a lactate dehydrogenase (LDH) level of greater than 1000 mg/dL [4]. Several studies have demonstrated level two evidence for using serial thoracentesis in addition to appropriate antibiotics for borderline complicated parapneumonic effusions [1, 20, 23]. It is recommended to remove less than 1500 mL of fluid with each drainage to reduce risk of re-expansion pulmonary edema.

Tube Thoracostomy

Tube thoracostomy has been shown to be effective for managing both complicated parapneumonic effusions and empyemas. Tube thoracostomy should be considered in patients with borderline complicated effusions who are progressing poorly with antibiotics alone [1, 9, 20, 21]. There are several options for tube thoracostomy size in the management of empyema [1, 25, 28]. The British Thoracic Society reviewed the optimal size to be used for tube thoracostomy, and they found that there was no difference in mortality and no difference in the need for surgical intervention between large bore (15–20 French (Fr)), medium bore (10–14 Fr), and small bore (less than 10 Fr) [1, 29]. Not surprisingly tube thoracostomy is most effective in complicated effusions compared to empyemas and more effective in simple empyemas than complex empyemas [30, 31].

The chest tube, once placed, should be flushed daily with sterile saline to reduce the risk of the tube clogging. The tube may be removed when the output over 24 hours is less than 50 mL, the draining fluid is clear yellow, and the empyema cavity has closed [1, 20, 32]. In reviewing several studies, the success rates of tube thoracostomies range widely from 35% to 80% [1, 9, 20, 31, 33].

Intrapleural Therapies

Empyemas progress through three stages if not managed effectively early in the course of treatment. They begin at an exudative phase characterized by inflammatory cells. If not drained, they progress to a fibrinopurulent phase when the pleura becomes involved. Finally, the empyemas progress to an organizing phase, which is more chronic in nature. Once the empyema has reached the transitional/fibrinopurulent stage, drainage with tube thoracostomy and antibiotics is generally not sufficient to provide effective treatment. When this stage has been reached, further medical management with intrapleural fibrinolytics with or without mucolytics is necessary [1, 20, 34, 35]. The use of intrapleural fibrinolytics is

widely debated. There have been many studies including MIST I and MIST II looking at the use of intrapleural fibrinolytics [34–37]. The body of evidence does not recommend the use of intrapleural fibrinolytics alone. A Cochrane review did not find any evidence of mortality benefit or decrease in the number of patients who progressed to surgical management [27]. Other studies did show a decrease in the length of stay [34, 35]. The benefit of intrapleural therapy is seen more clearly when fibrinolytics and mucolytics, such as tPA and DNAse, are combined [36–38]. The combination results in improvement in the radiographic appearance, a decreased rate of progression to surgical intervention, and an overall decreased length of stay [35, 37–39]. The recommendation from the British Thoracic Society and American College of Chest Physicians is to administer tPA and DNAse intrapleurally twice daily for 3 days if there is evidence of ongoing fever, leukocytosis, and anorexia [1, 20].

Complications and Prognosis

Complications occur in about 25% of patients with a parapneumonic effusion or empyema [1, 18]. Approximately half of all patients (51.6%) may require operative management including operative drainage, decortication, or closure of a bronchopleural fistula [20, 32]. The common complications associated with empyema include incomplete drainage, pleural peel, sepsis, empyema necessitans, and venous thromboembolism [18, 19, 32]. A pleural peel develops when the pleura thickens as a result of the increased inflammation in the pleural space. A pleural peel may require decortication or pleurectomy if it causes a clinically significant limitation in lung re-expansion [20, 32]. Empyema necessitans refers to spread of an infectious pleural effusion to the chest wall and surrounding structures. It may develop if there is a tract for infectious spread or presence of a highly virulent pathogen.

The American College of Chest Physicians created a risk score to aid in prognostic determinations [20]. The low-risk group includes patients with effusions or empyemas that take up less than half of the hemithorax on x-ray, a pH of greater than 7.2, and a negative gram stain and culture. The overall mortality rate in patients determined to have low-risk parapneumonic effusions is 10.8% [20, 32]. The high-risk group includes patients with a large effusion (greater than half of the hemithorax), any loculations or septations, a pH of less than 7.2, a positive culture, and the presence of purulence [20, 32]. The mortality rate also varies based on the infectious organism. Community-acquired streptococcal infections have the lowest 30-day mortality rate of 17% [19, 20]. However, gram-negative organisms, *Staphylococcus aureus*, and hospital-acquired infections have a mortality rate of greater than 44% [18, 19, 32].

Summary

In summary, pleural effusions are common in patients with bacterial pneumonia and of those approximately one quarter to one half will develop an empyema. Patients who have developed an empyema will often have progressive symptoms despite antibiotic therapy. Thoracentesis with both pleural fluid and serum laboratory testing should be completed to diagnose the empyema and determine the causative organism. Light's criteria are used to determine if the effusion is an exudative effusion. Depending on the presence of bacterial growth in pleural fluid, the presence of loculations, and the patient's clinical status, the empyema will need to be drained using serial thoracentesis, tube thoracostomy, or surgical intervention. Earlier drainage before the fibrinopurulent phase may prevent the need for an operative intervention.

References

1. Davies HE, Davies RJ, Davies CW. Management of pleural infection in adults: British Thoracic Society pleural disease guideline 2010. Thorax. 2010;65(Suppl 2):ii41–53.
2. Grijalva CG, Zhu Y, Nuorti JP, Griffin MR. Emergence of parapneumonic empyema in the USA. Thorax. 2011;66(8):663–8.

3. Wrightson JM, Davies RJ. The approach to the patient with a parapneumonic effusion. Semin Respir Crit Care Med. 2010;31(6):706–15.
4. Light RW. A new classification of parapneumonic effusions and empyema. Chest. 1995;108(2):299–301.
5. Light RW, Girard WM, Jenkinson SG, George RB. Parapneumonic effusions. Am J Med. 1980;69(4):507–12.
6. Wong CL, Holroyd-Leduc J, Straus SE. Does this patient have a pleural effusion? JAMA. 2009;301(3):309–17.
7. Koegelenberg CF, Diacon AH, Bolliger CT. Parapneumonic pleural effusion and empyema. Respiration. 2008;75(3):241–50.
8. Yu H. Management of pleural effusion, empyema, and lung abscess. Semin Interv Radiol. 2011;28(1):75–86.
9. Na MJ, Dikensoy O, Light RW. New trends in the diagnosis and treatment in parapneumonic effusion and empyema. Tuberkuloz ve toraks. 2008;56(1):113–20.
10. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44(Supplement_2):S27–72.
11. Hooper C, Lee YC, Maskell N. Investigation of a unilateral pleural effusion in adults: British Thoracic Society pleural disease guideline 2010. Thorax. 2010;65(Suppl 2):ii4–17.
12. Kearney SE, Davies CW, Davies RJ, Gleeson FV. Computed tomography and ultrasound in parapneumonic effusions and empyema. Clin Radiol. 2000;55(7):542–7.
13. Svigals PZ, Chopra A, Ravenel JG, Nietert PJ, Huggins JT. The accuracy of pleural ultrasonography in diagnosing complicated parapneumonic pleural effusions. Thorax. 2017;72(1):94–5.
14. Diacon AH, Brutsche MH, Soler M. Accuracy of pleural puncture sites: a prospective comparison of clinical examination with ultrasound. Chest. 2003;123(2):436–41.
15. Aquino SL, Webb WR, Gushiken BJ. Pleural exudates and transudates: diagnosis with contrast-enhanced CT. Radiology. 1994;192(3):803–8.
16. Leung AN, Muller NL, Miller RR. CT in differential diagnosis of diffuse pleural disease. AJR Am J Roentgenol. 1990;154(3):487–92.
17. Light RW, Macgregor MI, Luchsinger PC, Ball WC Jr. Pleural effusions: the diagnostic separation of transudates and exudates. Ann Intern Med. 1972;77(4):507–13.
18. Marks DJB, Fisk MD, Koo CY, Pavlou M, Peck L, Lee SF, et al. Thoracic empyema: a 12-year study from a UK tertiary cardiothoracic referral Centre. PLoS One. 2012;7(1):e30074.
19. Maskell NA, Batt S, Hedley EL, Davies CW, Gillespie SH, Davies RJ. The bacteriology of pleural infection by genetic and standard methods and its mortality significance. Am J Respir Crit Care Med. 2006;174(7):817–23.
20. Colice GL, Curtis A, Deslauriers J, Heffner J, Light R, Littenberg B, et al. Medical and surgical treatment of parapneumonic effusions: an evidence-based guideline. Chest. 2000;118(4):1158–71.
21. Light RW. The management of parapneumonic effusions and empyema. Curr Opin Pulm Med. 1998;4(4):227–9.
22. Parapneumonic effusion and empyema in adults [Internet]. Ipswich: EBSCO Information Services; 1995 (updated 2017 Jun 15) [cited 2018 April]. Record no. 435308. Available from: http://www.dynamed.com/login.aspx?direct=true&site=DynaMed&id=435308
23. Simmers TA, Jie C, Sie B. Minimally invasive treatment of thoracic empyema. Thorac Cardiovasc Surg. 1999;47(2):77–81.
24. Kesieme EB, Dongo A, Ezemba N, Irekpita E, Jebbin N, Kesieme C. Tube thoracostomy: complications and its management. Pulm Med. 2012;2012:256878.
25. Mahmood K, Wahidi MM. Straightening out chest tubes: what size, what type, and when. Clin Chest Med. 2013;34(1):63–71.
26. Espinosa CM, Fallat ME, Woods CR, Weakley KE, Marshall GS. An approach to the management of pleural empyema with early video-assisted thoracoscopic surgery and early transition to oral antibiotic therapy. Am Surg. 2016;82(4):295–301.
27. Redden MD, Chin TY, van Driel ML. Surgical versus non-surgical management for pleural empyema. Cochrane Database Syst Rev. 2017;(3):CD010651.
28. Rahman NM, Maskell NA, Davies CW, Hedley EL, Nunn AJ, Gleeson FV, et al. The relationship between chest tube size and clinical outcome in pleural infection. Chest. 2010;137(3):536–43.
29. Havelock T, Teoh R, Laws D, Gleeson F, Group BTSPDG. Pleural procedures and thoracic ultrasound: British Thoracic Society pleural disease guideline 2010. Thorax. 2010;65(Suppl 2):ii61–76.
30. Keeling AN, Leong S, Logan PM, Lee MJ. Empyema and effusion: outcome of image-guided small-bore catheter drainage. Cardiovasc Intervent Radiol. 2008;31(1):135–41.
31. Shankar S, Gulati M, Kang M, Gupta S, Suri S. Image-guided percutaneous drainage of thoracic empyema: can sonography predict the outcome? Eur Radiol. 2000;10(3):495–9.
32. Farjah F, Symons RG, Krishnadasan B, Wood DE, Flum DR. Management of pleural space infections: a population-based analysis. J Thorac Cardiovasc Surg. 2007;133(2):346–51.
33. Liu YH, Lin YC, Liang SJ, Tu CY, Chen CH, Chen HJ, et al. Ultrasound-guided pigtail catheters for drainage of various pleural diseases. Am J Emerg Med. 2010;28(8):915–21.
34. Cameron R, Davies HR. Intra-pleural fibrinolytic therapy versus conservative management in the treatment of adult parapneumonic effusions and empyema. Cochrane Database Syst Rev. 2008;(2):CD002312.

35. Nie W, Liu Y, Ye J, Shi L, Shao F, Ying K, et al. Efficacy of intrapleural instillation of fibrinolytics for treating pleural empyema and parapneumonic effusion: a meta-analysis of randomized control trials. Clin Respir J. 2014;8(3):281–91.
36. Maskell NA, Davies CW, Nunn AJ, Hedley EL, Gleeson FV, Miller R, et al. U.K. controlled trial of intrapleural streptokinase for pleural infection. N Engl J Med. 2005;352(9):865–74.
37. Rahman NM, Maskell NA, West A, Teoh R, Arnold A, Mackinlay C, et al. Intrapleural use of tissue plasminogen activator and DNase in pleural infection. N Engl J Med. 2011;365(6):518–26.
38. Brito V, Nair GB, Brar N. New treatments for idiopathic pulmonary fibrosis, empyema, and chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2012;185(6):680–1.
39. Janda S, Swiston J. Intrapleural fibrinolytic therapy for treatment of adult parapneumonic effusions and empyemas: a systematic review and meta-analysis. Chest. 2012;142(2):401–11.

Surgical Management of Acute Empyema

44

Dylan Russell and Neil Stockmaster

Introduction

Empyema is "pus in the chest." There are many causes to include bacterial pneumonia, malignancies, traumatic injuries, mediastinal pathology, and extension from an infradiaphragmatic source. It is most commonly a complication of bacterial pneumonia and subsequent parapneumonic effusion. It is also the most common complication of pneumonia. A parapneumonic effusion is a pleural effusion secondary to pneumonia. When the parapneumonic effusion is found to grow positive bacterial cultures, it is known as a complicated parapneumonic pleural effusion. It is known as an empyema when the pleural effusion is a purulent, thick, and viscous. In the United States, approximately one million patients per year will be hospitalized with pneumonia. Approximately 20–40% of these patients will develop a parapneumonic effusion; 5–25% of these patients will progress further to empyema [9]. Approximately, 15% of patients with an empyema die, and another 30% require surgical drainage. The incidence of empyema was initially declining after the introduction of antibiotics in the 1940s. However, since the 1990s, the worldwide incidence of empyema has been reportedly increasing yet again. The etiology of this resurgence is likely multifactorial and requires further investigation. An understanding of the appropriate management for this disease process will be critical for any acute care surgeon [2].

Diagnosis

There are three stages in the natural course of empyema: the exudative, fibrinopurulent, and organizing phases. These were originally defined in 1961 [17]. In the exudative (acute) stage, the fluid is thin and often sterile. Pleural inflammation allows for increased capillary permeability and therefore a small fluid collection. This stage only lasts 24–72 hours. The fibrinopurulent stage results from organism invasion into the pleural space, followed by inflammation and polymorphonuclear (PMN) leukocyte invasion. Fibrinous loculations, partitions, and protein accumulation occur; the fluid may appear purulent and thick at this point. In the final organizing stage, a thick pleural peel is formed by fibroblast proliferation, and the parenchyma of the lung is entrapped, forming a fibrothorax. This stage occurs 2–4 weeks after presentation [5].

Pleural effusions may be detected on imaging. Aside from suspicious signs and symptoms of parapneumonic effusion in a patient's clinical presentation, imaging is likely to be the first objective evidence that a parapneumonic effusion is present. A chest X-ray is often the most

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available imaging modality. A pleural effusion is often evident on chest X-ray and manifests as blunting of the costophrenic angles. Lateral decubitus films may demonstrate dependent layering. Complex parapneumonic effusions and empyemas may fail to layer dependently due to fibrinous loculations and may result in a false-negative radiographic interpretation. Approximately 10% of pleural effusions are missed on chest X-ray [1]. Therefore, although useful, a chest X-ray should be combined with additional imaging.

Pleural ultrasound is a safe, rapid, and effective imaging modality that is available at bedside. It can be adequately performed and interpreted by practiced non-radiologists. It is at least as effective as a lateral decubitus chest X-ray in identifying small pleural effusions and better at estimating volumes [8]. This makes it a valuable and useful tool for the acute care surgeon. The benefits of contrast-enhanced computed tomography in the diagnosis of pleural effusion are primarily in its ability to detect parenchymal abnormalities and potentially ascertain the cause for a pleural effusion (malignancy, trauma, etc.). Although it cannot definitively differentiate between a simple parapneumonic effusion and an empyema, certain findings may indicate a higher likelihood of purulence. These include parietal pleural thickening, pleural enhancement due to vascular ingrowth, increased attenuation of the extrapleural fat, division of the parietal and visceral layers of the pleura (the "split pleura sign"), and locules of gas within the pleural effusion [14, 16].

When a parapneumonic effusion is suspected, a pleural fluid analysis is mandatory. It can be difficult to differentiate a complicated parapneumonic effusion or empyema from a simple effusion on clinical presentation or radiology alone. Pleural fluid analysis will therefore aid in diagnosis and direct further management. Diagnostic thoracentesis should be performed under ultrasound guidance to reduce the risk of pneumothorax. The fluid pH should be measured with an arterial blood gas analyzer within 1 hour of sampling unless the pleural fluid is frankly purulent. In addition, laboratory analysis of the pleural fluid should include glucose, LDH, Gram's stain, and culture [11].

Immediate Intervention

Removing purulent material from the pleural space is the most fundamental treatment of empyema. This should be accomplished by ongoing pleural drainage and not by thoracentesis alone. The American Association for Thoracic Surgery (AATS) Consensus Guidelines for Management of Empyema published in 2017 strongly recommends that …

> The presence of pus, positive Gram's stain, or culture in the pleural fluid establishes the diagnosis of empyema which should be treated with tube thoracostomy followed by surgical intervention when appropriate [11].

Additionally, pleural fluid laboratory analysis that demonstrates pH <7.2, LDH >1000 IU/L, or glucose <40 mg/dL or a loculated pleural effusion evident on imaging in a patient with suspected pleural space infection should also prompt a tube thoracostomy [11]. Tube thoracostomy is traditionally performed with large-bore catheters; however, no substantial evidence exists to suggest that small-bore catheters perform substantially worse. A prospective, non-randomized, unblinded, multicenter study involving 405 patients and published in 2010 found that smaller chest tubes were associated with less pain than larger tubes without a significant change in clinical outcome in the treatment of pleural infection [10]. The British Thoracic Society guidelines suggest a small-bore chest tube is sufficient for infectious effusions [4]. The AATS does not make specific recommendations regarding chest tube size. Lacking randomized controlled trials, expert opinion remains that if there is concern for overly thick purulent fluid or extensively septated effusions, a large-bore tube should probably be used.

Drain occlusion is a common cause of drain failure and necessitates frequent flushing. Approximately 20 mL sterile saline every 8–12 hours should be sufficient [6]. Dislodgement is also common. Chest X-ray or CT may be used to assess for proper positioning; CT is a more sensitive modality. Loculations that remain undrained require additional or larger drains. Fibrinolytic therapy or surgery should be consid-

ered if complete drainage is not achieved [11]. Even if fibrinolytic therapy is attempted, the surgeon should be consulted for possible surgical intervention as the data regarding efficacy of fibrinolytic therapy is inconclusive.

Surgical Management

If the patient fails to improve radiographically and clinically or if there is concern for incomplete drainage, then surgical management is necessary [4]. The surgical management of empyema can occur in one of two ways: open or thoracoscopically. Goals of surgical therapy include complete evacuation of the infected pleural fluid, obliteration of dead space within the hemithorax, and complete re-expansion of the lung.

In fibrinopurulent (stage II) empyema, video-assisted thoracoscopic surgery (VATS) drainage should be the first-line treatment [11]. VATS for empyema is associated with multiple benefits relative to open thoracotomy in the treatment of empyema. These include shorter hospital stays, lower costs, improved pain control, less morbidity, and reduced 30-day mortality [3]. However, the studies which demonstrate these benefits are not randomized controlled trials and are subject to significant biases. It is possible that patients with a concerning surgical or clinical history were never considered for VATS; there exists a selection bias favoring VATS in these studies. There are potential drawbacks associated with VATS to include technical difficulty and increasing operative times. Surgeons less practiced with VATS may elect to proceed directly with an open thoracotomy. Uncontrollable bleeding and injury to structures that cannot be thoracoscopically repaired will require conversion to open thoracotomy. Inability to achieve the two main goals of surgical therapy will also require conversion. Patients that are unable to tolerate single lung ventilation or with severe coagulopathy will never be candidates for VATS. Conversion from VATS to open thoracotomy occurs in approximately 11.4% of cases; conversion occurs more in mixed or chronic empyema compared to acute empyema [15].

Despite the lack of convincing randomized controlled evidence demonstrating superior outcomes with VATS, the AATS recommends…

> VATS should be the first-line approach in all patients with stage II acute empyema [11].

Video-Assisted Thoracoscopic Surgery (VATS)

This procedure allows direct video imaging of the pleural space. It should allow the surgeon to convert a multi-loculated empyema into a single communicating space in order to facilitate complete debridement of purulent material and re-expansion of the lung with obliteration of dead space.

1. Achieve single lung ventilation with a double-lumen endotracheal tube, if possible. Simple endotracheal intubation without lung isolation may be performed if necessary.
2. Place the patient in the lateral decubitus position with the nonoperative lung down. Apply slight reverse Trendelenburg to allow the diaphragm to move down away from the surgical field.
3. If a thoracostomy tube is already present, this tube site may be used as a port site.
4. The camera port incision is made in the inferior mid-axillary region at a level consistent with the empyema location based on preoperative imaging.
5. A 0-degree or 30-degree scope may be passed into the pleural space.
6. Two more port incisions are placed within the ipsilateral chest wall in order to allow two thoracoscopic instruments to pass into the hemithorax.
7. Aspirate liquified purulent material. Fibrinous material too thick to be aspirated may be removed with ring forceps.
8. Mobilize the lung from attachments to the apical pleural cupula, the posterior costomediastinal gutter, the anterior pulmonomediastinal recess, and the diaphragm.
9. Explore the major and minor fissures for interlobar loculations.

10. Irrigate the pleural space thoroughly with antibiotic-containing sterile saline. There is no recommend choice of antibiotic.

If significant lung entrapment is discovered, this represents a more advanced empyema than an acute stage II empyema. A formal decortication should be performed using standard instrumentation as during an open thoracotomy. Conversion to open thoracotomy is not an unexpected consequence in this scenario as total pneumonolysis may require it.

Open Thoracotomy

This procedure allows direct examination and intervention within the pleural space. When necessary, a full thoracotomy offers the best, most efficient, means of accomplishing a true, complete decortication. A full, complete decortication is the most effective means of obtaining full lung re-expansion with pleural space obliteration.

1. Lung isolation is essential and often obtained thru the use of a dual-lumen endotracheal tube or a bronchial blocker.
2. The patient is positioned in a lateral decubitus position, with the affected lung up. Ensure all pressure points are padded, to include use of an axillary roll.
3. Generally, a skin incision is made overlying the fourth or fifth intercoastal space. Dissection carries down thru the skin and soft tissues to the level of the major named thoracic musculature.
4. Either a muscle splitting or muscle sparing approach can be utilized without compromising visualization.
5. The pleural space is entered most commonly on the "top" of the rib. The intercostal muscles and intercostal space can then be mobilized completely from within the pleural space.
6. Once the intercostal space is fully mobilized, the pleural space can be fully explored. All intra- and extralobar adhesions can be divided.
7. After fully mobilizing the effected lung, attention is then turned to decorticating the lung and chest wall itself. This can be done most effectively with a careful combination of sharp and blunt dissection.
8. In areas where complete decortication is not possible, the thickened pleura may be divided in a series of "cross-like" patterns, to release as much constriction as possible.
9. Once the lung is completely mobilized and decorticated, meticulous hemostasis is obtained.
10. One or two pleural (chest) tubes are then placed appropriately within the hemithorax to afford optimal postoperative pleural drainage.
11. It is not uncommon for patient to have an air leak following a complete decortication. This usually resolves in several days.
12. Pleural tubes remain until drainage has slowed to an acceptable amount. Antibiotics are continued for recommended duration of therapy.

Pediatric Patients

The management of empyema in children is similar to adults but with specific considerations. Regarding the diagnosis of empyema, ultrasound should be the initial and primary imaging modality in children with suspected pleural space disease on chest X-ray. If further characterization of the disease is necessary, especially for surgical preoperative planning, computed tomography may be obtained. It is best practice to limit computed tomography in children due to the increase in long-term cancer risk [7].

The AATS recommends pediatric patients be managed similarly to adult patients presenting with empyema. A strong recommendation is made that a tube thoracostomy should be placed initially for pediatric patients presenting with an empyema. Patients who fail to respond adequately to a tube thoracostomy should undergo surgical evacuation of the infected pleural fluid with VATS debridement preferred over an open thoracotomy [11]. Be aware that a tube thoracostomy in a pedi-

atric patient may be significantly more challenging than in an adult due to noncompliance with tube placement. General anesthesia may be required to safely and properly perform a tube thoracostomy. A small-bore tube (<14F) should be used in children when possible, even for complicated and multiloculated pleural effusions [7].

Tube thoracostomy with fibrinolytic instillation in children is known to be equivocal in terms of therapeutic or recovery benefits compared to VATS and superior to tube thoracostomy alone. A prospective randomized trial involving 36 pediatric patients that compared VATS to tube thoracostomy with fibrinolytic therapy found no difference in length of hospitalization, required days of O_2 support, time until defervescence, or analgesic requirement. The only significant difference between the two groups was in the cost of hospitalization, with VATS being more expensive ($11.7 K ± $2.9 K vs. $7.6 K ± $5.4 K, $P = 0.02$) [13]. A second near-identical prospective, randomized trial involving 60 pediatric patients was published contemporaneously. This study also failed to demonstrate a difference in the primary outcome (length of hospitalization) and also demonstrated an increased cost of VATS. The failure rate of fibrinolytic therapy requiring conversion to VATS was 16.6% in both studies [12].

In both of these studies, the first fibrinolytic dose was given upon chest tube placement with one dose in 24 hour increments for the following 48 hours (three doses total). The first described study used tPA with 1-hour dwell time and the second described study used urokinase with a 4-hour dwell time.

Conclusions

The surgeon usually becomes involved for treatment of an empyema when antibiotics and tube drainage fail to resolve the effusion or control the infection. Patients with an empyema may also present more acutely with sepsis or severe pulmonary compromise if the previous attempts at drainage fail due to dense fluid, loculations, or difficult to access areas of the thoracic cavity. In these situations, immediate surgical intervention is indicated. The acute care surgeon should be familiar with the tenets of adequate open lung decortication and thoracic cavity drainage, especially if a thoracic surgeon is not immediately available. Current evidence suggests that VATS drainage has better outcomes than open thoracotomy; the acute care surgeon should also be familiar with this procedure. The need for conversion to an open thoracotomy is not uncommon due to bleeding, significant lung entrapment, and advanced empyema disease. Pediatric patients should be managed similarly to adults in that VATS debridement is preferred over open thoracotomy. In the pediatric population, intrapleural fibrinolytic therapy may be as effective as VATS debridement.

References

1. Brixey AG, Luo Y, Skouras V, Awdankiewicz A, Light RW. The efficacy of chest radiographs in detecting parapneumonic effusions. Respirology. 2011;16(6):1000–4.
2. Burgos J, Falco V, Pahissa A. The increasing incidence of empyema. Curr Opin Pulm Med. 2013;19(4):350–6.
3. Chambers A, Routledge T, Dunning J, Scarci M. Is video-assisted thoracoscopic surgical decortication superior to open surgery in the management of adults with primary empyema? Interact Cardiovasc Thorac Surg. 2010;11(2):171–7.
4. Davies HE, Davies RJO, Davies CWH. Management of pleural infection in adults: British Thoracic Society pleural disease guideline 2010. Thorax. 2010;65(Suppl 2):ii41–53.
5. Gupta K, Rastogi B, Jain M, Gupta P, Sharma D. Electrolyte changes: an indirect method to assess irrigation fluid absorption complications during transurethral resection of prostate: a prospective study. J Indian Assoc Pediatr Surg. 2005;10(3):142–6. Retrieved from http://www.jiaps.com/article.asp?issn=0971-9261;year=2005;volume=10;issue=3;spage=142;epage=146;aulast=Gupta
6. Havelock T, Teoh R, Laws D, Gleeson F. Pleural procedures and thoracic ultrasound: British Thoracic Society pleural disease guideline 2010. Thorax. 2010;65(Suppl 2):ii61–76.
7. Islam S, Calkins CM, Goldin AB, Chen C, Downard CD, Huang EY, et al. The diagnosis and management of empyema in children: a comprehensive review from the APSA Outcomes and Clinical Trials Committee. J Pediatr Surg. 2012;47(11):2101–10.
8. Kocijancic I, Vidmar K, Ivanovi-Herceg Z. Chest sonography versus lateral decubitus radiography in the diagnosis of small pleural effusions. J Clin Ultrasound JCU. 2003;31(2):69–74.

9. Light RW. Parapneumonic effusions and empyema. Proc Am Thorac Soc. 2006;3(1):75–80. https://doi.org/10.1513/pats.200510-113JH.
10. Rahman NM, Maskell NA, Davies CWH, Hedley EL, Nunn AJ, Gleeson FV, Davies RJO. The relationship between chest tube size and clinical outcome in pleural infection. Chest. 2010;137(3):536–43.
11. Shen KR, Bribriesco A, Crabtree T, Denlinger C, Eby J, Eiken P, et al. The American Association for Thoracic Surgery consensus guidelines for the management of empyema. J Thorac Cardiovasc Surg. 2017;153(6):e129–46. https://doi.org/10.1016/j.jtcvs.2017.01.030.
12. Sonnappa S, Cohen G, Owens CM, van Doorn C, Cairns J, Stanojevic S, et al. Comparison of urokinase and video-assisted thoracoscopic surgery for treatment of childhood empyema. Am J Respir Crit Care Med. 2006;174(2):221–7.
13. St. Peter SD, Tsao K, Harrison C, Jackson MA, Spilde TL, Keckler SJ, et al. Thoracoscopic decortication vs tube thoracostomy with fibrinolysis for empyema in children: a prospective, randomized trial. J Pediatr Surg. 2009;44:106–11. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3086274/
14. Stark DD, Federle MP, Goodman PC, Podrasky AE, Webb WR. Differentiating lung abscess and empyema: radiography and computed tomography. AJR Am J Roentgenol. 1983;141(1):163–7.
15. Tong BC, Hanna J, Toloza EM, Onaitis MW, D'Amico TA, Harpole DH, Burfeind WR. Outcomes of video-assisted thoracoscopic decortication. Ann Thorac Surg. 2010;89(1):220–5.
16. Waite RJ, Carbonneau RJ, Balikian JP, Umali CB, Pezzella AT, Nash G. Parietal pleural changes in empyema: appearances at CT. Radiology. 1990;175(1):145–50.
17. Watkins E, Fielder CR. Management of nontuberculous empyema. Surg Clin N Am. 1961;41(3):681–93. Retrieved from http://www.sciencedirect.com/science/article/pii/S0039610916363915

Part XVII

Bleeding from Idiopathic Thrombocytopenic Purpura

45

Bleeding from Immune Thrombocytopenia: Medical Management – Steroids, Immunoglobulins, and New Therapies

Jeffrey Lew and Jeffrey Berenberg

Immune thrombocytopenia (ITP), formerly called idiopathic thrombocytopenic purpura, is an autoimmune phenomenon resulting in the reduction of circulating platelets.

ITP presents as an isolated thrombocytopenia and is considered when the platelet count is persistently below $<100 \times 10^9$/L without an alternative explanation. Left untreated, ITP can lead to bleeding complications with a 5% risk of mortality. Patients with ITP can be a challenge to diagnose and manage in the perioperative and the emergent surgical setting.

ITP has an incidence between 1 and 9 cases per 100,000 people [1]. It can occur at any age although the clinical course differs between children and adults. In children ITP is mostly self-limiting, but in adults it is a chronic condition predominantly affecting the elderly. The pathophysiology of ITP is now understood to be from multiple mechanisms to include antiplatelet antibodies, impaired production and maturation of megakaryocytes [2], and T-cell-mediated destruction of platelets [3]. The most common mechanism of ITP is destruction from antiplatelet IgG antibodies against surface glycoproteins, GPIIb/IIIa and GP1b/IX/V [4]. ITP can be a primary process or secondary to autoimmune diseases (systemic lupus erythematosus, rheumatoid arthritis, antiphospholipid antibody syndrome), infection (HCV, HIV, *H. pylori*), lymphoproliferative disorders, or medications. When the cause is from medication, it is referred to as drug-induced thrombocytopenia (DITP).

The clinical presentation of ITP can range in severity from asymptomatic to life-threatening bleeding. Mild symptoms can be self-limited and restricted to the skin with petechiae, ecchymosis, and purpura resulting from vessels bleeding into the skin. Patients with ITP will not always present with purpura which is why the International Working Group has removed "purpura" from the nomenclature of ITP. Other mild symptoms include mucosal bleeding when brushing teeth and spontaneous epistaxis [5]. The more severe symptoms are rare but can be life-threatening when platelets are below 30×10^9/L to include visceral and intracerebral hemorrhage.

Immune thrombocytopenia is a diagnosis of exclusion requiring a thorough history and physical with appropriate laboratory analysis to rule out other causes of thrombocytopenia. History should focus on the onset and location of bleeding, family history, menstrual history, and risk factors for secondary causes of ITP. It is an acquired disorder, with a bimodal distribution peaking in childhood and in the elderly; therefore

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a family history of bleeding and a lifelong history of bleeding are not consistent with ITP and should prompt workup for inherited thrombocytopenias. However, inherited thrombocytopenias can occasionally present in adulthood [6]. Physical exam should focus on the skin for petechiae and ecchymosis and mucosal surfaces such as the mouth. Lymphadenopathy and organomegaly are not found in ITP and should prompt workup of other causes of thrombocytopenia. Hemarthrosis and bleeding into muscles would be very uncommon in ITP and would suggest a disorder of clotting factors, such as factor deficiency or acquired factor inhibitors.

Laboratory tests and studies should exclude other causes of thrombocytopenia. A complete blood count is important to determine the degree of thrombocytopenia and if other cell lines are involved. A peripheral smear is recommended to look for platelet clumping or schistocytes in the blood, suggesting a microangiopathic hemolytic process such as thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), or disseminated intravascular coagulation (DIC). In ITP the peripheral smear would characteristically show large platelets due to young immature platelets being released into the circulation; this may be reflected as an elevated mean platelet volume on the complete blood count. Renal function tests are also recommended because an elevated creatinine would also raise suspicion of thrombocytopenic purpura. Coagulation studies are recommended because activated partial thromboplastin time (aPTT) and partial thromboplastin time (PTT) would be elevated in DIC but should be normal in patients with ITP. In addition, evaluation of secondary causes of ITP should be in the initial workup such as serologies for HIV, HCV, and *H. pylori* [7]. Although ITP is associated with autoimmune diseases, testing for antinuclear antibodies, rheumatoid factor is not generally recommended but should be considered if other autoimmune symptoms are present. Antiplatelet antibodies are not recommended because they lack sensitivity and specificity for ITP [8] (Table 45.1). In absence of other cytopenias, bone marrow biopsy is not recommended.

Table 45.1 Lab tests for work up of ITP

Initial labs	Comments
Complete blood count	Assess degree of thrombocytopenia
Basic metabolic panel	Assess for kidney damage
Peripheral blood smear	Rule out microangiopathic hemolytic process
HIV	HIV 0/1 test
Coagulation studies (PT, aPTT, INR)	Rule out coagulopathy
Hepatitis C	Hepatitis C IgG ab
H. pylori	Stool ag, urea breath test
Quantitative immunoglobulins	Rule out IgA deficiency prior to transfusion of IVIG. Also recommended in children to reassess for common variable immunodeficiency
Direct antiglobulin test (DAT)	DAT and blood group are recommended in anticipation for first-line therapy anti-D immunoglobulin
Blood group (Rh)	
Tests to consider if clinically indicated	
Bone marrow biopsy	If other cell lines affected
Anti-nuclear antibodies, rheumatoid factor antiphospholipid antibodies	If other symptoms of autoimmune disease present, for example, joint pain, venous thromboembolism, recurrent miscarriages
Pregnancy test	Rule out ITP of pregnancy

The treatment goals of ITP are to achieve adequate hemostasis and an increase in platelet count. The decision to initiate treatment differs between adults and children due to the majority of cases being self-limiting in children. As a result, ITP treatment in children with mild bleeding restricted to bruising and petechiae should be observed regardless of platelet count. Treatment of children should be initiated if there is moderate to severe bleeding. In adults, the majority of ITP is chronic and will not improve spontaneously; therefore treatment is initiated when the platelet count falls below 30×10^9/L because of the increased risk for spontaneous bleeding. Except in life-threatening bleeding, platelet transfusions are not used to treat chronic ITP because it would be destroyed by the immune system within hours.

Special considerations are made in patients with ITP undergoing surgery based on whether the surgery is emergent or elective. For elective

procedures the goal is to achieve platelet counts required for hemostasis, which for most surgeries is >50 × 10^9/L and >100 × 10^9/L for neurosurgical procedures. If patients cannot meet these thresholds, then surgery should be delayed for consultation of a hematologist for medical management of ITP. This allows for time to treat the underlying cause of ITP and for platelet counts to increase to safe levels for procedures. For patients with chronic ITP requiring an emergent surgery, the platelet count must be increased quickly. Therefore, certain agents are selected for the emergent and non-emergent settings based on their time to initial response. See Fig. 45.1 for treatment algorithm for ITP.

Medical management of chronic ITP in the non-emergent setting starts with treating the underlying etiology of secondary ITP to include retroviral therapy for underlying HIV or HCV, eradication of *H. pylori*, and treatment of underlying autoimmune disease or lymphoma. In addition, any medications known to cause DITP should be discontinued, and the patient should be monitored to see if the platelet counts improve. It may take weeks to months for platelet recovery, depending on the underlying etiology, and surgical procedures should be delayed until platelets recover. After secondary causes have been treated or if there is no secondary cause, then medical treatment for the underlying immune mechanism

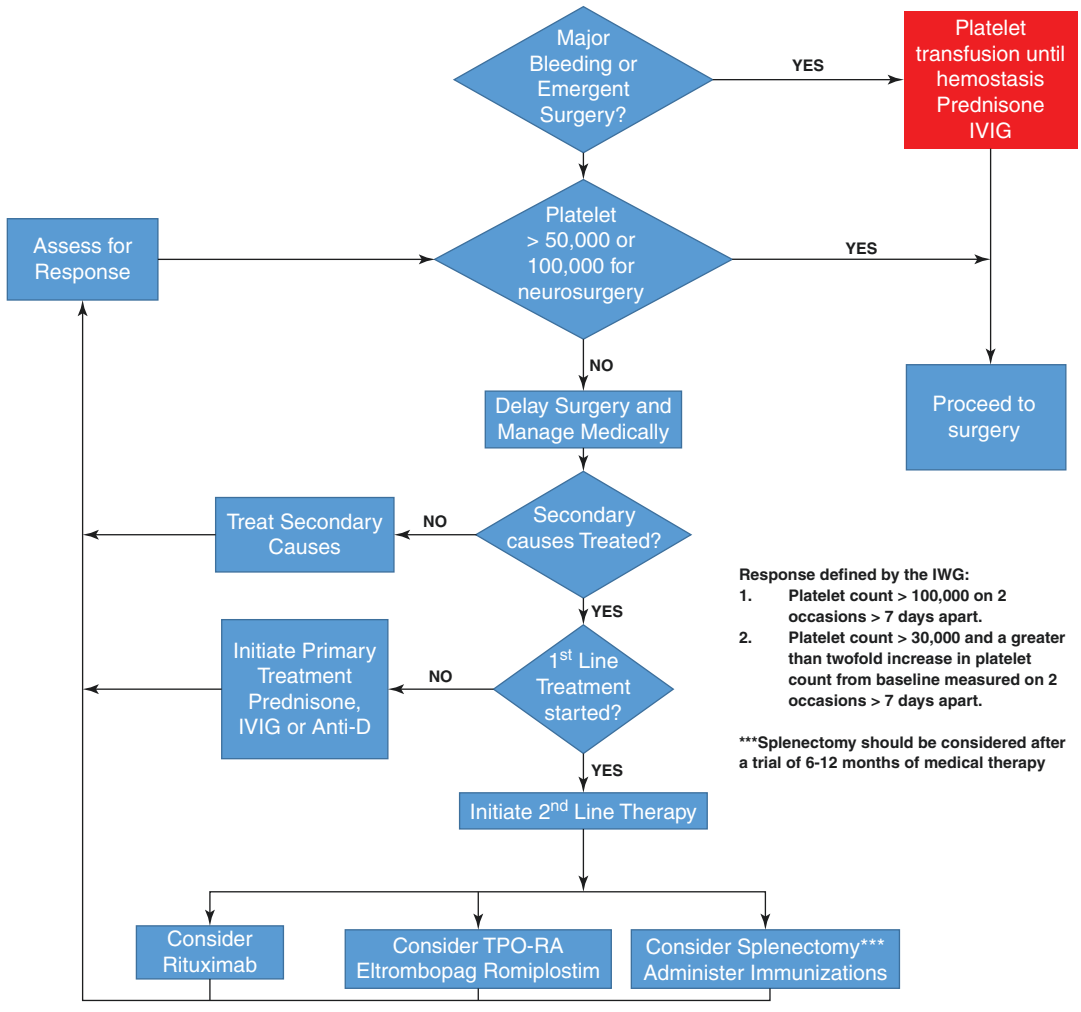

Fig. 45.1 ITP treatment algorithm

Table 45.2 Timing and response rate for treatment of ITP

Treatment/dose	Initial response/peak response	Response rate	Comments
First-line agents			
IVIG 1 g/kg daily for 1–2 days	1–3 days 7–28 days	85%	Fastest onset of action. Rare infusion reactions
Anti-D immunoglobulin 50-75mcg/kg	2–14 days 4–28 days	70–80%	Must be Rh + and monitored for hemolysis
Prednisone 1–2 mg/kg daily	4–14 days 7–28 days	70–80%	Requires steroid taper
Dexamethasone 40 mg/d for 4 days per cycle 6 cycles total	2–14 days 4–28 days	90%	Faster than prednisone and higher rates of remission
Second-line agents			
Splenectomy	1–56 days 7–56 days	80%	Increased risk of infections, thrombotic events
Eltrombopag 50–75 mg daily	7–28 days 14–90 days	80%	Hepatotoxicity, thrombotic events
Romiplostim 1 mcg/kg SC once weekly	14–21 days Not reported	80%	Thrombotic events, arthralgias
Rituximab 375 mg/m^2 over 4 hours weekly for 4 consecutive weeks	7–56 days 14–180 days	60%	Infusion reactions, infection, neutropenia

is targeted. First-line treatment for ITP is immunosuppression with prednisone 1 mg/kg/day for 2–4 weeks for adults and 2 mg/kg/day for children followed by a steroid taper. Prednisone takes 4–14 days for an initial response and up to 28 days for a peak response. High-dose dexamethasone has also been studied and is effective at 40 mg/day orally for 4 days for six different treatment cycles. This treatment has been found to have slightly faster initial onset of action than prednisone and higher (up to 77%) rates of remission [9]. For patients where steroids are contraindicated, intravenous immunoglobulins (IVIG) are an alternative first-line therapy and have the benefit of getting a more rapid rise in platelet count in a short time period. IgA levels should be checked prior to infusion to screen for IgA deficiency, where IVIG may lead to anaphylactic reaction. In IgA-deficient patients, steroids are a better first-line option to treat ITP. Anti-D immunoglobulins are also first-line treatment for Rh+, non-splenectomized patients; however, it is contraindicated in patients with hemolytic anemia; therefore, the direct antiglobulin test (DAT) should be obtained with blood typing prior to its initiation [6]. Both IVIG and anti-D immunoglobulin have the fastest initial response times of 1–2 days, respectively, and peak response times as early as 7 and 4 days making them more useful for urgent surgery and major bleeds (Table 45.2).

If there is no response after first-line therapy, there are multiple second-line options to include thrombopoietin receptor agonists (TPO-RA), rituximab, and splenectomy. Splenectomy was previously the most effective second-line treatment for ITP with over 80% response rates. Postsplenectomy response times have been variable between 1 and 56 days. During this postsplenectomy time period, a hematologist would expect a response as defined by a platelet count of >30 × 10^9/L and a greater than twofold increase in platelet count from baseline measured on two occasions >7 days apart. If a patient does not meet this threshold, then a failed splenectomy should be considered and a search accessory splenic tissue can be done. During long-term follow-up, it was found that refractory ITP can be due to accessory splenic tissue in 10% of refractory cases [10]. In such cases, remaining splenic tissue can be located using radiolabeled platelets and an intraoperative gamma probe. However, there must be a high index of suspicion for accessory splenic

tissue for a repeat surgical procedure to be considered in patients with no evidence of platelet response and absence of Howell-Jowell bodies on peripheral blood smear. In addition, splenectomy has multiple risks and complications to include postsplenectomy sepsis syndrome, hemorrhage, and long-term increased venous thromboembolism risk. As a result, splenectomy is considered starting 6–12 months after the diagnosis of ITP and is unresponsive to medical therapy. If splenectomy is considered, vaccination for encapsulated organisms, *Neisseria meningitidis*, *Strep pneumoniae*, *Haemophilus influenzae.* Vaccination should occur at least 2 weeks before or after splenectomy for proper response to vaccine. However, if a patient is on immunosuppressive therapy (>2 weeks of therapy of 20 mg or 2 mg/kg body weight prednisone equivalent), then live vaccines should be administered 1 month post-splenectomy. Laparoscopic splenectomy is preferred over open splenectomy due to lower bleeding complication rates, decreased postoperative pain, and decreased hospitalization time.

In patients who are not surgical candidates, medical therapy with rituximab infusions is an alternative. Rituximab has been studied extensively; however, the overall platelet response rates are variable and are not comparable to splenectomy with initial response and peak response times highly variable from weeks to months [11]. Patients refractory to rituximab will often require repeat infusions or alternative therapy. In the past decade, TPO-RA such as eltrombopag and romiplostim have been FDA approved for treating ITP, and more recently long-term data demonstrates overall response rates of 85%, which are comparable to splenectomy [12, 13]. Although, in the past, TPO-RA have been reserved for ITP refractory to splenectomy and rituximab, it is now being used earlier in the ITP treatment algorithm. Additionally, romiplostim has been found to raise platelet counts more effectively prior to splenectomy and can be considered as a medical alternative to splenectomy [14]. However, eltrombopag and romiplostim are oral therapies requiring long-term compliance unlike definitive splenectomy. Eltrombopag has an initial response 7–28 days and peak response times up to 90 days [15]. Romiplostim can take 14–21 days for initial response with peak response not reported [16]. The most common side effects are headache, nasopharyngitis, elevated liver enzymes, and increased risk of thrombosis. Recently in April 2018, the FDA has approved for treatment of chronic ITP fostamatinib, a splenic tyrosine kinase inhibitor preventing antibody-mediated destruction of platelets. This agent has been proven to increase platelet counts above $>50 \times 10^9$/L in 12 weeks in patients previously treated with second-line agents to include splenectomy, TPO-RA, and rituximab [17]. However, guidelines have not been updated to reflect where it falls in the algorithm.

For emergent surgery with life-threatening bleeds in a patient with known ITP, IVIG with corticosteroids should be given concurrently for rapid immune control due to their fastest time to initial response. Although platelets would be consumed quickly, they are indicated in emergent bleeds to temporarily increase platelet counts until hemostasis is achieved [18]. Through retrospective studies in patients with life-threatening hemorrhage, massive platelet transfusions from presentation through the postoperative period resulted in successful control of hemorrhage [19]. Once hemostasis is achieved, platelet transfusions can stop, and initial response in platelet counts should be seen in 2–5 days. TPO-RA and rituximab have slower times to initial response and have no role in the emergent setting. Antifibrinolytic agents have been studied but have no mortality benefit.

Conclusions

ITP can be a challenging hematologic condition to manage in the emergent and non-emergent setting. Although there have not been many advances of ITP management in the emergent setting, there have been multiple advances in the treatment of chronic ITP in the non-emergent setting. In the past decade, a larger body of evidence has emerged to support using TPO-RA as second-line

treatment of ITP, and there is now data supporting the use of splenic tyrosine kinase inhibitors. This in turn can result in lower rates of splenectomy and expanding second-line and third-line options for patients with refractory ITP who experienced multiple treatments.

References

1. Terrell DR, et al. Prevalence of primary immune thrombocytopenia in Oklahoma. Am J Hematol. 2012;87(9):848–52.
2. Khodadi E, et al. Bone marrow niche in immune thrombocytopenia: a focus on megakaryopoiesis. Ann Hematol. 2016;95(11):1765–76.
3. Olsson B, Andersson PO, Jernås M, et al. T-cell-mediated cytotoxicity toward platelets in chronic idiopathic thrombocytopenic purpura. Nat Med. 2003;9(9):1123–4.
4. Cines DB, Cuker A, Semple JW. Pathogenesis of immune thrombocytopenia. Presse Med. 2014;43(4 Pt 2):e49–59.
5. Altomare I, et al. Rate of bleeding-related episodes in adult patients with primary immune thrombocytopenia: a retrospective cohort study using a large administrative medical claims database in the US. Clin Epidemiol. 2016;8:231.
6. Balduini CL, Savoia A, Seri M. Inherited thrombocytopenias frequently diagnosed in adults. J Thromb Haemost. 2013;11(6):1006–19.
7. Neunert C, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117(16):4190–207.
8. Lambert MP, Gernsheimer TB. Clinical updates in adult immune thrombocytopenia. Blood. 2017;129(21):2829–35.
9. Cheng Y, et al. Initial treatment of immune thrombocytopenic purpura with high-dose dexamethasone. N Engl J Med. 2003;349(9):831–6.
10. Ahmed R, et al. Long-term outcome following splenectomy for chronic and persistent immune thrombocytopenia (ITP) in adults and children. Ann Hematol. 2016;95(9):1429–34.
11. Bennett CM, et al. Prospective phase 1/2 study of rituximab in childhood and adolescent chronic immune thrombocytopenic purpura. Blood. 2006;107(7):2639–42.
12. Saleh MN, et al. Safety and efficacy of eltrombopag for treatment of chronic immune thrombocytopenia: results of the long-term, open-label EXTEND study. Blood. 2013;121(3):537–45.
13. Cines DB, et al. Integrated analysis of long-term safety in patients with chronic immune thrombocytopaenia (ITP) treated with the thrombopoietin (TPO) receptor agonist romiplostim. Int J Hematol. 2015;102(3):259–70.
14. Cines DB, et al. Safety and efficacy of romiplostim in splenectomized and nonsplenectomized patients with primary immune thrombocytopenia. Haematologica. 2017;102(8):1342–51. Haematol-2016.
15. George JN, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood. 1996;88(1):3–40.
16. Khan AM, Mydra H, Nevarez A. Clinical practice updates in the management of immune thrombocytopenia. Pharm Ther. 2017;42(12):756.
17. Bussel J, et al. Fostamatinib for the treatment of adult persistent and chronic immune thrombocytopenia: results of two phase 3, randomized, placebo-controlled trials. Am J Hematol. 2018;93(7):921–30.
18. Salama A, et al. Massive platelet transfusion is a rapidly effective emergency treatment in patients with refractory autoimmune thrombocytopenia. Thromb Haemost. 2008;100(05):762–5.
19. Spahr JE, Rodgers GM. Treatment of immune-mediated thrombocytopenia purpura with concurrent intravenous immunoglobulin and platelet transfusion: a retrospective review of 40 patients. Am J Hematol. 2008;83(2):122–5.

46 Immune Thrombocytopenia: Incidence, Diagnosis, Presentation, and Surgical Management

Kenneth John Bogenberger and Chan W. Park

Immune thrombocytopenia (ITP), previously referred to in literature and practice as idiopathic thrombocytopenic purpura, is an acquired disorder of immune-mediated destruction of platelets. Platelet destruction is believed to be mediated by the presence of circulating platelet-reactive IgG antibodies that bind with platelets, subsequently resulting in splenic sequestration and opsonization [1]. ITP is a heterogeneous syndrome with many genetic and pathologic associations. It may be encountered in association with an inciting event, illness, or drug (secondary ITP) or may present itself independently with another unrelated process (primary). Molecular mimicry of certain foreign antigens is thought to contribute to many cases of ITP, along with possible variations in the genetics of initiation and maintenance of the immune response, as well as platelet clearance and production [2]. The multitude of genetic factors makes it a difficult disease to characterize and likely contributes to the wide range of clinical presentations.

The prevalence of ITP ranges from 2.5 to 9.6 per 100,000 person-years [3, 4]. A recent population study in Korea showed the incidence to be 5.3 per 100,000 person-years, and the data suggests a slight female predilection for the disease, though gender data in many of these studies are mixed [4, 5]. In the USA, the incidence of ITP is estimated to be as high as 3.9 per 100,000 person-years and is encountered in both adult and pediatric populations, though rates of chronic ITP are higher in adults.

ITP is a heterogeneous disease process with variable presentation. As such, categorizing ITP has been difficult. A 2009 international working group of clinicians and researchers provided updates to definitions and terminology in an attempt to decrease ambiguity and improve collaboration [2, 6, 7]. Relevant examples of such terminology are included in Table 46.1.

Table 46.1 International working group descriptive terminology for ITP [2, 6, 7]

Terminology	Description
Newly diagnosed	Less than 3 months' duration of thrombocytopenia
Persistent	3–12 months' duration of thrombocytopenia
Chronic	More than 12 months' duration of thrombocytopenia
Severe	Significant bleeding requiring treatment, additional interventions, or an increase in drug dosage
Refractory	Persistence of severe ITP after splenectomy
Response	Platelet count greater than 30 × 10^9/L and a greater than twofold increase in platelet count versus baseline measures, taken on two occasions more than 7 days apart
Complete response	Platelet count greater than 100 × 10^9/L, measured on two occasions greater than 7 days apart

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Table 46.2 Causes of secondary immune thrombocytopenia [1, 6, 8–12]

Autoimmune disorders	Infections	Drugs	Vaccinations
Systemic lupus erythematosus	HIV	Heparin	Measles
Antiphospholipid syndrome	Hepatitis C	Penicillin	Mumps
Leukemia	*H. pylori*	Nonsteroidal anti-inflammatory	Rubella
Lymphoma	*Cytomegalovirus*		Varicella
	Herpes zoster		
	Tuberculosis		

Primary ITP is defined as an autoimmune disorder characterized by thrombocytopenia (peripheral blood platelet count <100 × 10^9/L) in the absence of other causes or disorders that may be associated with thrombocytopenia. There is no specific laboratory test or clinical diagnostic criteria that defines the condition and as a result is difficult to diagnose with accuracy.

Secondary ITP refers to forms of immune-mediated thrombocytopenia except primary ITP. Secondary ITP is additionally referred to by the condition which is the apparent cause, i.e., "drug-induced ITP" [7]. Examples of such causes are included in Table 46.2.

Initial Presentation

Pertinent patient history and a physical exam are always obtained. Important risk factors for life-threatening hemorrhage should be elicited, including recent surgery, any previous history of gastrointestinal bleeding or intracranial hemorrhage, anticoagulation, or antiplatelet therapy. On physical exam, signs of a bleeding diathesis should be evaluated including the presence of bruising, petechiae, or purpura. A neurologic exam should also be performed, as well as fecal occult blood testing. Physical exam may give important clues as to the presence of anemia or hypovolemia, which can be suggestive of acute blood loss including poor skin turgor, dry mucous membranes, and pallor.

Patients with acute ITP may present with bleeding, ecchymosis, or hematoma as a result of critically low platelet counts. Bleeding may be relatively limited, e.g., bruising, purpura, or epistaxis. Bleeding may be life-threatening, e.g., intracerebral, gastrointestinal, or postoperative surgical site bleeding. In such patients, bleeding may not stop as platelet transfusion only provides a transient response before those platelets also succumb to targeting by antiplatelet antibodies. Priorities during initial presentation should be rapid evaluation of the patient's volume status and need for resuscitation, presence of active bleeding, and, if so, the degree of anemia.

In addition to a complete blood count, a peripheral smear is important to distinguish thrombocytopenia from pseudothrombocytopenia due to clumping. A smear from a patient with ITP will show a low number of otherwise normal platelets. Platelets may be larger than average, because of their immaturity as a result of their high turnover rate. In patients presenting with suspected ITP, abnormalities in the complete blood count and peripheral blood smear related to causes other than thrombocytopenia should also be further investigated. A bone marrow biopsy should be considered if there are other suspected derangements of hematopoiesis. Routine use of antiplatelet, antiphospholipid, and antinuclear antibodies is not recommended by current guidelines and may not be reliable in establishing the diagnosis. Certain laboratory tests for infectious sources are indicated (see Table 46.3). In clinically significant cases of ITP, neither the magnitude of the decline in platelet count nor the velocity at which it declines is necessarily indicative of prognosis in patients. This is most evident in children who may have profound thrombocytopenia secondary to viral illness, with subsequent bleeding sequelae, only to recover spontaneously without further relapses.

Table 46.3 Laboratory evaluation of ITP

Routine diagnostic tests [13]		
Complete blood count	Blood group and Rh typing	Hepatitis C
Coagulation studies (pt/ptt)	*H. pylori* diagnostic testing	Direct antiglobulin test
Blood smear	HIV	Pregnancy testing in women
Diagnostic tests to consider in select cases [13]		
Bone marrow biopsy	Autoimmune antibody panel	Bleeding time
Thrombopoietin	Platelet-associated IGG	Platelet survival study
Thyroid function tests and antithyroid antibodies		

Treatment

The initiation of treatment for ITP must be individualized for patients based on a number of considerations. The patient's absolute platelet count and presence of bleeding are the two major determinants; however other considerations include the patient's need for therapeutic anticoagulation or antiplatelet therapy, the need for surgical procedures in the near future, and patient lifestyle choices that increase the risk of bleeding, e.g., contact sports. Severe bleeding is rare and normally occurs when platelet counts are below 10 × 10^9/L [14]. The mainstay of initial treatment are corticosteroids. The medical management was discussed in more detail in the previous chapter.

Splenectomy for ITP

Historically, the rates of response for splenectomy are between 60% and 80% [6, 15, 16], making it a mainstay of treating severe and chronic ITP for patients who failed conventional medical therapy. The most recently published guidelines from the American Society of Hematology still recommend splenectomy for patients with chronic ITP who are good surgical candidates [11]. However, with the advent of new medical therapies, the desire to minimize surgery-related morbidity, and to avoid long-term effects on immune function of splenectomy, rates of splenectomy for ITP have consequently decreased. As novel medical therapies and treatment regimens are studied and long-term efficacy data grows, splenectomy is increasingly becoming a third-line treatment approach [13]. In one study from Korea with 10,814 patients, only 104 patients were found to have undergone splenectomy [5]. This means that the patients who need splenectomy have failed medical management and, as such, may be in more dire need of splenectomy. Moreover, splenectomy remains an important intervention for ITP and has the potential to provide durable results in patients where medical therapy and second-line therapies have failed. A recent 2016 study notes, however, that as splenectomy is increasingly relegated to third-line therapy, durable response rates to splenectomy remain similar [17]. In all cases, the indications for splenectomy must be weighed against individual patient factors including age, ability to tolerate anesthesia, the duration and magnitude of response while on medical therapy, and the presence of comorbid conditions.

Indications for splenectomy currently include cases of ITP that are clinically severe and are unresponsive to medical therapy, i.e., associated with significant morbidity to the patient. At a minimum, patients considered for an elective splenectomy should have failed corticosteroid therapy [11]. The acceptable platelet threshold for treatment is 30 × 10^9/L, though patient factors may play a role in choosing a different threshold. For example, patients with a history of previous serious bleeding, e.g., requiring hospitalization, transfusion, or intracranial bleeding, may require consideration for splenectomy at a higher platelet count. Ultimately the risk of bleeding needs to be assessed against the morbidity associated with surgery. The mortality rate of patients undergoing splenectomy for ITP is from 0.2% to 1%, and the overall complication rate is between 9% and 13% [15]. The most common postoperative complications are postoperative bleeding, cardiovascular events, and infectious complications (discussed later in the section) [15].

Preoperative Evaluation and Planning

Providers who are planning to refer patients for surgery should assess the patient's ability to undergo surgery. Patients who are high risk for surgery based on cardiovascular and other risk factors may require further risk stratification or diagnostic evaluation, i.e., cardiac or pulmonary evaluation, prior to surgery. Evaluation done prior to or in combination with surgical consultation will help to expedite the process. In some patients, initiation or continuation of antiplatelet agents may be indicated, and this need may have to be balanced against the degree of thrombocytopenia and should be individualized to the patient based on the severity of thrombocytopenia, presence of bleeding, and indication for antiplatelet therapy. Patients should have received all necessary vaccinations based on age, provided they are otherwise without contraindications. CDC guidelines also recommend pneumococcal, meningococcal, haemophilus influenzae type b, and zoster vaccinations for elective splenectomy [18].

There are no universal guidelines to determine timing of splenectomy. At a minimum there should be enough time between initiation of medical treatment and the decision for surgery to assess for platelet response. In patients who have undergone second-line therapies, e.g., rituximab, 6–8 weeks may be necessary to assess for response [14]. In the elective setting, vaccination should be done 4 weeks prior to splenectomy when possible, or alternatively 2 weeks postoperatively if necessary. In order to decrease the risk of postsplenectomy sepsis, vaccinations for *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis* are required. These vaccines may not be effective in patients who have received rituximab in the 6 months prior to splenectomy [19].

Splenectomy can be performed laparoscopically or as an open procedure. Patients undergoing surgery must be able to tolerate general anesthesia. In general, laparoscopy is preferred because it is associated with less morbidity and quicker patient recovery than open splenectomy [20]. Contraindications for a laparoscopic procedure may include splenomegaly and inability to tolerate pneumoperitoneum. Patients undergoing open or laparoscopic surgery should have a platelet count above 50,000/L. In patients who are severely thrombocytopenic at the time of surgery (less than 50,000), platelets should be available for transfusion.

The incidence rate for detecting accessory spleen tissue is as high as 30% [21]. Accessory spleen tissue not removed at the time of index surgery may result in treatment failure. Studies investigating laparoscopic splenectomy have found lower rates for detecting accessory splenic tissue than in open procedures [21, 22]. In patients with persistent thrombocytopenia postoperatively, and evidence of inadequate splenectomy on blood smear, a radionuclide scan can be used to localize splenunculi missed on initial operation. In patients undergoing laparoscopic splenectomy, consideration should be given to performing the scan preoperatively to assist in planning and decreasing rates of inadequate resection [21].

Postoperative Management

In the immediate postoperative period, splenectomy patients should, at the very least, be admitted to a monitored ward where they can be placed on continuous telemetry and pulse oximetry. Patients who were unstable intraoperatively and subjected to long operative times or whose burden of chronic disease makes them high risk for complications should be monitored in the intensive care unit (ICU). Important postoperative complications include bleeding, portal venous thrombosis, subphrenic abscess, intestinal ischemia, pancreatic leak, and overwhelming postsplenectomy infection (OPSI) [23].

Portal venous thrombosis (PVT) is a common and potentially lethal complication of splenectomy. The incidence is 22% and typically present by postoperative day 7. Symptoms include abdominal pain, nausea, diarrhea, dyspnea, and fever; symptoms are often nonspecific and may be confused with other common postoperative etiologies for sepsis [24]. In general, laboratory

studies are nonspecific but may include elevated lactate dehydrogenase, white blood cell count, or derangement in liver-associated enzymes [24, 25]. The diagnosis is typically made with imaging, either ultrasound or IV contrast CT scan [23]. PVT is managed with appropriate resuscitation and therapeutic anticoagulation. In the setting of severe venous congestion, bowel ischemia may result and require emergent surgical resection. Rates of PVT are higher in persons undergoing splenectomy for hematologic disorders, and the presence of splenomegaly is also a risk factor for the complication [26]. The incidence of PVT is also increased with laparoscopic splenectomy [23] and is associated with longer operative times [25]. PVT is not associated with thrombocytosis and was not found to be reduced with administration of aspirin. However, an extended course of thromboprophylaxis was found to decrease rates of PVT, and consideration for an extended course of thromboprophylaxis should be given for such patients, particularly if additional risk factors for thrombotic events exist [25]. Additionally, routine screening postoperatively is recommended in patients undergoing splenectomy for ITP and can be performed as early as 7 days postoperatively [27, 28].

Overwhelming postsplenectomy infection is another unique, potentially fatal complication of splenectomy for which clinicians should maintain a high clinical suspicion in the postoperative period. Prodromal symptoms may be nonspecific, including flu-like symptoms, malaise, fever, headache, or gastrointestinal complaints, and can progress rapidly toward septic shock; [29] rapid diagnosis and treatment are essential in these patients. Early administration of fluid and antibiotics is critical in septic patients, with ICU admission being warranted. Clinical sequelae of the disease include development of disseminated intravascular coagulation (DIC), bilateral adrenal hemorrhage, and peripheral gangrene. The role of prophylactic antibiotics has been shown to reduce morbidity and mortality in pediatric patients, though for adults it is controversial and generally not indicated [29].

Pancreatic leak is a dreaded complication associated with splenectomy. Because of the organ's proximity to the spleen, the pancreatic tail is at risk of injury during dissection and ligation of the hilar vessels. In the setting of a suspected pancreatic injury, a distal pancreatectomy may be performed along with splenectomy. In the setting of an unrecognized pancreatic injury, the patient may present clinically with pancreatitis, elevated lipase, and a peripancreatic fluid collection.

Outcomes for splenectomy vary widely in studies; in one systematic review, the median complete response rate was 67% [15]. Cumulative rates of response, including complete and partial responders, are as high as 86%, while 23% of patients with an initial response to splenectomy will relapse [30]. Most relapses occur within 2 years of splenectomy.

Multidisciplinary Considerations

Management of ITP requires a true multidisciplinary approach. As previously discussed, ITP is treated primarily through medical therapies, but when indicated, surgical intervention can be utilized to supplement failing or unresponsive medication regimens. Effective communication and interdisciplinary collaboration among hematologists, internists, and surgical specialists are necessary for success. Basic knowledge of both medical and surgical treatment modalities, as well as the sequelae of these therapies, will help to minimize treatment complications and facilitate enhanced patient care. Timing of certain treatments and coordination of care in ITP is also of utmost importance, and primary care physicians are ideally situated to provide this care coordination and oversight of specialized treatment modalities. For example, providers referring patients for surgery, either for splenectomy or unrelated procedure, must individually consider patient characteristics and comorbid conditions when deciding between treatment modalities. These include the patient's cardiovascular health, the presence of chronic infectious disease, the effects of immune-modulating therapy, and ultimately the patient's expectations and goals of treatment.

Nursing Considerations

With regard to nursing care of patients with ITP, special attention must be given to thoroughly assessing patients' risk of falling and implementing prevention measures to minimize that risk. While this is true for all patients, it is more so for a patient population at risk of severe complications from bleeding. If a fall does occur, a thorough evaluation of the patient and prompt notification of the physician are essential in identifying and preventing life-threatening bleeding. Most medical facilities have well-defined protocols and procedures for preventing and reporting falls, and these measures should be strictly adhered to in all patients hospitalized for ITP. Patients with ITP should also have a thorough skin survey performed to identify and document any bruising or wounds on admission and should be periodically assessed for growth or hemorrhage. Even without active hemorrhage, the patient will likely have blood type crossmatched for use.

ITP patients are frequently treated by oncology nurses who have experience with blood product transfusions and therapies. Familiarity with hospital protocols regarding transfusion therapy is essential. Patients undergoing blood- or antibody-based therapies should be monitored for evidence of transfusion-related side effects. These reactions are common and range from mild side effects including fever or exanthem, to severe including anaphylaxis, hemolysis, or acute organ failure. Nurses and other members of the care team with direct interaction with the patient should be aware of these potential side effects and pay particular attention to their presence, notifying the clinician whenever there is suspicion for a transfusion-associated reaction.

Considerations for Patients with ITP Undergoing Surgery

Patients with ITP who undergo concomitant surgery for diseases other than ITP are an important subset for consideration. Such patients may present considerable challenge as the need for an operation versus risk of sequelae secondary to ITP must be balanced. Patients may present with or develop coagulopathy secondary to thrombocytopenia or have undergone immune-modulating therapies that would potentially impact surgical outcomes. Additionally, patients with ITP in general experience higher rates of postoperative complications including renal failure, sepsis, pneumonia, and stroke [31]. In the setting of clinically significant thrombocytopenia, consideration should be given to delaying definitive surgical management in certain situations until the patient is stable.

Patients with ITP who present with surgical emergencies or urgent surgical indications may present with severe thrombocytopenia that puts the patient at significant risk for bleeding. Platelets should be given to patients who are thrombocytopenic just prior to or at the start of the surgery. Platelets should not be given significantly ahead of time because platelet survival is significantly reduced to 1–4 hours following transfusion. Whenever possible, platelets should be transfused after ligation of the splenic artery to decrease the risk of sequestration and opsonization.

Conclusion

In summary, acute ITP is frequently a self-limited disease, with few long-term consequences, should platelet counts rebound appropriately. This is most commonly seen in the setting of secondary ITP, where the inciting cause or offending agent is resolved and the host immune response subsides. In the acute setting, the principal goals of the clinical team should be to prevent or stop life-threatening hemorrhage, evaluate for secondary causes, and promptly initiate treatment while monitoring for adverse events. The treatment of chronic ITP is a more complicated problem, and one that requires discussion with multiple members of the care team including primary care, hematology, and surgery. Patients with chronic ITP require a multidisciplinary team whose job is to navigate important decisions with regard to treatment and management of the patient's comorbidities and mitigate the risk of deleterious

effects caused by many of these therapies. The treatment of chronic ITP has evolved over the last 20 years, and with new therapeutic targets, improving rates of remission with medical therapy alone is possible. Nonetheless, surgery remains an important intervention in medically refractory cases and should be considered as a second-line treatment modality. In the appropriately selected surgical patient, laparoscopic splenectomy is a great option with decreased hospital stay and improved morbidity.

Bibliography

1. Kistangari G, McCrae KR. Immune thrombocytopenia. Hematol Oncol Clin North Am. 2013;27(3):495–520.
2. Cines DB, Bussel JB, Liebman HA, Luning Prak ET. The ITP syndrome: pathogenic and clinical diversity. Blood. 2009;113(26):6511–21.
3. Segal JB, Powe NR. Prevalence of immune thrombocytopenia: analyses of administrative data. J Thromb Haemost. 2006;4(11):2377–83.
4. Wu S-R, Kuo H-C, Huang W-C, et al. Incidence, clinical characteristics, and associated diseases in patients with immune thrombocytopenia: a nationwide population-based study in Taiwan. Thromb Res. 2018;164:90–5.
5. Lee JY, Lee J-H, Lee H, et al. Epidemiology and management of primary immune thrombocytopenia: a nationwide population-based study in Korea. Thromb Res. 2017;155:86–91.
6. Khan AM, Mydra H, Nevarez A. Clinical practice updates in the management of immune thrombocytopenia. P T. 2017;42(12):756–63.
7. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood. 2009;113(11):2386–93.
8. Dal MS, Karakus A, Dal T, et al. Assessment of the underlying causes of the immune thrombocytopenia: ten years experience. J Pak Med Assoc. 2017;67(7):1004–8.
9. Liebman H. Other immune thrombocytopenias. Semin Hematol. 2007;44(4 Suppl 5):S24–34.
10. Reese JA, Li X, Hauben M, et al. Identifying drugs that cause acute thrombocytopenia: an analysis using 3 distinct methods. Blood. 2010;116(12):2127–33.
11. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117(16):4190–207.
12. Cecinati V, Principi N, Brescia L, Giordano P, Esposito S. Vaccine administration and the development of immune thrombocytopenic purpura in children. Hum Vaccin Immunother. 2013;9(5):1158–62.
13. Lambert MP, Gernsheimer TB. Clinical updates in adult immune thrombocytopenia. Blood. 2017;129(21):2829–35.
14. Palau J, Jarque I, Sanz MA. Long-term management of chronic immune thrombocytopenic purpura in adults. Int J Gen Med. 2010;3:305–11.
15. Kojouri K. Splenectomy for adult patients with idiopathic thrombocytopenic purpura: a systematic review to assess long-term platelet count responses, prediction of response, and surgical complications. Blood. 2004;104(9):2623–34.
16. Katkhouda N, Grant SW, Mavor E, et al. Predictors of response after laparoscopic splenectomy for immune thrombocytopenic purpura. Surg Endosc. 2001;15(5):484–8.
17. Palandri F, Polverelli N, Sollazzo D, et al. Have splenectomy rate and main outcomes of ITP changed after the introduction of new treatments? A monocentric study in the outpatient setting during 35 years. Am J Hematol. 2016;91(4):E267–72.
18. Kim DK, Riley LE, Hunter P, on behalf of the Advisory Committee on Immunization Practices. Recommended immunization schedule for adults aged 19 years or older, United States, 2018*. Ann Intern Med. 2018;168(3):210.
19. Provan D, Newland AC. Current management of primary immune thrombocytopenia. Adv Ther. 2015;32(10):875–87.
20. Chater C, Terriou L, Duhamel A, et al. Reemergence of splenectomy for ITP second-line treatment? Ann Surg. 2016;264(5):772–7.
21. Morris KT, Horvath KD, Jobe BA, Swanstrom LL. Laparoscopic management of accessory spleens in immune thrombocytopenic purpura. Surg Endosc. 1999;13(5):520–2.
22. Gigot J-F, Gigot F, Jamar F, et al. Inadequate detection of accessory spleens and splenosis with laparoscopic splenectomy A shortcoming of the laparoscopic approach in hematologic diseases. Surg Endosc. 1998;12(2):101–6.
23. Moris D, Dimitriou N, Griniatsos J. Laparoscopic splenectomy for benign hematological disorders in adults: a systematic review. In Vivo. 2017;31(3):291–302.
24. Rattner DW, Ellman L, Warshaw AL. Portal vein thrombosis after elective splenectomy. An underappreciated, potentially lethal syndrome. Arch Surg. 1993;128(5):565–569; discussion 569-570.
25. Rottenstreich A, Kleinstern G, Spectre G, Da'as N, Ziv E, Kalish Y. Thromboembolic events following splenectomy: risk factors, prevention, management and outcomes. World J Surg. 2018;42(3):675–81.
26. de'Angelis N, Abdalla S, Lizzi V, et al. Incidence and predictors of portal and splenic vein thrombosis after pure laparoscopic splenectomy. Surgery. 2017;162(6):1219–30.
27. Bouvier A, Gout M, Audia S, Chalumeau C, Rat P, Deballon O. Routine screening of splenic or portal

vein thrombosis after splenectomy. Rev Med Interne. 2017;38(1):3–7.
28. Tran T, Demyttenaere SV, Polyhronopoulos G, et al. Recommended timing for surveillance ultrasonography to diagnose portal splenic vein thrombosis after laparoscopic splenectomy. Surg Endosc. 2010;24(7):1670–8.
29. Brigden ML, Pattullo AL. Prevention and management of overwhelming postsplenectomy infection--an update. Crit Care Med. 1999;27(4):836–42.
30. Vianelli N, Galli M, de Vivo A, et al. Efficacy and safety of splenectomy in immune thrombocytopenic purpura: long-term results of 402 cases. Haematologica. 2005;90(1):72–7.
31. Chang CC, Chang HC, Wu CH, Chang CY, Liao CC, Chen TL. Adverse postoperative outcomes in surgical patients with immune thrombocytopenia. Br J Surg. 2013;100(5):684–692; discussion 693.

Part XVIII

Esophageal Achalasia

Esophageal Achalasia

47

Chan W. Park and Brooke Pati

Incidence and Pathogenesis

Most studies evaluating the incidence and prevalence of esophageal achalasia indicate that the disease process occurs equally in men and women affecting 1 in 100,000 individuals annually, with a prevalence of 10 in 100,000 [1, 2]. The peak incidence is cited to occur between 30 and 60 years of age, and in most studies the mean age at diagnosis was over 50 years of age [3–8]. Currently, there are no racial predilections identified.

The primary etiology of achalasia is not fully understood and may be neurodegenerative, autoimmune, or viral immune in pathogenesis [1, 2]. Current literature and pathologic examination favors there to be a degeneration of inhibitory ganglion cells in the myenteric plexus of the esophageal body and the LES. Although the cause for this degenerative process is unclear, the end result is an inflammatory process with subsequent loss of the inhibitory neurotransmitters nitrous oxide and vasoactive intestinal peptide. This leads to an imbalance between the excitatory and inhibitory neurons, and as a result there is unopposed cholinergic activity that promotes incomplete relaxation of the LES and aperistalsis due to a loss of latency gradient along the esophageal body.

Etiology

One theory suggests that autoantibodies play a role in the degenerative process of this disease because an increased number of circulating antibodies against the myenteric plexus is observed in some patients with achalasia [9]. It is thought that autoimmune destruction occurs in genetically susceptible people; however no definite trigger has been identified. Further studies report that these circulatory antibodies are likely secondary to a nonspecific reaction to the disease process and not the cause of the disease. This idea is further supported by the finding that similar antibodies are detected in patients without achalasia.

Another postulated cause of achalasia is the idea that there is an inherited component of the disease process. Multiple case-control studies have reported a significant association with human leukocyte antigen (HLA) class II antigens in the development of achalasia [10, 11]. Although HLA association suggests an immunogenetic predisposition for the disease, not all

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achalasia patients have associated HLA antigens. Of note, a recent genetic association study in 4242 controls and 1068 achalasia patients imputed classical HLA haplotype and amino acid polymorphisms suggesting immune-mediated processes in idiopathic achalasia [12].

Several studies have found an association between achalasia and viral infections such as measles and varicella zoster virus; however no causal relationship has been determined. Interestingly, one strong piece of evidence that favors infection as part of the pathogenesis of achalasia is the fact that Chagas disease, caused by the *Trypanosoma cruzi*, does closely mimic the pathophysiology of primary achalasia [13].

Diagnosis

The diagnosis of esophageal achalasia is typically suspected in a patient who presents with dysphagia to both solids and liquids with associated regurgitation of undigested food. Upper endoscopy is an essential first step to exclude structural abnormalities such as esophageal carcinoma, stricture, or eosinophilic esophagitis. Various diagnostic modalities can be utilized to assist in making the diagnosis of esophageal achalasia; however, esophageal manometry is considered the gold standard for definitive diagnosis [14].

Conventional Manometry

Using a flexible catheter, esophageal pressures are measured along the length of the esophagus. The manometric finding of aperistalsis of the esophageal body and incomplete relaxation of the LES in the absence of mechanical obstruction strongly supports the diagnosis of achalasia [15]. Other findings that are suggestive of the diagnosis but are not required include an increased resting LES pressure and simultaneous non-propagating contractions of the esophageal musculature [16].

High-Resolution Manometry

Recent advances in manometry to include the evolution from conventional manometry with pressure sensors spaced 3–5 cm apart utilizing solid-state or water-perfused catheters to newer high-resolution manometry (HRM) where sensors are placed 1 cm apart have led to a greater understanding and improved diagnostic algorithms for achalasia [14]. HRM enables esophageal pressure data to be displayed as esophageal topography plots. Esophageal topography using HRM as a diagnostic method was originally developed by Clouse and resulted in an improved understanding of peristaltic contractile activity [17–22]. Seminal work that characterized HRM using Clouse plots in both asymptomatic and symptomatic individuals eventually led to the creation of a new classification scheme for motility disorders, called the Chicago Classification [23].

The Chicago Classification provides a standardized approach for analysis and categorization of abnormalities that has led to a significant increase in our knowledge regarding the diagnosis and management of motility disorders. This hierarchical system of analysis has four major categories that are classified based on LES relaxation and motility of the esophageal body: (1) incomplete LES relaxation (achalasia or esophagogastric junction outflow obstruction), (2) other major motility disorders (absent contractility, distal esophageal spasm, and hypercontractile or jackhammer esophagus), (3) minor motility disorders (ineffective esophageal motility or fragmented peristalsis), and (4) normal esophageal motility [24].

This classification further delineated achalasia into three clinically relevant subclassifications on the basis of the pattern of contractility in the esophageal body which have important therapeutic outcome implications (Fig. 47.1). Subtype I is considered classical achalasia without evidence of pressurization, subtype II is esophageal achalasia with compression or ≥2 test swallows associated with an esophageal pressurization >30 mm Hg, and subtype III or spastic achalasia is defined by ≥2 spastic contractions with or without a

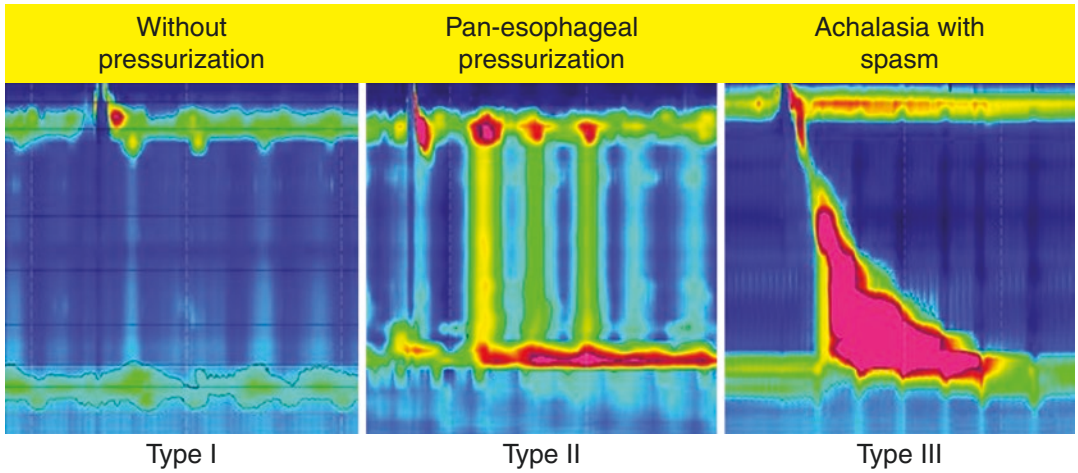

Fig. 47.1 Esophageal pressure topography (EPT) based on the three types of achalasia from the Chicago Classification (https://www.mayoclinic.org/~/media/kcms/gbs/patient%20consumer/images/2016/05/10/15/53/velafigures1_lg.jpg)

period of compartmentalized pressurization [17, 18]. This last subtype is the most difficult to treat, and investigators used logistic regression analysis to determine that type II achalasia patients are more likely to have good symptom response and less likely to require multiple treatments when compared to the other subtypes [19, 20].

Barium Esophagram

Barium esophagram provides another adjunct for diagnosing esophageal achalasia. Esophageal dilation with a gradual taper down to the gastroesophageal junction giving a "bird's-beak" appearance is the classic description of achalasia (Fig. 47.2). Additional findings include aperistalsis and poor emptying of barium. Signs suggestive of late- or end-stage achalasia include tortuosity, angulation, sigmoidization, and megaesophagus [14].

Endoscopy

As noted previously it is imperative that esophagogastroduodenoscopy be performed in patients presenting with dysphagia primarily to rule out a mechanical obstruction due to malignancy. On manometry mechanical obstruction can similarly

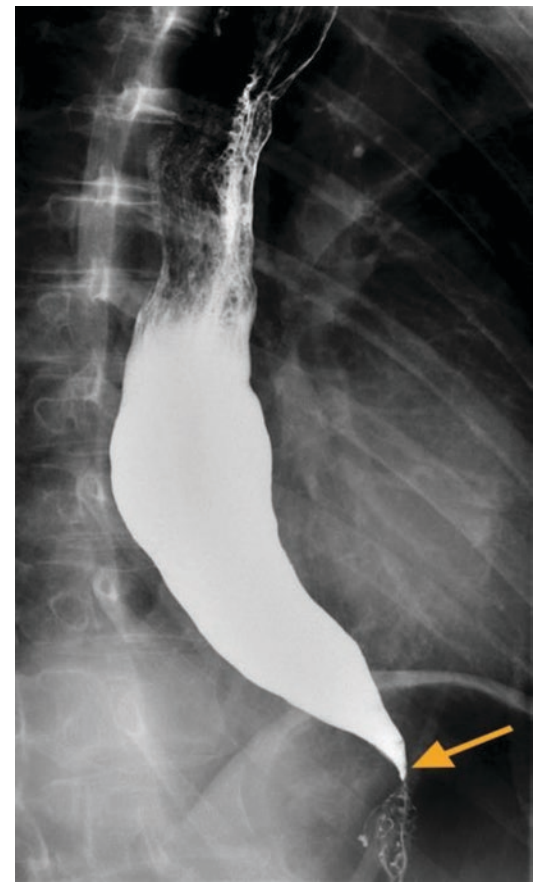

Fig. 47.2 Classic bird's-beak appearance of achalasia barium swallow. (From http://www.svuhradiology.ie/case-study/achalasia-barium-swallow/ courtesy of Dr. Eric Heffernan)

result in impaired LES relaxation and aperistalsis or spastic contractions of the esophageal body; therefore endoscopic evaluation aids as a diagnostic tool [25]. The term "pseudoachalasia" is used when mechanical obstruction mimics achalasia both clinically and manometrically. Endoscopy also allows for diagnostic evaluation of other esophageal disorders such as gastroesophageal reflux disease (GERD), Barrett's esophagus, and eosinophilic esophagitis. It is routine practice that individuals with dysphagia have random biopsies sampled from the distal and proximal esophagus to assess for eosinophilic esophagitis. Additionally, if signs of Barrett's esophagus are identified on endoscopy, the length of mucosal involvement should be measured, and multiple biopsies should be taken to evaluate for dysplasia or malignancy.

Multidisciplinary Approach

The diagnostic process incorporates a multidisciplinary approach and involves collaboration among numerous medical specialties. Gastroenterologists and foregut surgeons are often called upon to perform diagnostic endoscopy and interpret pH/manometry results. Radiologists analyze barium esophagrams and other imaging studies in anticipation of achalasia treatments and procedures. Nurses and procedure technicians administer manometry exams, assist physicians with pH testing and analysis, and support patients through the multiple testing and procedures. It is helpful for all allied health providers to be knowledgeable about the various procedures necessary in the diagnosis of achalasia, and this will enhance the effectiveness of the multidisciplinary team in facilitating achalasia patient care.

Other Esophageal Motility Disorders

There are several distinct esophageal motility disorders that may present with similar patient complaints as achalasia, and it is helpful to consider/exclude these disorders in diagnosis and management of achalasia.

Nutcracker Esophagus

Hypercontractile or "nutcracker" esophagus is an esophageal motility disorder characterized by high amplitude peristaltic contractions in the distal esophagus or excessive duration of peristalsis. The diagnosis is made using manometry in patients with either noncardiac chest pain or dysphagia when esophageal pressures are >180 mm Hg during peristalsis or there is a long duration of swallow responses (>7 seconds) [26]. This differs from achalasia in that patients with "nutcracker" esophagus have an LES that relaxes normally and peristaltic contractions that propagate normally. Also distinct from achalasia, treatment for patients with "nutcracker" esophagus involves medications typically aimed at symptom relief (e.g., nitrates, sildenafil, proton pump inhibitors, tricyclic antidepressants, etc.), while endoscopic and surgical interventions have little therapeutic role.

Diffuse Esophageal Spasm

Although an uncommon disease accounting for only 10% of esophageal motility disorders, diffuse esophageal spasm (DES) should be considered on the differential when a patient presents with symptoms of dysphagia. Using conventional manometry, DES is diagnosed by the presence of simultaneous contractions in the distal esophagus in ≥20% of wet swallows with amplitude contractions of ≥30 mmHg alternating with normal peristalsis [27]. When HRM is utilized as a diagnostic tool, the Chicago Classification accounts for a new parameter called distal latency that is only visualized on esophageal topography plots. Current guidelines define DES by HRM as a normal LES relaxation pressure and a distal latency of <4.5 s in 20% of wet swallows. Treatment for DES utilizes medical therapies similar to the treatment of hypertensive esophagus, and in refractory patients, endoscopic and surgical

interventions such as surgical myotomy and per oral endoscopic myotomy (POEM) can be attempted [28]. These alternative treatment modalities will be described in detail below.

Presentation

It is well documented that progressive dysphagia to both solids and liquids is a hallmark symptom associated with a diagnosis of esophageal achalasia. Tsuboi and colleagues performed a single-center review of all patients who underwent manometry during a 24-year time period (1984–2008) and found that patients diagnosed with achalasia most commonly presented with dysphagia and heartburn [29]. Other common symptoms include regurgitation of undigested food or saliva, noncardiac chest pain, cough, hoarseness, or sore throat. Patients frequently report retrosternal burning and discomfort similar to heartburn and typical of gastroesophageal reflux disease. These reported symptoms may, in fact, be due to gastroesophageal reflux. However, other causes include direct irritation of the esophageal lining by undigested food, retained pills, or lactate production from bacterial fermentation of retained carbohydrates [29, 30]. Abnormal esophageal motility might also trigger the sensation of heartburn. It is important to understand that there is significant overlap of the characteristic symptoms of achalasia and more common disorders such as gastroesophageal reflux disease, mechanical obstruction (secondary to stricture or rings), or malignancy. Therefore, it is often necessary to rule out these disorders prior to referral for an esophageal motility disorder evaluation.

Due to the symptoms that patients with achalasia experience, they are at an increased risk of complications that may require more urgent intervention such as aspiration pneumonia or malnourishment. It is common for patients with regurgitation of undigested food or accumulated saliva to wake up from sleep because of coughing and choking, thus increasing their risk for aspirating. Additionally those individuals who have been unable to tolerate solids or liquids by mouth intake secondary to dysphagia are often malnourished, and it is recommended these individuals have more urgent intervention to prevent worsening nutritional status.

Natural History

Over time, patients with achalasia who do not undergo treatment can develop progressive dilation of the esophagus. Characteristic findings of late- or end-stage achalasia include esophageal tortuosity, angulation, and severe dilation or megaesophagus (diameter >6 cm). Despite undergoing treatment for achalasia, approximately 10–15% of these patients will develop late- or end-stage achalasia, and some case series report that up to 5% of patients require esophagectomy [31, 32].

Although patients with esophageal achalasia are at increased risk for developing esophageal cancer, the absolute risk for esophageal cancer is low. One study followed 448 patients for a median time of 9.6 years and found that 15 patients (3.3%) developed esophageal cancer after a mean symptom duration of 13 years [33]. Of note, the risk of esophageal cancer was increased 28-fold (95% CI 17–46) as compared with controls.

Patients with esophageal achalasia who develop esophageal cancer typically get squamous cell carcinoma; however some studies have demonstrated there is also an increased risk of developing esophageal adenocarcinoma. Despite this increased risk of esophageal cancer, endoscopic surveillance in patients with achalasia remains controversial and is currently not routinely recommended. One population-based study in Sweden followed 1062 patients with achalasia for up to 24 years and found the risk of esophageal cancer was increased 16-fold (95% CI 8.8–28.3) compared to population controls [34]. In this study esophageal cancer was diagnosed an average of 14 years following the diagnosis of achalasia. Additionally, the authors estimated that annual surveillance endoscopy after the first year would be required in 406 men and 2200 women to detect one cancer.

Multidisciplinary Management of Achalasia

Achalasia is a chronic, progressive disease that currently has no cure. Treatment options for achalasia are undertaken to reduce the hypertonicity of the LES by pharmacologic, endoscopic, or surgical means. However, because no intervention significantly affects the aperistalsis associated with achalasia and because the LES hypertonicity often returns over time despite therapeutic intervention, repeat interventions are often required. Thus the goals in treating achalasia are to relieve the patient's symptoms, improve esophageal emptying, and prevent further dilation of the esophagus. In order to achieve these goals, a multidisciplinary approach tailoring the available therapeutic options to the symptoms of the achalasia patient should be utilized.

Medical Therapy

Oral pharmacologic therapies such as calcium channel blockers and long-acting nitrates provide a noninvasive treatment option for achalasia. However, these agents are considered the least effective intervention for achalasia due to their short-lived clinical response and unfavorable side effect profile [35]. These medications aim to relax the smooth muscle and are effective in reducing LES pressure and temporarily relieving dysphagia, but they do not improve LES relaxation or peristalsis. Therefore, they do not provide complete alleviation of symptoms and are generally reserved for those patients who have comorbid conditions that prevent them from undergoing definitive but more invasive therapies.

Especially in medically complicated or compromised patients, the initiation of pharmacotherapy should be carefully undertaken. A number of these medications will decrease systemic blood pressure and even end organ perfusion. Patients must be warned about the side effect profiles of these medications such as orthostatic hypotension and dizziness, which could result in traumatic falls. Overall, pharmacotherapy plays a very limited role in the treatment of patients with achalasia and should be used in very early stages of the disease, prior to more definitive treatments, or for patients who fail or are not candidates for other more invasive treatments. Endoscopic therapy is to be discussed in another chapter.

Surgical Therapy

In 1913 Ernest Heller performed the first surgical myotomy for achalasia, and since then several different technical approaches have been described to accomplish surgical management of achalasia. The original approach involved both an anterior and posterior division of the circular muscle fibers of the LES without disruption of the mucosa using a thoracotomy [36]. A decade later Zaaijer modified the technique to a single anterior extramucosal myotomy showing equivalent results [36]. Since the 1990s recent advances in minimally invasive surgical techniques have enabled surgeons to perform a surgical myotomy effectively through both thoracoscopic and laparoscopic approaches. A left thoracoscopic approach was associated with a shorter hospital stay, diminished postoperative discomfort, and a faster overall recovery [37]. Furthermore, long-term follow-up showed that almost 90% of patients achieved relief of dysphagia. However, this was in the setting of 60% of patients having abnormal reflux postoperatively. The laparoscopic approach was then favored as it offers better exposure of the gastroesophageal junction, the ability to perform an extended myotomy onto the gastric wall, and the ability to perform a partial fundoplication with the goal of reducing postoperative reflux [38].

Surgical Myotomy

As described earlier the myotomy has changed over time, and the current standard approach uses an extended myotomy which is defined as

a 3 cm incision onto the cardia of the stomach. The extended esophageal myotomy incision has been shown to provide long-term dysphagia relief due to disruption of the gastric sling, which consists of short transverse muscle fibers on the lesser curve of the stomach. The extended myotomy is performed by individually dividing the esophageal and gastric muscle fibers. First, the longitudinal muscles are divided, which exposes the underlying circular muscles and this allows for their division next. Division through the longitudinal and circular muscle fibers further reveals a smooth and white mucosal plane. It is described that the most critical and challenging step is creating a 3 cm myotomy caudal to the gastroesophageal junction. The challenge arises because the tissue plane becomes less readily identifiable, the gastric sling can blur the dissection, and the stomach mucosa is thinner and more prone to perforation here. After this step the esophageal portion of the myotomy should be approximately 6 cm in length with the total length of the entire myotomy being 9 cm. It is recommended that endoscopic inspection of the mucosa and the myotomy is performed prior to proceeding in order to identify and repair any mucosal perforations. If a partial fundoplication is to be performed, it would follow next [39].

The 2012 guidelines from the Society of American Gastrointestinal and Endoscopic Surgeons recommend that patients who undergo myotomy should have a fundoplication to prevent reflux [34]. Laparoscopic Heller myotomy with a partial fundoplication has now become the gold standard for treatment of achalasia in the United States. One meta-analysis demonstrated that laparoscopic myotomy combined with an antireflux procedure provided better symptom relief than all endoscopic and other surgical approaches with a low complication rate (6.3%) [40]. In addition, the incidence of postoperative gastroesophageal reflux was less than 10% when fundoplication was performed with a laparoscopic myotomy, while it is much higher (32%) without fundoplication. Although it is widely recommended that a fundoplication should be performed to reduce the rate of reflux after myotomy, it is not well known which approach, an anterior Dor or posterior Toupet, is better for accomplishing this benefit. One multicenter randomized controlled trial comparing these two approaches found similar improvement rates in dysphagia and regurgitation in both groups and a nonsignificant higher percentage of abnormal pH test results in 24 patients who received a Dor fundoplication compared to 19 patients with a Toupet fundoplication (41% vs 21%) [41]. Currently, additional studies aimed at comparing the two approaches are needed to determine which partial fundoplication provides the best reflux control after myotomy.

Esophagectomy

Treatments for achalasia are palliative in nature, and success of therapy is based most importantly on relief of symptoms such as dysphagia and regurgitation. Even if patients respond to one of the aforementioned therapies, they should be advised regarding the risk of developing "end-stage" achalasia. This is characterized by massive esophageal dilation (megaesophagus) of >6 cm in diameter or esophageal body tortuosity (sigmoid esophagus). Patients who reach this stage of the disease often have failed multiple interventions involving the LES, and esophagectomy is necessary for relief of disabling manifestations of end-stage disease to include dysphagia and delayed emptying. There are relative indications for esophagectomy such as a sigmoid esophagus and in particular when there is a tortuous segment above the diaphragm that empties poorly (Fig. 47.3) [42]. There is significant morbidity associated with esophagectomy, and now that studies are consistently demonstrating symptom improvement in greater than 90% of patients after laparoscopic Heller myotomy with fundoplication, esophagectomy should be reserved for those who have failed all other treatment modalities or have concomitant esophageal pathology requiring resection.

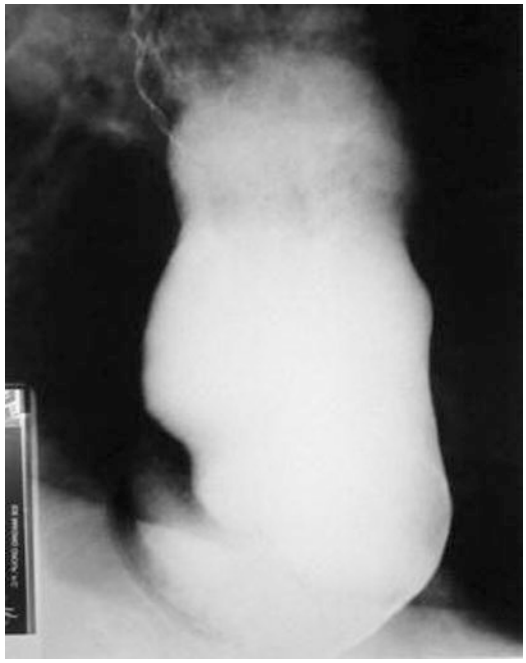

Fig. 47.3 Barium upper gastrointestinal radiograph of a sigmoid esophagus from end-stage achalasia. (https://link.springer.com/article/10.1007/s00268-015-3012-x#Fig3)

Summary

Achalasia is a rare primary esophageal motility disorder characterized by incomplete relaxation of the LES and esophageal aperistalsis. As described earlier, no current medical therapy is curative for achalasia; therefore all available treatment options are aimed at relieving symptoms. It is recommended that given the complexity of the disease process, patient-specific differences, and the wide array of management options, a multidisciplinary approach should be implemented. Through a multidisciplinary approach, nurses, radiologists, gastroenterologists, surgeons, and ancillary support members can work with the patient to determine which treatment option will provide the best long-term symptom relief and reduce the risk of needing an esophagectomy or developing esophageal cancer. Effective pharmacologic options do not exist. Recent advances in endoscopic therapy provide less invasive means for treating achalasia; however, their durability is still in question. Surgical options remain a primary treatment option for many individuals.

References

1. Vaezi MF, Richter JE. Diagnosis and management of achalasia. American College of Gastroenterology Practice Parameter Committee. Am J Gastroenterol. 1999;94:3406–12.
2. Francis DL, Katzka DA. Achalasia: update on the disease and its treatment. Gastroenterology. 2010;139:369–74.
3. Farrukh A, DeCaestecker J, Mayberry JF. An epidemiological study of achalasia among the south Asian population of Leicester, 1986–2005. Dysphagia. 2008;23:161–4.
4. Sadowski DC, Ackah F, Jiang B, et al. Achalasia: incidence, prevalence and survival. A population-based study. Neurogastroenterol Motil. 2010;22:e256–61. 15.
5. Birgisson S, Richter JE. Achalasia in Iceland, 1952–2002: an epidemiologic study. Dig Dis Sci. 2007;52:1855–60.
6. Gennaro N, Portale G, Gallo C, et al. Esophageal achalasia in the Veneto region: epidemiology and treatment. Epidemiology and treatment of achalasia. J Gastrointest Surg. 2011;15:423–8.
7. Marlais M, Fishman JR, Fell JM, et al. UK incidence of achalasia: an 11-year national epidemiological study. Arch Dis Child. 2011;96:192–4.
8. Enestvedt BK, Williams JL, Sonnenberg A. Epidemiology and practice patterns of achalasia in a large multi-centre database. Aliment Pharmacol Ther. 2011;33:1209–14. 19 Booy JD, Takata J, Tomlinson G, et al.
9. Storch WB, Eckardt VF, Wienbeck M, et al. Autoantibodies to Auerbach's plexus in achalasia. Cell Mol Biol (Noisy-le-Grand). 1995;41(8):1033–8.
10. Verne GN, Sallustio JE, Eaker EY. Anti-myenteric neuronal antibodies in patients with achalasia. A prospective study. Dig Dis Sci. 1997;42(2):307–13.
11. Verne GN, Hahn AB, Pineau BC, et al. Association of HLA-DR and -DQ alleles with idiopathic achalasia. Gastroenterology. 1999;117(1):26–31.
12. Gockel I, Becker J, Wouters MM, et al. Common variants in the HLA-DQ region confer susceptibility to idiopathic achalasia. Nat Genet. 2014;46(8):901–4.
13. Ates F, Vaezi MF. The pathogenesis and management of Achalasia: current status and future directions. Gut Liver. 2015;9(4):449–63.
14. Vaezi MF, Pandolfino JE, Vela MF. ACG clinical guideline: diagnosis and management of achalasia. Am J Gastroenterol. 2013;108(8):1238–49.
15. Pandolfino JE, Kahrilas PJ. American gastroenterological A. AGA technical review on the clinical use of esophageal manometry. Gastroenterology. 2005;128(1):209–24.

16. Spechler SJ, Castell DO. Classification of oesophageal motility abnormalities. Gut. 2001;49(1):145–51.
17. Fox M, Hebbard G, Janiak P, et al. High-resolution manometry predicts the success of oesophageal bolus transport and identifies clinically important abnormalities not detected by conventional manometry. Neurogastroenterol Motil. 2004;16(5):533–42.
18. Pandolfino JE, Ghosh SK, Zhang Q, Jarosz A, Shah N, Kahrilas PJ. Quantifying EGJ morphology and relaxation with high-resolution manometry: a study of 75 asymptomatic volunteers. Am J Physiol Gastrointest Liver Physiol. 2006;290(5):G1033–40.
19. Pandolfino JE, Ghosh SK, Rice J, Clarke JO, Kwiatek MA, Kahrilas PJ. Classifying esophageal motility by pressure topography characteristics: a study of 400 patients and 75 controls. Am J Gastroenterol. 2008;103(1):27–37.
20. Ghosh SK, Pandolfino JE, Zhang Q, et al. Quantifying esophageal peristalsis with high-resolution manometry: a study of 75 asymptomatic volunteers. Am J Physiol Gastrointest Liver Physiol. 2006;290(5):G988–97.
21. Scherer JR, Kwiatek MA, Soper NJ, et al. Functional esophagogastric junction obstruction with intact peristalsis: a heterogeneous syndrome sometimes akin to achalasia. J Gastrointest Surg. 2009;13(12):2219–25.
22. Ghosh SK, Pandolfino JE, Rice J, et al. Impaired deglutitive EGJ relaxation in clinical esophageal manometry: a quantitative analysis of 400 patients and 75 controls. Am J Physiol Gastrointest Liver Physiol. 2007;293(4):G878–85.
23. Kahrilas PJ, Bredenoord AJ, Fox M, et al. International high resolution Manometry Working Group. The Chicago Classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil. 2015;27(2):160–74.
24. Rohof WOA, Bredenoord AJ. Chicago Classification of esophageal motility disorders: lessons learned. Curr Gastroenterol Rep. 2017;19(8):37.
25. Krill JT, Naik RD, Vaezi MF. Clinical management of achalasia: current state of the art. Clin Exp Gastroenterol. 2016;9:71–82.
26. Achem SR, Gerson LB. Distal Esophageal spasm: an update. Curr Gastroenterol Rep. 2013;15(9):325.
27. Lufrano R, Heckman MG, Diehl N, et al. Nutcracker esophagus: demographic, clinical features, and esophageal tests in 115 patients. Dis Esophagus. 2015;28(1):11–8.
28. Bashashati M, Andrews C, Gosh S, et al. Botulinum toxin in the treatment of diffuse esophageal spasm. Dis Esophagus. 2010;23(7):554–60.
29. Tsuboi K, Hoshino M, Srinivasan A, et al. Insights gained from symptom evaluation of esophageal motility disorders: a review of 4,215 patients. Digestion. 2012;85(3):236–42.
30. 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(9):1974–9.
31. Spechler SJ, Souza RF, Rosenberg SJ, et al. Heartburn in patients with achalasia. Gut. 1995;37:305–8.
32. Eckardt VF, Hoischen T, Bernhard G. Life expectancy, complications, and causes of death in patients with achalasia: results of a 33-year follow-up investigation. Eur J Gastroenterol Hepatol. 2008;20:956.
33. Vela MF, Richter JE, Wachsberger D, et al. Complexities of managing achalasia at a tertiary referral center: use of pneumatic dilatation, Heller myotomy, and botulinum toxin injection. Am J Gastroenterol. 2004;99:1029.
34. Leeuwenburgh I, Scholten P, Alderliesten J, et al. Long-term esophageal cancer risk in patients with primary achalasia: a prospective study. Am J Gastroenterol. 2010;105:2144–9.
35. Vaezi MF, Richter JE. Current therapies for achalasia: comparison and efficacy. J Clin Gastroenterol. 1998;27(1):21–35.
36. Pellegrini C, Wetter LA, Patti M, et al. Thoracoscopic esophagomyotomy. Initial experience with a new approach for the treatment of achalasia. Ann Surg. 1992;216:291–6.
37. Stefanidis D, Richardson W, Farrell TM, et al. SAGES guidelines for the surgical treatment of esophageal achalasia. Surg Endosc. 2012;26:296–311.
38. Patti MG, Pellegrini CA, Horgan S, et al. Minimally invasive surgery for achalasia: an 8-year experience with 169 patients. Ann Surg. 1999;230:587–93.
39. Watson TJ. Esophagectomy for end-stage achalasia. World J Surg. 2015;39:1634.
40. Sandler RS, Nyrén O, Ekbom A, et al. The risk of esophageal cancer in patients with achalasia. A population-based study. JAMA. 1995;274:1359.
41. Hirota WK, Zuckerman MJ, Adler DG, et al. ASGE guideline: the role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. Gastrointest Endosc. 2006;63:570–80.
42. Eckardt AJ, Eckardt VF. Editorial: cancer surveillance in achalasia: better late than never? Am J Gastroenterol. 2010;105:2150–2.

48 Esophageal Achalasia: Endoluminal Therapy

Brett C. Parker and Eleanor C. Fung

Pneumatic Dilation

Pneumatic dilation has been considered the first-line nonsurgical therapy for achalasia in which the goal of the procedure is to dilate the lower esophageal sphincter through disrupting its circular muscle fibers via radial force. It is generally performed under sedation with either endoscopic or fluoroscopic guidance to aid with positioning of the balloon across the lower esophageal sphincter. Graded sized polyethylene balloons are used for intraluminal dilation and come in diameters of 3.0, 3.5, and 4.0 cm which are larger than standard through-the-scope balloons. The balloon is generally distended to a pressure of 8–15 psi and maintained for 15–60 seconds to confirm radiologic obliteration of the balloon waist at the lower esophageal sphincter (Figs. 48.1 and 48.2). Pneumatic dilation is generally performed in a graded fashion starting with a 3.0 cm balloon, and patients are evaluated based on symptom and endoscopic evaluation correlated with LES pressures every 4–6 weeks to determine if a larger dilatation or subsequent dilatations are necessary. Gastrografin followed by barium esophagrams are also typically performed following dilatation to rule out esophageal perforation, which is one of the inherent risks of the procedure and occurs in approximately 2–5% of cases [6]. Other complications of pneumatic dilation include intramural hematoma, post-dilation chest pain, gastroesophageal reflux, and traumatic diverticuli [1].

The success rate of pneumatic dilatation for symptom regression was found to range from 54% to 91% in numerous longitudinal cohort studies [4]. However, published follow-up studies at 5–10 years have shown that approximately 20–75% of patients then required repeated dilatations in which it was found that treatment effect and symptom remission decrease with time [13, 14]. Risk factors which predict relapse following pneumatic dilatation include younger age (age <40 years), male sex, single dilation session with a 3.0 cm balloon, immediate or 3-month post-treatment LES pressure >15 mmHg, poor esophageal emptying on timed barium swallow, and classic achalasia [5].

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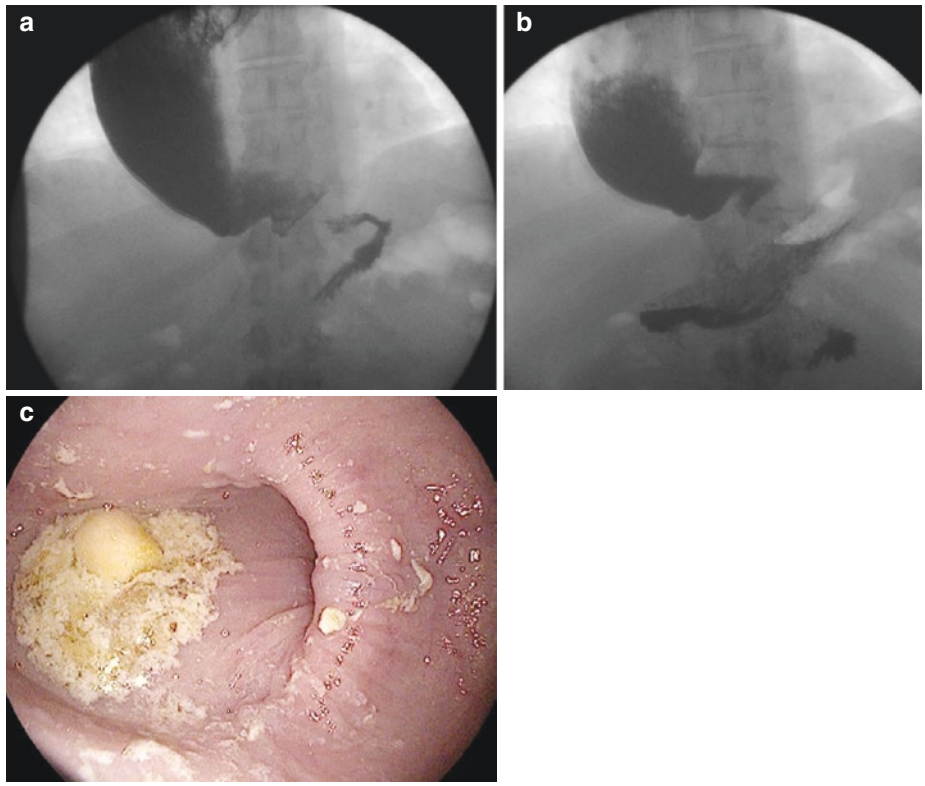

Fig. 48.1 Endoscopic and radiologic findings in achalasia. (**a**) Conventional barium esophagram of a patient with achalasia showing the classic "birds beak" appearance of the esophagus with tapering at the gastroesophageal junction. (**b**) Radiologic evidence of achalasia with a dilated esophagus and air-fluid level. (**c**) Evidence of dilated esophagus with retained food particles commonly encountered during endoscopy

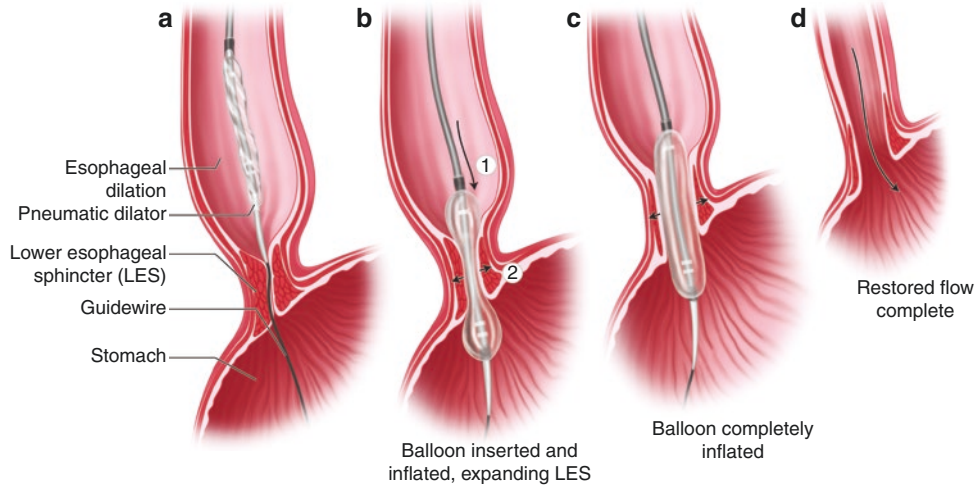

Fig. 48.2 Technique for pneumatic dilation of the lower esophageal sphincter for achalasia. A guidewire is used to aid positioning of the pneumatic balloon across the gastroesophageal junction. The balloon is then inflated until the balloon waist is obliterated to ensure adequate dilation of the GEJ. (**a**) Under endoscopic guidance, a guidewire is passed through the gastroesophageal junction, followed by the pneumatic dilater. (**b**) The waist of the pneumatic balloon is positioned in the center of the GEJ. (**c**) The balloon is inflated to desired diameter, generating radial force and tearing the muscle fibers. (**d**) The GEJ lumen is enlarged, and flow into the stomach is restored

Endoscopic Botulinum Toxin Injection

Botulinum toxin inhibits the release of acetylcholine from nerve endings, thus reversing the unopposed excitatory state leading to increased LES contraction seen in achalasia. These pharmacological actions of the neuromuscular junction were first described in 1980 [2]. The technique for injecting botulinum toxin into the LES as a treatment for achalasia was subsequently published by Pasricha et al. in 1994. This procedure has since become the most common initial therapy for achalasia, being used in 41% of cases [7]. Although there is no agreement on a universal technique for botulinum toxin injection, there has been little variation since it was originally described. The original protocol consists of performing a complete upper endoscopy under conscious sedation with light air insufflation and withdrawing the scope to identify the LES. This landmark is typically described as a sphincter rosette, the Z-line, or the squamocolumnar junction (Fig. 48.3). Once the GEJ has been identified, a 5 mm sclerotherapy needle is used to inject 20–25 U/mL of botulinum toxin into each of the four quadrants of the LES under direct vision, resulting in a total of 80–100 U reconstituted in 4–5 mL of saline, taking care not to raise a submucosal bleb [11].

Although botulinum toxin injection has a great initial response rate of approximately 78%, major limitations of this treatment option include its short duration of effect which typically lasts 6–9 months on average, as well as its decreased effectiveness over time with little to no effect seen after 2–3 injections [8]. Studies have shown that only 40.6% of patients report improved symptoms at 1 year follow-up and nearly half of patients require a second injection [3]. Despite the limited efficacy of this therapy as definitive treatment, it has an excellent safety profile and is typically very well tolerated by patients. Therefore, it is considered a viable treatment option for high-risk surgical patients, the elderly, and patients with shortened life expectancy.

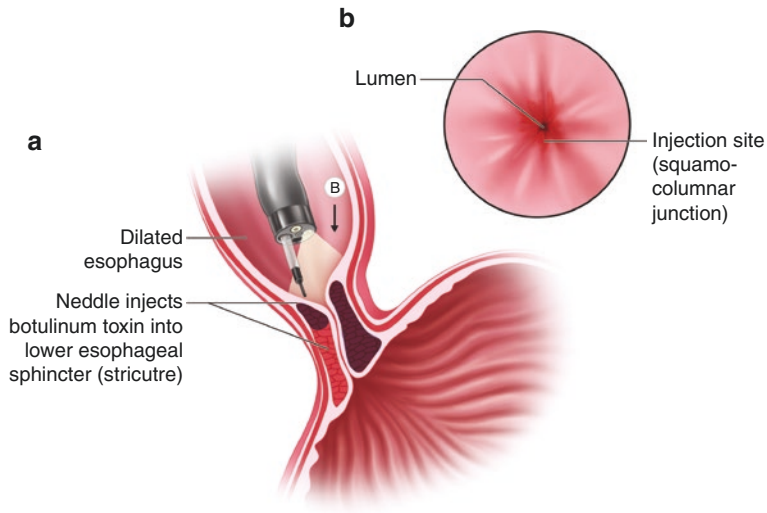

Fig. 48.3 Technique for endoscopic botox injection. A sclerotherapy needle is used to make four-quadrant injections of botulinum toxin into the squamocolumnar junction at the lower esophageal sphincter. (**a**) A sclerotherapy needle is passed through the endoscope, positioned perpendicular to the esophageal wall, and used to make four-quadrant injections of botulinum toxin, avoiding the creation of a submucosal bleb. (**b**) The injection site should be at the squamocolumnar junction of the lower esophageal sphincter, or "Z-line"

Other Endoscopic Therapies

POEM, per oral endoscopic myotomy, will be described in another chapter. Ethanolamine oleate is a sclerosing agent that induces an inflammatory response and fibrosis that has been used in the treatment of achalasia by causing excitatory neuron damage to decrease the LES pressure. The use of intersphincteric ethanolamine oleate injections at the gastroesophageal junction has been found to be a clinically comparable and a cheaper alternative to endoscopic botulinum toxin injections in initial case series [10]. Another novel technique is the use of temporary self-expanding metallic stents measuring up to 30 mm in diameter placed across the gastroesophageal junction for symptom improvement. The stents are left in place for 4–5 days before being retrieved. A single-center study showed a long-term clinical success rate of over 80% with greater efficacy in comparison to pneumatic dilation; however, complications included stent migration, gastroesophageal reflux, and chest pain [5].

Conclusion

The choice of treatment for achalasia should be clinically tailored based on the patient's age, medical comorbidities, operative risk, symptom severity, and local expertise of the managing physicians. Endoscopy plays a key role, not only in the diagnostic work-up for achalasia and surveillance for esophageal malignancy, but also as a therapeutic tool in providing viable minimally invasive treatment options for symptom relief. More studies are required to determine the long-term efficacy and safety of these endoscopic therapies in comparison to surgical myotomy.

References

1. Arora Z, Thota PN, Sanaka MR. Achalasia: current therapeutic options. Ther Adv Chronic Dis. 2017;8:101–8.
2. Bigalke H, Habermann E. Blockade by tetanus and botulinum toxin of postganglionic cholinergic nerve endings in the myenteric plexus. Naunyn Schmiedeberg's Arch Pharmacol. 1980;312:255–63.
3. Campos GM, Vittinghoff E, Rabl C, Takata M, Gadenstätter M, Lin F, Ciovica R. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. Ann Surg. 2009;249:45–57.
4. Chuah SK, Wu KL, Hu TH, Tai WC, Changchien CS. Endoscope-guided pneumatic dilation for treatment of esophageal achalasia. World J Gastroenterol. 2010;16:411–7.
5. Chuah SK, Chiu CH, Tai WC, Lee JH, Lu HI, Changchien CS, Tseng PH, Wu KL. Current status in the treatment options for esophageal achalasia. World J Gastroenterol. 2013;19:5421–9.
6. Dunst CM, Kurian AA, Swanstrom LL. Endoscopic Myotomy for Achalasia. Adv Surg. 2014;48:27–41.
7. Enestvedt BK, Williams JL, Sonnenberg A. Epidemiology and practice patterns of achalasia in a large multicentre database. Aliment Pharmacol Ther. 2011;33:1209–11.
8. Kumar AR, Schnoll-Sussman FH, Katz PO. Botulinum toxin and pneumatic dilation in the treatment of achalasia. Tech Gastrointest Endosc. 2014;16:10–9.
9. 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;42:265–71.
10. Mikaeli J, Veisari AK, Fazlollahi N, Mehrabi N, Soleimani HA, Shirani S, Malekzadeh R. Ethanolamine oleate versus botulinum toxin in the treatment of idiopathic achalasia. Ann Gastroenterol. 2015;28:229–35.
11. Pasricha PJ, Ravich WJ, Hendrix TR, Sostre S, Jones B, Kalloo AN. Treatment of achalasia with intrasphincteric injection of botulinum toxin. A pilot trial. Ann Intern Med. 1994;121:590–1.
12. Vaezi MF, Pandol JE, Vela MF. ACG clinical guideline: diagnosis and management of achalasia. Am J Gastroenterol. 2013;108:1238–49.
13. West RL, Hirsch DP, Bartelsman JF, de Borst J, Ferwerda G, Tytgat GN, Boeckxstaens GE. Long term results of pneumatic dilation in achalasia followed for more than 5 years. Am J Gastroenterol. 2002;97:1346–51.
14. Zerbib F, Thetiot V, Richy F, Benajah DA, Message L, Lamouliatte H. Repeated pneumatic dilations as long-term maintenance therapy for esophageal achalasia. Am J Gastroenterol. 2006;101:692–7.

49 Surgical Therapy of Esophageal Achalasia: Peroral Endoscopic Myotomy

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Introduction

The traditional surgical approach for achalasia is Heller myotomy, commonly performed laparoscopically, with and without robot assistance. The addition of a partial fundoplication is used to minimize postoperative reflux. While the Heller myotomy is considered the gold standard with excellent long-term results, the advent of peroral endoscopic myotomy (POEM) provides a less invasive interventional approach for the management of achalasia.

Indications and Contraindications

For patients to be considered POEM candidates, a diagnosis of achalasia is necessary, and malignancy must be ruled out. Indications for POEM include classic achalasia, complicated achalasia (like a dilated "sigmoid" esophagus and failure of previous myotomy), as well as other spastic esophageal motility disorders. Contraindications to POEM include severe pulmonary disease, coagulopathy, and prior interventions that compromise esophageal mucosal integrity like an endoscopic mucosal resection, radiofrequency ablation, and radiation therapy.

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Patient Preparation

Preoperative assessment includes esophagogram, upper endoscopy, high-resolution manometry, and pH testing. Patients are routinely placed on a clear liquid diet for at least 2 days prior to the procedure to aid in decreasing residual food particles in the esophagus. Some surgeons prescribe fluconazole for 5 days for candidiasis prophylaxis from esophageal stasis.

Principles of POEM Operative Technique

The principles of POEM procedure are (1) mucosal incision and submucosal access, (2) submucosal tunnel creation, (3) esophageal myotomy, and (4) mucosal incision closure. POEM is usually performed in the operating room under general anesthetic. A high-definition gastroscope, fitted with a plastic distal cap attachment and carbon dioxide insufflation, is used to minimize the risk of mediastinal emphysema and barotrauma if pneumoperitoneum were to occur. Prior to initiating the actual myotomy, the LES is identified. A submucosal bleb is created in the mid-esophagus using saline solution mixed with indigo carmine. A 1.5–2 cm longitudinal mucosal incision is made with an endoscopic submucosal dissection knife. The submucosal space is dissected, and the submucosal tunnel is extended until passing the

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LES and at least 2–3 cm into the stomach. Subsequently, an anterior or posterior myotomy of the muscle bundles is performed starting 2 cm distal to the mucosal entry point and extending distally 2–3 cm into the gastric cardia. After completion of the myotomy, the gastroscope is introduced into the esophageal lumen, and smooth passage into the stomach through the GEJ is confirmed. The mucosal incision site is closed using endoscopic clips.

Postoperative Care and Follow-Up

Patients are typically admitted post-procedure for observation. An esophagogram or CT esophagogram is obtained 24 hours after the procedure to evaluate for submucosal tunnel leak, extra-esophageal leakage, or esophageal outlet obstruction. A submucosal tunnel leak should prompt re-intervention. If no leakage (submucosal or extra-esophageal) or obstruction is noted, an oral diet is started. The possibility of a leak should be considered in patients with fever, chest pain, or signs consistent with sepsis after the procedure. Most small leaks can be managed non-operatively with no oral intake and intravenous antibiotic therapy, while significant leaks may require interventional drainage, esophageal stent placement, and/or re-intervention. Patients are maintained on soft diets for several weeks and gradually increased to normal oral intake. Patients are typically started on proton pump inhibitor therapy following the procedure, although protocols seem to differ widely on duration of therapy. Follow-up protocols for POEM vary according to each center and usually include a post-procedure upper endoscopy and pH studies.

Outcomes

POEM has demonstrated safety and efficacy in short-term studies (success as high as 98% at 6 months) when compared to laparoscopic Heller myotomy, although limited long-term follow-up is available. There is limited data on the effectiveness of POEM over 2 years; however, single-institution studies seem to indicate that POEM remains as effective as laparoscopic Heller myotomy. Although rare in occurrence, the most commonly reported POEM complications are mucosal perforation, pneumothorax, pneumoperitoneum, subcutaneous emphysema, pleural effusion, and pneumonia. Most of these complications can be minimized with the use of carbon dioxide insufflation.

Factors associated with long-term clinical failure after POEM include an Eckardt score >3–4 and a history of previous pneumatic dilation. The biggest concern associated with POEM is post-procedure gastroesophageal reflux. Laparoscopic Heller myotomy with anterior or posterior fundoplication is associated with a 10% symptomatic reflux rate. The rate of reflux in post-POEM patients is as high as 40%. Full-thickness myotomy seems to be a risk factor for postoperative reflux esophagitis. Inner-circular myotomy, as opposed to full-thickness myotomy, preserves the longitudinal outer esophageal muscular layer, which may help prevent post-POEM reflux. Although higher rates of reflux are reported with POEM compared to Heller myotomy, the post-POEM reflux seems to be well controlled with PPI therapy and most commonly does not require any further therapy, and no other reflux-associated complications have been reported.

No difference in cost-effectiveness, operative time, hospital length of stay, or complication rates have been observed between POEM and laparoscopic Heller myotomy. Patients who undergo POEM have no physical restrictions post-procedure, report reduced postoperative pain scores, and have decreased narcotic use.

Other Applications of POEM

POEM may have an advantage to surgical myotomy in type III achalasia since this technique allows for a longer-segment esophageal myotomy. POEM has also been employed to manage diffuse esophageal spasm and hypertensive LES and extrapolated to perform endoscopic myotomy of the pylorus for delayed gastric emptying.

Additionally it may be used to perform a posterior myotomy after a previously failed anterior Heller myotomy.

Summary

POEM combines the minimal invasiveness of an endoscopic procedure with the safety and efficacy of surgical myotomy. Benefits of POEM, over surgical myotomy, include its flexibility to adjust the length and location of myotomy and the ability to extend the myotomy proximally without thoracoscopy or thoracotomy. Similar to Heller myotomy and pneumatic dilation, long-term efficacy of POEM decreases slightly over time. After POEM, as with other standard therapies for achalasia, patients require ongoing follow-up to assess for recurring symptoms and the need for additional treatment when indicated. Long-term follow-up results of POEM are still awaited.

Selected References

1. Awaiz A, Yunus RM, Khan S, Memon B, Memon MA. Systematic review and meta-analysis of perioperative outcomes of Peroral Endoscopic Myotomy (POEM) and Laparoscopic Heller Myotomy (LHM) for achalasia. Surg Laparosc Endosc Percutan Tech. 2017;27(3):123–31.
2. Benedict JJ, Golas AA, Richter JE, Velanovich V. Health-related quality of life and physiological outcomes of peroral endoscopic myotomy for achalasia. J Laparoendosc Adv Surg Tech A. 2017;27(8):778–83. https://doi.org/10.1089/lap.2017.0087. Epub 2017 Jun 28.
3. Crespin OM, Liu LWC, Parmar A, Jackson TD, Hamid J, Shlomovitz E, Okrainec A. Safety and efficacy of POEM for treatment of achalasia: a systematic review of the literature. Surg Endosc. 2017;31(5):2187–201.
4. DeMeester SR. Per-oral endoscopic myotomy for achalasia. J Thorac Dis. 2017;9(Suppl 2):S130–4. https://doi.org/10.21037/jtd.2016.09.39.
5. Docimo S Jr, Mathew A, Shope AJ, Winder JS, Haluck RS, Pauli EM. Reduced postoperative pain scores and narcotic use favor per-oral endoscopic myotomy over Laparoscopic Heller Myotomy. Surg Endosc. 2017;31(2):795–800.
6. Friedel D, Modayil R, Iqbal S, Grendell JH, Stavropoulos SN. Per-oral endoscopic myotomy for achalasia: an American perspective. World J Gastrointest Endosc. 2013;5(9):420–7.
7. Greenleaf EK, Winder JS, Hollenbeak CS, Haluck RS, Mathew A, Pauli EM. Cost-effectiveness of per oral endoscopic myotomy relative to laparoscopic Heller Myotomy for the treatment of achalasia. Surg Endosc. 2017; https://doi.org/10.1007/s00464-017-5629-3.
8. Grimes KL, Inoue H. Per oral endoscopic myotomy for achalasia: a detailed description of the technique and review of the literature. Thorac Surg Clin. 2016;26(2):147–62.
9. Haito-Chavez Y, Inoue H, Beard KW, Draganov PV, Ujiki M, Rahden BHA, Desai PN, Pioche M, Hayee B, Haji A, Saxena P, Reavis K, Onimaru M, Balassone V, Nakamura J, Hata Y, Yang D, Pannu D, Abbas A, Perbtani YB, Patel LY, Filser J, Roman S, Rivory J, Mion F, Ponchon T, Perretta S, Wong V, Maselli R, Ngamruengphong S, Chen YI, Bukhari M, Hajiyeva G, Ismail A, Pieratti R, Kumbhari V, Galdos-Cardenas G, Repici A, Khashab MA. Comprehensive analysis of adverse events associated with per oral endoscopic myotomy in 1826 patients: an international multicenter study. Am J Gastroenterol. 2017;112(8):1267–76. https://doi.org/10.1038/ajg.2017.139.
10. Hoppo T, Thakkar SJ, Schumacher LY, Komatsu Y, Choe S, Shetty A, Bloomer S, Lloyd EJ, Zaidi AH, VanDeusen MA, Landreneau RJ, Kulkarni A, Jobe BA. A utility of peroral endoscopic myotomy (POEM) across the spectrum of esophageal motility disorders. Surg Endosc. 2016;30(1):233–44.
11. Hungness ES, Sternbach JM, Teitelbaum EN, Kahrilas PJ, Pandolfino JE, Soper NJ. Per-oral Endoscopic Myotomy (POEM) after the learning curve: durable long-term results with a low complication rate. Ann Surg. 2016;264(3):508–17.
12. Jones EL, Meara MP, Pittman MR, Hazey JW, Perry KA. Prior treatment does not influence the performance or early outcome of per-oral endoscopic myotomy for achalasia. Surg Endosc. 2016;30(4):1282–6.
13. Kim WH, Cho JY, Ko WJ, Hong SP, Hahm KB, Cho JH, Lee TH, Hong SJ. Comparison of the outcomes of peroral endoscopic myotomy for achalasia according to manometric subtype. Gut Liver. 2017;11(5):642–7.
14. Leeds SG, Burdick JS, Ogola GO, Ontiveros E. Comparison of outcomes of Laparoscopic Heller Myotomy versus per-oral endoscopic myotomy for management of achalasia. Proc (Bayl Univ Med Cent). 2017;30(4):419–23.
15. Martinek J, Svecova H, Vackova Z, Dolezel R, Ngo O, Krajciova J, Kieslichova E, Janousek R, Pazdro A, Harustiak T, Zdrhova L, Loudova P, Stirand P, Spicak J. Per-oral endoscopic myotomy (POEM): mid-term efficacy and safety. Surg Endosc. 2018;32(3):1293–302. https://doi.org/10.1007/s00464-017-5807-3.
16. Miller HJ, Neupane R, Fayezizadeh M, Majumder A, Marks JM. POEM is a cost-effective procedure: cost-utility analysis of endoscopic and surgical treatment options in the management of achalasia. Surg Endosc. 2017;31(4):1636–42.

17. Nabi Z, Ramchandani M, Chavan R, Tandan M, Kalapala R, Darisetty S, Lakhtakia S, Rao GV, Reddy DN. Peroral endoscopic myotomy in treatment-naïve achalasia patients versus prior treatment failure cases. Endoscopy. 2017; https://doi.org/10.1055/s-0043-121632.
18. Ngamruengphong S, Inoue H, Chiu PW, Yip HC, Bapaye A, Ujiki M, Patel L, Desai PN, Hayee B, Haji A, Wong VW, Perretta S, Dorwat S, Pioche M, Roman S, Rivory J, Mion F, Ponchon T, Garros A, Nakamura J, Hata Y, Balassone V, Onimaru M, Hajiyeva G, Ismail A, Chen YI, Bukhari M, Haito-Chavez Y, Kumbhari V, Maselli R, Repici A, Khashab MA. Long-term outcomes of per-oral endoscopic myotomy in patients with achalasia with a minimum follow-up of 2 years: an international multicenter study. Gastrointest Endosc. 2017;85(5):927–33.
19. Patti MG, Andolfi C, Bowers SP, Soper NJ. POEM vs Laparoscopic Heller Myotomy and Fundoplication: which is now the gold standard for treatment of achalasia? J Gastrointest Surg. 2017;21(2):207–14. https://doi.org/10.1007/s11605-016-3310-0.
20. Repici A, Fuccio L, Maselli R, Mazza F, Correale L, Mandolesi D, Bellisario C, Sethi A, Kashab M, Rösch T, Hassan C. Gastroesophageal reflux disease after per-oral endoscopic myotomy as compared with Heller's Myotomy with fundoplication: a systematic review with meta-analysis. Gastrointest Endosc. 2017. pii: S0016-5107(17)32419-7; https://doi.org/10.1016/j.gie.2017.10.022.
21. Schlottmann F, Luckett DJ, Fine J, Shaheen NJ, Patti MG. Laparoscopic Heller Myotomy versus Peroral Endoscopic Myotomy (POEM) for achalasia: a systematic review and meta-analysis. Ann Surg. 2018;267(3):451–60. https://doi.org/10.1097/SLA.0000000000002311.
22. Shiwaku H, Inoue H, Sasaki T, Yamashita K, Ohmiya T, Takeno S, Nimura S, Yamashita Y. A prospective analysis of GERD after POEM on anterior myotomy. Surg Endosc. 2016;30(6):2496–504.
23. Swanstrom LL, Kurian A, Dunst CM, Sharata A, Bhayani N, Rieder E. Long-term outcomes of an endoscopic myotomy for achalasia: the POEM procedure. Ann Surg. 2012;256(4):659–67. https://doi.org/10.1097/SLA.0b013e31826b5212.
24. Teitelbaum EN, Dunst CM, Reavis KM, Sharata AM, Ward MA, DeMeester SR, Swanström LL. Clinical outcomes five years after POEM for treatment of primary esophageal motility disorders. Surg Endosc. 2018;32(1):421–7. https://doi.org/10.1007/s00464-017-5699-2.
25. Tuason J, Inoue H. Current status of achalasia management: a review on diagnosis and treatment. J Gastroenterol. 2017;52(4):401–6.
26. Youn YH, Minami H, Chiu PWY, Park H. Peroral endoscopic myotomy for treating achalasia and esophageal motility disorders. J Neurogastroenterol Motil. 2016;22:14–24. https://doi.org/10.5056/jnm15191.
27. Zhang X, Modayil RJ, Friedel D, Gurram KC, Brathwaite CE, Taylor SI, Kollarus MM, Modayil S, Halwan B, Grendell JH, Stavropoulos SN. Per-oral endoscopic myotomy in patients with or without prior Heller Myotomy: comparing long-term outcomes in a large U.S. single-center cohort (with videos). Gastrointest Endosc. 2018;87(4):972–85. https://doi.org/10.1016/j.gie.2017.10.039.

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https://doi.org/10.1007/978-3-030-12823-4