POEM Contraindications and Pitfalls

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Introduction

Peroral endoscopic myotomy (POEM), as the first Natural Orifice Transluminal Endoscopic Surgery (NOTES) procedure to gain widespread clinical success, represents a novel type of minimally invasive surgery outside the safe confines of the gastrointestinal lumen, and outside the comfort zone of most endoscopists, particularly gastroenterologists, who are unfamiliar with the hazards of surgery in their day-to-day practice. As such, it carries a much higher risk of severe or life-threatening complications than traditional therapeutic endoscopy. Furthermore, it requires a high level of skill as it attempts to replicate the results of a time-honored laparoscopic operation, the Heller myotomy, with much more basic tools than are available to the laparoscopic surgeon. It follows that in order to maximize efficacy and safety in this technically complex and risky undertaking, the operator needs to be acutely aware of potential pitfalls along with preventive and corrective strategies to address such pitfalls. These strategies consist of "tips and tricks" painstakingly acquired by pioneers and early adopters at high-volume centers, often via an arduous trial-and-error process. Unfortunately, this type of experiential practical

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information is hard to come by in the peer-reviewed literature which focuses heavily on evidence-based aggregate data to the point of near exclusion of empirical data. We hope that this chapter will help address this knowledge gap particularly for POEM operators early in their learning curve. We review the scant information regarding POEM pitfalls and contraindications gleaned from the literature and augment it with pitfalls, practical tips, and advice from our own extensive experience derived from the largest Western single-operator series at well over 300 POEMs spanning a period of 7 years.

POEM Contraindications and Pitfalls in Patient Selection

POEM Contraindication Due to Comorbidities

An international survey of 16 pioneering POEM centers in 2012 (including all high-volume centers at that time) used 17 brief clinical scenarios illustrating comorbid diseases of varying severity to poll respondents on whether POEM was contraindicated in each of these clinical scenarios. A majority of respondents considered POEM to be relatively or absolutely contraindicated in the following scenarios [1]:

1. Extensive esophageal wall fibrosis due to prior irradiation of the esophagus/mediastinum or extensive endoluminal mucosal resection or ablative therapy (e.g. endoscopic mucosal resection, radiofrequency ablation, photodynamic therapy).
2. Severe pulmonary disease (e.g. extensive bullous disease or prior lung resection, home oxygen dependence, ASA class III, FEV1 or FVC < 70%, $pCO_2 \geq 45$, or $pO_2 < 75$).
3. High risk of major intraoperative bleeding due to uncorrectable coagulopathy (e.g. baseline platelet count <30,000 due to disorders such as ITP, myelodysplasia) or cirrhosis with portal hypertension (even in the absence of gastric or esophageal varices).

Another potential contraindication to POEM is severe cachexia due to malnutrition. In these patients, poor immune function and tissue healing as well as thin and structurally unsound mucosal and submucosal layers may complicate POEM. In such patients, we defer POEM until optimal nutritional status can be achieved via feeding tube alimentation.

Patients in Whom POEM May Not Represent Appropriate Therapy

1. *Patients with poorly defined and/or treatment-naïve nonachalasia esophageal motility disorders.* In the IPOEMS survey of 16 pioneering centers, surprisingly, nearly one quarter of the 841 POEMs reported was performed for nonachalasia disorders [jackhammer/nutcracker esophagus, hypertensive lower esophageal sphincter (LES), and distal esophageal spasm (DES)]. Most cen-

ters applied POEM almost exclusively to typical achalasia patients, whereas a small number of centers such as The Oregon Clinic and Shanghai reported over 25% of POEMs performed to treat nonachalasia conditions [1]. Several studies have demonstrated reasonable efficacy of POEM for spastic nonachalasia conditions but, nevertheless, inferior efficacy compared to that seen in POEM for classic achalasia [2–4]. POEM when applied injudiciously to such patients may not provide relief and may even exacerbate the patient's symptoms [5]. Therefore, in nonachalasia spastic disorders, it is prudent to reserve myotomy for patients refractory to pharmacological therapy options such as proton pump inhibitors, calcium channel blockers, phosphodiesterase inhibitors, pain modulators, or botulinum toxin injections [6]. A treatment plan for these poorly understood disorders should be developed within an expert multidisciplinary team including motility specialists and surgeons. In patients refractory to pharmacological therapy that are being considered for POEM, detailed discussion with the patient regarding outcomes and expectations is important prior to proceeding with POEM.

2. *Previously myotomized achalasia patients in whom LES-related outflow obstruction may not be the cause of symptom relapse or persistence.*

   Symptom persistence after Heller myotomy is most often due to inadequate myotomy usually due to inadequate extension through the gastroesophageal junction (GEJ) and cardia, especially if the myotomy was performed by a low-volume operator. In these patients, POEM is an extremely effective therapy [7–10]. Probably, the best predictor of POEM success in this setting is a high pre-POEM LES pressure, which has also been reported as one of the best predictors of laparoscopic Heller success [11, 12]. During POEM, the sphincter high-pressure zone can be identified very easily and precisely and effectively ablated.

   Less commonly, a failed Heller myotomy may be due to a tight fundoplication. It is difficult to distinguish a tight fundoplication from residual sphincter. Amyl nitrite enhanced barium esophagram has been used anecdotally in this setting. It has been theorized that improved transit after administration of amyl nitrite (a LES relaxant) would be consistent with inadequate myotomy, whereas the absence of such an effect would be consistent with a tight fundoplication. However, this technique has not been adequately studied and, in practice, clinical judgment needs to be applied. When significant uncertainty remains, POEM can in some cases be performed empirically prior to attempting a take-down of the fundoplication since it may be less invasive than this type of surgical revision.

   One needs to be cautious in patients who display a cycle of initial excellent durable response to therapy including Heller myotomy or aggressive pneumatic dilation only to be followed by late relapse of symptoms years later. Unlike patients with persistence of symptoms signifying a failed Heller discussed above, in many of the patients with late relapse of symptoms, the relapse is not due to LES-related outflow obstruction and will not respond to POEM. Detailed evaluation including timed barium esophagram, pH studies, and endoscopy is very important to exclude conditions for which POEM would not be appropriate therapy. Such conditions include GERD, peptic stricture, or end-stage failed esophagus:

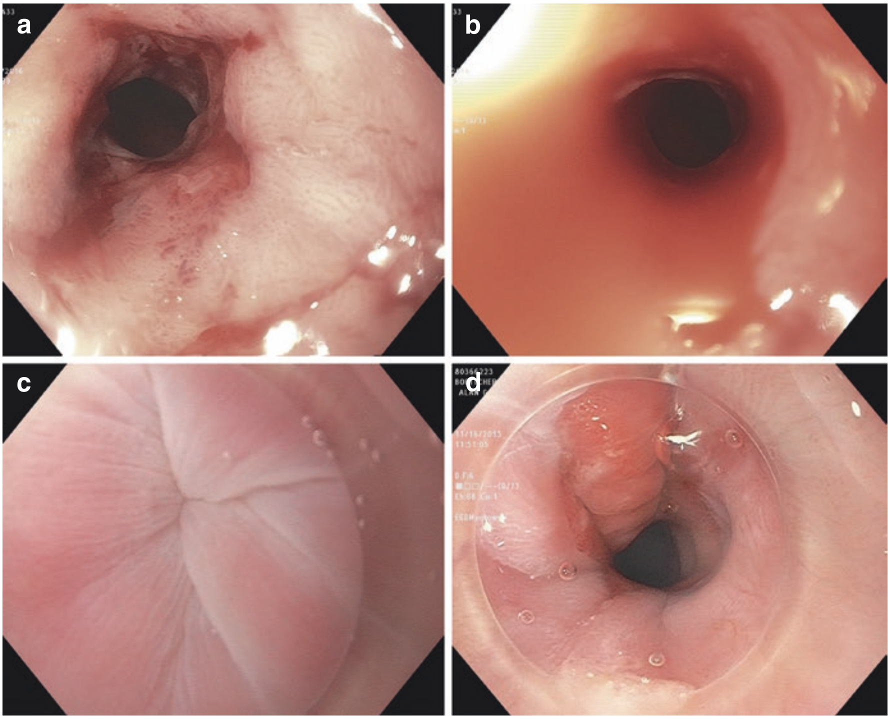


Fig. 7.1 (**a**, **b**) Demonstration of luminal narrowing secondary to peptic strictures after Heller myotomy. (**c**, **d**) Demonstration of luminal narrowing secondary to achalasic sphincter

(a) GERD in postmyotomy achalasia patients may manifest with symptoms such as globus sensation, dysphagia, regurgitation, and chest pain that may be indistinguishable from classic achalasia symptoms. On EGD, one often encounters erosive esophagitis and a patulous LES. If endoscopic findings are equivocal, pH studies performed off-medication can help confirm presence of GERD. Appropriate treatment would include an antacid regimen or partial fundoplication rather than POEM which would further exacerbate GERD symptoms.
(b) Peptic strictures due to long-standing GERD resulting from effective initial therapy for achalasia may cause dysphagia and may mimic “residual sphincter” on barium esophagram. However, on endoscopy, peptic strictures can be easily identified as unyielding firm tight stenoses quite different from the short elastic high-pressure zone of a nonrelaxing LES associated with achalasia that yields to scope insertion (Fig. 7.1).
(c) A failed, end-stage esophagus can be diagnosed by the following findings on barium esophagram, endoscopy and high resolution manometry: On

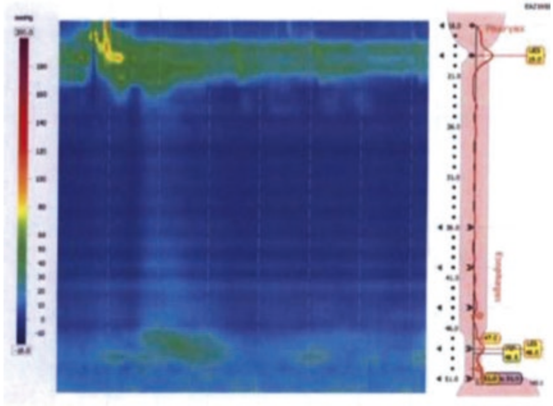


Fig. 7.2 Patient status after prior remote Heller with good initial response now referred for possible POEM for recurrent dysphagia and poor emptying on barium. HRM shows minimal residual LES pressure (mean LES pressure of 9.6, residual pressure of −1.2!) and common cavity between the stomach and esophagus. This patient would not benefit from POEM and should be considered for possible esophagectomy

endoscopy, findings include the presence of significant dilation of the esophageal body and patulous GEJ. On barium esophagram there will be marked esophageal dilation, with the absence of the "bird-beak" sign. On high-resolution manometry/impedance, findings include lack of any contractile activity, very low LES pressure, very low esophageal body pressure with equalization of esophageal and gastric pressures and no bolus transit on impedance (Fig. 7.2).

3. *Achalasia in the setting of prior bariatric surgery.* Patients that have undergone bariatric surgery such as gastric bypass or sleeve gastrectomy may suffer from idiopathic achalasia or achalasia secondary to the bariatric surgery itself [13]. POEM has been anecdotally reported to be efficacious in patients that have had prior bariatric surgery. However, based on our preliminary unpublished experience, some caution is indicated. The excellent efficacy of POEM in disrupting the LES (which underlies its dramatic and durable relief of dysphagia and, on the downside, clinically relevant GERD in approximately 30–40% of patients) may be a cause of concern in patients with prior bariatric surgery. POEM may significantly increase the severity of GERD in sleeve patients and may facilitate regurgitation from the surgically restricted small-capacity gastric pouch in bypass patients and the high-pressure narrow stomach in sleeve gastrectomy patients. In these patients, severe GERD or regurgitation can diminish any post-POEM quality-of-life improvement from dysphagia relief. Effective management of such symptoms can be difficult since surgical revision or antireflux procedures are limited in these patients.

Procedural Pitfalls

Preprocedure Preparation

POEM is unique in that it is a mediastinal surgical procedure that can be performed in endoscopy units where procedure protocols may be somewhat less stringent than in formal operating rooms, as they are geared toward traditional endoscopic procedures in which reaction time delays, omissions, or other errors are much less likely to result in mission-critical disruptions compared to surgery. To minimize serious and potentially life-threatening events, it is important to replicate operating room protocols including detailed equipment checklists that ensure that all devices that may be needed, particularly ones that may be needed infrequently (such as overtubes, stents, and specialized clips or sutures) or emergently (such as Veress needles or angiocaths for decompression), are readily available. Detailed "time-out" protocols are essential, including, for example, confirmation that air insufflation has been turned off and appropriate antibiotics have been administered. It is instructive to look at air insufflation as an example of a potentially catastrophic event that may result from a minor oversight that would be of little import in most other endoscopic procedures. The high frequency of adverse events and severe adverse events resulting from use of air rather than CO_2 was amply illustrated in a study by a group that intentionally utilized air in their first 119 POEMs [14]. Endoscopy consoles at the present time still have air as the default insufflation setting with add-on appended equipment required to use carbon dioxide. To avoid air insufflation one needs to ensure prior to the procedure that the unit's default air insufflation is switched off. Including the "air switch-off" step in the standard procedure "time-out" minimizes the risk of inadvertent air insufflation which can occur even in expert centers. Inadvertent air insufflation was reported as the cause of the single occurrence of pneumothorax requiring chest drainage in a recent study by Inoue et al. following a series of 500 POEM cases [15]. This is not a "learning curve" related event and is most likely to occur when the procedure becomes more routine, and vigilance by the operator and support team decreases. We recommend including an "air-off/CO_2 on" check to the preprocedure "time-out", as we have done at our institution, and positioning an angiocath and betadine wipes at a standard location within immediate reach of the operator to minimize any delay in emergent venting of capnothorax or capnoperitoneum.

Other routine preprocedure setup tasks should be included in the preprocedure checklist. For example, routine taping of the distal cap attachment with a water-resistant tape can avoid dislodgment of the cap in the submucosal tunnel, which can result in a quite cumbersome and time-consuming extraction of the dislodged cap [16, 17].

It is also important to have a highly trained dedicated team. Since achalasia is a rare disorder and POEM is performed in small numbers in most centers, errors can result without a dedicated team. The anesthesiology team needs to be prepared for circumstances that may result in severe morbidity. For example they need to anticipate the presence of massive amounts of food debris in patients with advanced or end-stage achalasia and severely dilated esophagus and preemptively apply cricoid pressure and rapid sequence intubation. At our center, on some occasions, we employ additional maneuvers such as semi-erect intubation in certain severe end-stage patients with the history of aspiration episodes during prior endoscopies. An endoscopy team that is unfamiliar with POEM may also fail to correctly interpret signs of pneumothorax or pneumoperitoneum. Delay in diagnosis of such conditions may result in cardiac arrest, whereas prompt recognition allows correction by desufflation or venting with an angiocath, thus minimizing morbidity. Anesthesiologists familiar with traditional endoscopic procedures performed under general anesthesia but unfamiliar with POEM need to recognize signs of emerging tension pneumothorax or pneumoperitoneum (e.g. difficulty in ventilating the patient and high airway pressures) versus endotracheal tube displacement by the endoscope, bronchospasm, or inadequate paralysis. The latter sort of differential diagnosis would be appropriate for a traditional endoscopic procedure performed under general anesthesia such as endoscopic retrograde cholangiopancreatography, but in the case of POEM, it could result in delay in diagnosis of tension pneumothorax or pneumoperitoneum. If having a dedicated POEM-operative team is not feasible, it is incumbent upon the surgeon or gastroenterologist to discuss with the anesthesiologist the potential POEM anesthesia pitfalls prior to the procedure.

Tunnel Initiation and Orientation

On insertion of the endoscope, one may encounter a situation where excessive loss of insufflation from the upper esophageal sphincter is encountered with the resultant inability to properly distend the esophageal lumen (or submucosal tunnel lumen later in the procedure). In such cases, insertion of a short esophageal overtube with an air-tight silastic ring around the shaft of the endoscope may be helpful (Guardus Overtube, US Endoscopy, Mentor OH).

After removal of any debris from the esophagus, we recommend irrigation with at least 500–1000 cm^3 of saline based on studies regarding NOTES indicating significant reduction in bacterial colonies after copious irrigation with similar reductions, whether or not a disinfectant was included in the irrigant [18].

During this step, a common mistake involves aggressively and repeatedly inserting the endoscope through the GEJ, which in patients with an extremely tight LES results in mucosal tears compromising the mucosal flap which serves as the essential barrier that prevents leaks in POEM.

Careful measurement of the location of the GEJ from the incisors is required to determine the proximal and distal extents of the tunnel and myotomy. A common pitfall here involves overly rigid adherence to standard recommendations such as initiating the tunnel at a certain fixed distance proximal to the LES to the GEJ. Recent data suggest that a standard surgical myotomy of at least 8 cm may be longer than necessary in the esophageal body for nonspastic achalasia patients (type 1 and 2) [19]. Employing this approach in patients with advanced disease and dilated esophagus with mild (S1) or severe (S2) sigmoidization is likely excessive since these patients have a very short obstructing segment consisting of the LES only. Extension of the myotomy proximal to the LES on the expansive esophageal body may be of no benefit and even predispose the patient to diverticulum formation in the area of weakened muscle. Furthermore, in these advanced stage patients, severe angulation and lumen-indenting folds in the dilated distal esophageal body can make POEM technically challenging unless tunneling is initiated close to the LES distal to the meandering expansive lumen. With proper technique, POEM can provide substantial symptomatic improvement even in patients with sigmoid esophagus [20, 21]. Other scenarios that may complicate POEM can also be alleviated by judicious selection of the initiation site. Orientation that would require traversing areas of ulceration, diverticula, severe angulations, or a prior Heller myotomy should be avoided. It should also be noted that initiating the tunnel in an area that may make tunnel initiation and, importantly, tunnel closure difficult should be avoided even if this requires selecting a more proximal site by creating a longer submucosal tunnel than required for the planned myotomy length. This approach allows one to avoid areas with scarring and scant submucosa from recurrent ulcerations due to food stasis, areas in which a sigmoid esophagus "dives posteriorly" (making contact with the endoscope for a posterior POEM tenuous) or "ascends anteriorly" (causing the endoscope to be perpendicular to the wall or nearly retroflexed rather than in the optimal tangential position). Selecting an initiation site that is more proximal, away from areas where chronic food stasis may have caused the mucosa and submucosa to be thickened, may also facilitate closure as reviewed below in the "Tunnel Closure" section of this chapter.

Although a specific discussion regarding anterior vs posterior orientation is offered below in the "Submucosal Tunnel" section, we should note here that there is no consensus regarding the optimal orientation among expert centers with some favoring the anterior approach popularized by Inoue and some the posterior approach favored by the group in Shanghai and our group [1] (Fig. 7.3).

Initial Submucosal Injection

In achalasia patients, injection into the submucosa may be difficult due to alterations in the thickness of the layers of the esophageal wall. For example, in patients with long-standing achalasia, the entire wall of the esophagus may be severely thickened including the mucosa which may result in inadvertent injection of the deep mucosa superficial to the muscularis mucosae. In this case, attempts to establish a submucosal tunnel will be in vain unless the operator appreciates that what he/she considers to be muscularis propria is in fact a hypertrophic muscularis mucosae and proceeds to incise it (Fig. 7.4).

In severely malnourished patients in whom the submucosal layer may be very thin and in some early nonspastic achalasia patients with thin esophageal wall layers, the operator may inadvertently inject deep to the submucosa into the muscularis propria, adventitia, or mediastinal pleura. This may be recognized by appreciating that the resultant bleb is flatter than usual and has a pale white coloration with very little blue hue seen due to lack of transmission of the color of the injectate through the thickened overlying layers (Fig. 7.5). If not recognized, this deep

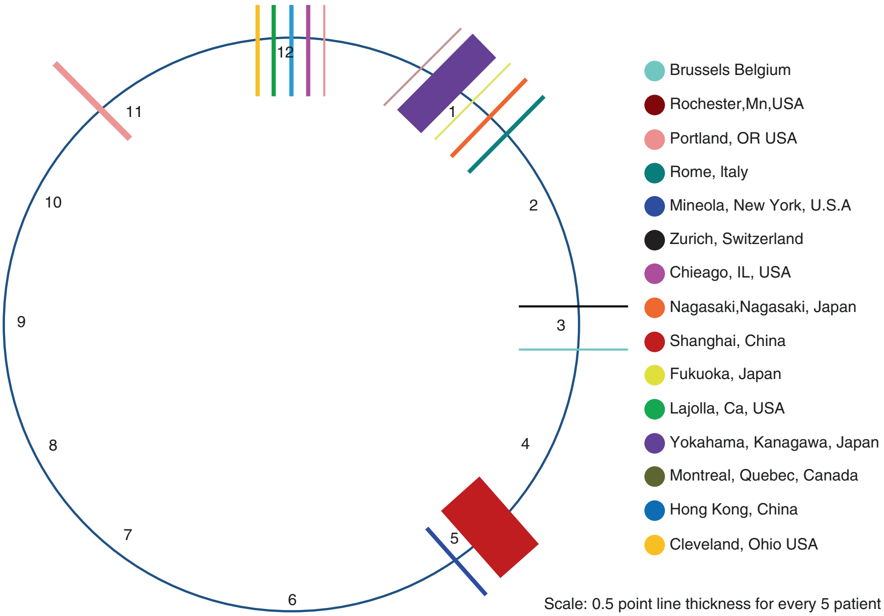


Fig. 7.3 POEM orientation among pioneering centers polled in the International POEM Survey (IPOEMS), including all centers having performed >30 POEMs at that time. Only two centers favored a posterior orientation (Mineola, Shanghai) at that time. (Figure from Stavropoulos SN, Modayil RJ, Friedel D, Savides T. The International Per Oral Endoscopic Myotomy Survey (IPOEMS): a snapshot of the global POEM experience. Surg Endosc. 2013 Sep;27(9):3322-38. doi: 10.1007/s00464-013-2913-8). Permission obtained

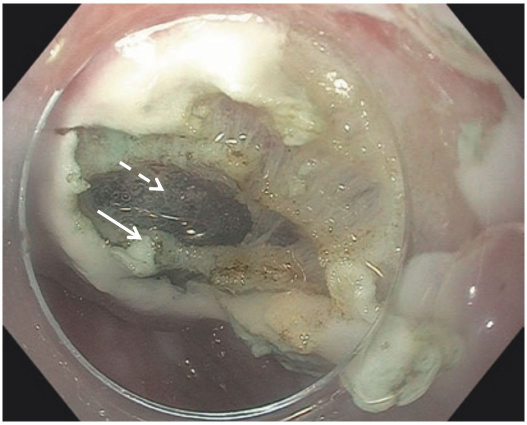


Fig. 7.4 Patient with long-standing achalasia with thick muscularis mucosae (*full arrow*) that can be confused for muscularis propria. Incision of this thickened muscularis mucosae reveals the submucosal space (*dashed arrow*)

bleb can result in layer confusion since the injected areolar tissue of the adventitia and pleura can mimic the submucosa. This can induce even experienced operators to incise through the muscularis propria and start tunneling in the adventitia or pleura plane deep to the muscularis propria with high attendant risks to injury to adjacent organs [22]. Once this is recognized, correction would necessitate closure

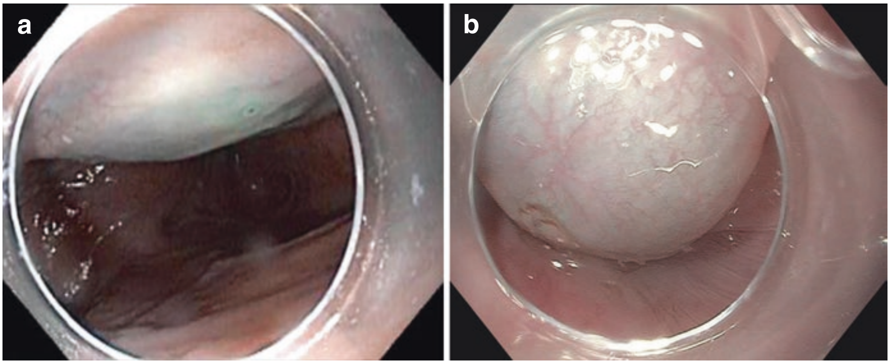


Fig. 7.5 Initial submucosal injection. (**a**) Shows a flat pale mount with very little blue hue suggesting that an inadvertent deeper injection into the muscularis propria or beyond has been performed rather than the desired submucosal injection (demonstrated in (**b**) as a markedly raised translucent bleb)

of the full thickness perforation leading to this deep mediastinal tunnel with a secure modality such as suturing [22].

Regarding the injectate used for submucosal injection, unlike endoscopic submucosal dissection, most operators avoid epinephrine due to the risk of necrosis of the devascularized mucosal flap. Such severe necrosis has been reported by one group [3].

Initial Mucosal Incision

Optimal incision is important in order to facilitate tunnel entry and facilitate secure closure at the conclusion of the procedure.

To avoid oozing from the edges of the incision from sizable mucosal and submucosal veins present in the midesophagus, we recommend selecting a site with the lowest density of such visible vessels and using a current with a significant coagulation component (e.g. dry-cut current in the ERBE VIO generator) for the initial incision.

As noted above, site selection and orientation should also take into account esophageal morphology in that area. Extensive nodularity from chronic food stasis likely represents cycles of ulcerations and healing that may make establishing a submucosal tunnel difficult. Even mild angulations of the esophagus may make tunnel entry and closure technically difficult.

Generally, it is accepted that a longitudinal incision allows easier closure with endoscopic clips than a transverse incision. Our group has used endoscopic suturing for closure in the last 250 POEMs and we prefer a transverse incision to avoid luminal narrowing. It should be noted, however, that even for closure with endoscopic clips, at least one group has advocated initially a transverse incision [23] and more recently an “inverted-T” incision [24]. Their argument, as we understand it, is that a transverse incision allows easier entry into the tunnel and also allows better escape of CO_2 from the tunnel, thus potentially decreasing insufflation-related adverse events. One would think, however, that this might also result in poor tunnel distension and decreased visibility. Furthermore, the closure issue remains since placement of clips along a transverse incision in the esophagus is more challenging.

The initial submucosal dissection at the entry site should be made close to the muscularis propria in order to avoid denuding the underside of the mucosal flap of submucosa, resulting in a structurally weakened flap at the tunnel opening that can tear during endoscope manipulations within the tunnel. Such tearing results in a much larger opening with devitalized torn edges that may be hard to approximate securely at the time of tunnel closure.

Initial Entry into the Submucosal Space and Tunnel Initiation

Operators early in their learning curve may have some difficulty in achieving initial entry into the submucosal space. As noted in the "Initial Incision" section, it is helpful to select a propitious entry site based on flat favorable morphology, lack of visible vascularity, and lack of submucosal scarring. Methods that may assist in submucosal entry include use of an oblique transparent distal cap attachment as initially used by Inoue or a tapered distal cap attachment (e.g. ST Hood; Fujifilm, Tokyo, Japan). In our first few POEMs in 2009–2010, we employed balloon dilation to establish the submucosal tunnel [25]. This technique greatly facilitates entry into the submucosal space and also carries the risk of balloon catheter perforation of the muscularis propria or mucosa during the blunt insertion prior to inflation [26].

For posterior POEM, which is our favored orientation currently, entry into the tunnel may be hampered by the much lower maximum down-angulation versus up-angulation capacity of gastroscopes (e.g. 90° vs 220° for Olympus GIF-HQ190 gastroscope). Therefore, we have developed and taught a technique that facilitates posterior entry which consists of reversing the orientation of the endoscope during entry by torqueing 180° while simultaneously using irrigation to retract the mucosal flap (demonstrated in Video 7.1).

Submucosal Tunnel Dissection

Submucosal tunnel dissection is usually the most time-consuming and challenging portion of POEM (e.g. mean duration of 44 min for submucosal access and tunnel creation vs. 25 min for the myotomy in a recent US study) [27]. Less intraprocedural bleeding and faster procedure durations have been reported with the use of the multifunctional ERBE hybrid T-type knife (ERBE, Tubingen, Germany) which allows injection and dissection by the same device compared to the triangular tip knife (TT knife, Olympus America, Center Valley PA) [28, 29]. However, neither effect appeared to have a significant impact on clinical outcomes, and, therefore, use of the hybrid knife is not a substitute for careful, precise, deliberate dissection which is the best strategy for preventing errors such as accidental mucosal injuries and excessive bleeding. Novice operators often attempt to use blunt dissection by

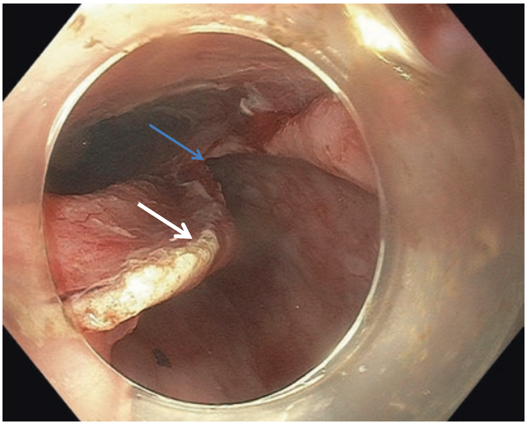


Fig. 7.6 Tearing of the tunnel opening caused by aggressive maneuvering of the endoscope during submucosal tunnel dissection. *White arrows* indicate the cautery changes that mark the original distal extent of the tunnel opening. The *blue arrow* demonstrates the distal extent of the now much larger opening after tearing occurred (note the absence of cautery along the tear confirming that this extension was caused by mechanical tissue tearing rather than electrical energy)

forceful endoscope insertion to achieve faster or easier tunnel dissection. Although this technique is often successful in the less vascular and softer porcine submucosa used in preclinical training, in humans it can have the following undesirable consequences: (1) Multiple small submucosal veins which would normally be obliterated by the electrosurgical dissection of the submucosa without any specific hemostatic maneuvers required can be avulsed via the technique of mechanical blunt dissection which then necessitates time-consuming coagulation of multifocal oozing. (2) Unrecognized buckling of the endoscope at the tunnel insertion site which may result in tearing of the opening may in turn make closure more challenging (Fig. 7.6) (3) "Muscle splitting" especially in the area of a tight LES, an important pitfall of submucosal dissection, is discussed in detail below.

Although submucosal tunnel dissection in the esophageal body is usually straightforward, occasionally certain challenging scenarios and pitfalls can occur. One such scenario is that of thin, absent, or fibrotic submucosa thwarting the endoscopist's attempts to create a submucosal tunnel. Aborted POEMs due to this phenomenon have been reported anecdotally even by expert operators. However, the best described series of such cases comes from a group in Rome, Italy [30]. This group reported a 6% early termination rate on their first 100 POEMs, with all five cases halted due to this phenomenon. We submit here an excerpt from their report as it describes this pitfall of submucosal dissection. They state that "*In 5 cases, the procedure failed because of inadequate lifting of the mucosa and the impossibility to proceed with submucosal dissection. Two patients had received radiation therapy for breast cancer. The esophageal wall appeared very thin, sclerotic, and any attempt at submucosal injection of glycerol solution ultimately failed, more likely because of severe submucosal fibrosis after radiation. The other 3 patients had no peculiar clinical history. Nevertheless, in these patients, the mucosal lifting was incomplete and submucosal dissection impossible: 2 of these patients had a* *very dilated and tortuous esophagus, which additionally complicated submucosal lifting and dissection. Any attempt at dissection resulted only in a laceration of the mucosa, which was repaired with clips.*" We focus the reader's attention on the fact that in three of the patients described, there was no clearly identifiable cause for this "absent submucosa" phenomenon which occurred in 3% of the patients in this Italian series. Based on observations from our series of over 300 POEMs [31] with no aborted POEMs, this phenomenon can usually be overcome with the maneuvers described below. It is encountered in patients with long-standing disease and severe food stasis likely resulting in pervasive inflammation and cycles of mucosal injury and healing that cause widespread submucosal sclerosis. This is most prevalent along the posterior wall of the esophagus or in patients with severe malnutrition in whom the absent submucosa is probably a sign of a severe prolonged catabolic state. We suggest the following maneuvers to overcome this challenging phenomenon: (1) Abandon the original site where tunnel initiation attempts have failed and reattempt at a new tunnel orientation (e.g. move from the posterior wall to a lateral wall) and/or new location (more distally or sometimes more proximally to the initial site, attempting to target an area with the least amount of mucosal nodularity, thickening, or other surface abnormalities). (2) Use of the I-type Hybrid knife (ERBE, Tubingen, Germany). The I-type Hybrid knife, which we have used in our last 280 POEMs, delivers a saline injection at pressures of up to 1400 PSI, which is powerful enough to dissect tissue via a tiny 0.12 μm port at the tip of this straight knife. In our experience, this can often achieve enough injection to delineate a submucosal dissection plane even in cases of very minimal fibrotic submucosa. Needless to say, even though these maneuvers may make a seemingly impossible dissection feasible, it would still remain an expert-level, slow, meticulous dissection requiring as much patience as skill.

Once the submucosal tunneling is initiated, a common pitfall involves spiraling of the tunnel dissection. Spiraling occurs due to preferential dissection on one flank of the tunnel more than the other and usually results in progressive clockwise rotation of the orientation of the tunnel. In patients with a relatively straight esophagus, it can be recognized by the operator as a progressive change in the angle between the long axis of the tunnel and the circular muscle fibers from a 90° angle to a more oblique angle [32]. Potential problems due to spiraling include the following: (1) Spiraling of the myotomy which results in a less powerful disruption of the ability of the circular muscle to achieve lumen-effacing contractions (2) Moving from an anterior POEM (2 o' clock orientation) or a posterior POEM (5 o' clock orientation) to a greater curvature-oriented POEM at a 7 o' clock position. A greater curvature POEM is much more challenging as it involves dissection across the angle of His [33]. One simple methodology first proposed by our group to avoid tunnel spiraling involves placing a marker on the shaft of the endoscope that indicates the torque rotation of the endoscope that maintains the desired orientation within the tunnel which is illustrated in our open-access narrated POEM technique video [34]. Advanced sigmoidization constitutes one of the most challenging and time-consuming POEM clinical scenarios [20, 21, 35]. The main challenge in these patients consists of completing a properly oriented submucosal tunnel. Proper orientation can be so challenging in these scenarios that experienced practitioners in India have described inadvertent retroflexion of the endoscope during tunneling, with the tunnel making a U-turn just prior to the GE junction and leading back to the esophageal body. This was recognized and corrected by the use of fluoroscopy which this group has used and now advocates in difficult sigmoid patients to help maintain orientation [36]. We have found our endoscope shaft torque marker method to be adequate in these patients, but we feel that it is important to be knowledgeable about the full armamentarium of useful adjunctive techniques such as fluoroscopy that can help avoid POEM pitfalls, particularly early in one's experience and in exceptionally challenging cases.

Submucosal tunnel dissection in the area of the GE junction can be challenging due to two potential reasons: a very tight LES or fibrosis from a variety of causes such as prior biopsies (frequently performed by referring physicians to exclude neoplasia or eosinophilic esophagitis), reflux or stasis erosions and ulcerations, prior Botox injections, or prior surgery including Heller myotomy. Fibrosis encountered as the tunnel approaches the GEJ is best approached via a detour, whereby the direction of the tunnel is deviated to the left or right of the fibrotic area depending on which side is most convenient and provides the best submucosal expansion [37]. A very tight LES can present a formidable obstacle to tunnel extension into the cardia and may also complicate the myotomy portion of the procedure. The Chinese group from Harbin has proposed a POEM technique, whereby myotomy is performed without prior separate submucosal tunnel dissection achieved by injecting the submucosa and then cutting the muscle by dissecting it off the injected submucosa as the endoscope advances in a proximal to distal direction [38, 39]. This technique may be of value in the hands of experienced operators. In the hands of less-experienced operators, it may result in "layer confusion" with resultant "splitting" of the esophageal muscle, thus leaving an unrecognized, and thus uncut, portion of the LES on the underside of the mucosal flap. This allows us to segue into a discussion of muscle "splitting," an important pitfall of submucosal tunnel dissection particularly in the area of a thick, tight LES. LES splitting is one of the two main technical causes of POEM clinical failures, with the other being inadequate myotomy extension onto the cardia to be addressed below. Muscle splitting is mainly an early learning curve pitfall which occurs as the novice operator, duly concerned about causing an inadvertent mucosal injury injects and dissects ever closer to the muscular layer, especially within the tight quarters of a high-pressure LES zone or in areas of scant fibrotic submucosa in the esophageal body. Splitting of the muscle may be initiated by excessive forward mechanical force with the endoscope in and ill-advised attempt to add blunt dissection with the endoscope to electrosurgical dissection in areas where the latter appears risky (such as segments with minimal submucosal expansion or a tight GE junction). Injection near the split muscle fibers can expand the fascia between circular muscle bundles, thus leaving some bundles attached to the mucosa camouflaged by injected fascia that mimics injected submucosa. Recognition of this pitfall of POEM can be difficult. It may be suspected in the following circumstances: (1) Once the myotomy is completed, the exposed cut edges of the LES are not significantly thicker than the cut edges of the muscle of the gastric cardia as is the norm. (2) Apparent premature entry into the peritoneal cavity, as heralded by exposure of omental fat while there is still a substantial high-pressure narrowing of the GE junction as assessed by intraluminal endoscope insertion. (3) Substantial residual narrowing and resistance to endoscope insertion at completion of the myotomy which can also be confirmed by functional luminal assessment using the EndoFLIP device (Crospon, Dublin, Ireland) [40]. Recovery from this pitfall is simple in theory but may require some experience in practice. The operator needs to "back-track" along the tunnel to the point where the muscle split originated. This can usually be determined by noting that the cut edges of the muscle appear thinner than expected and usually occurs in an area of difficult tunnel dissection. At that point, careful dissection of the underside of the mucosal flap is performed using ample submucosal injection, pure cutting current, and if necessary a specialized knife such as the hook knife (Olympus America, Center Valley, PA) to avoid injury to the mucosa. This delicate dissection exposes the true submucosal plane and isolates the split muscle bundles that remained attached to the mucosa. Figure 7.7 illustrates a case of muscle splitting in the distal esophageal body just proximal to the GEJ which was recognized and treated as discussed above. The technique for isolating and incising the missed muscle fibers in this case is

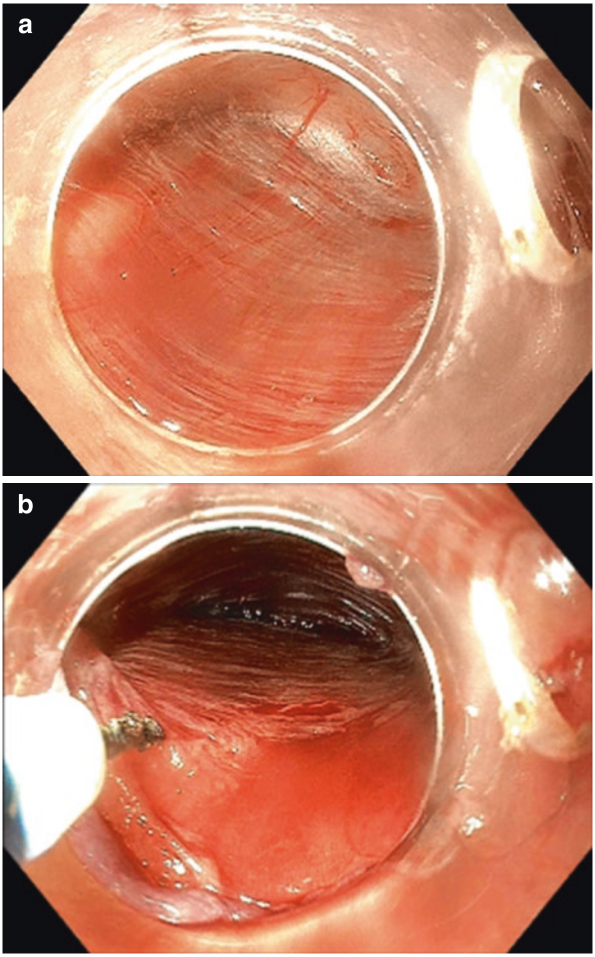
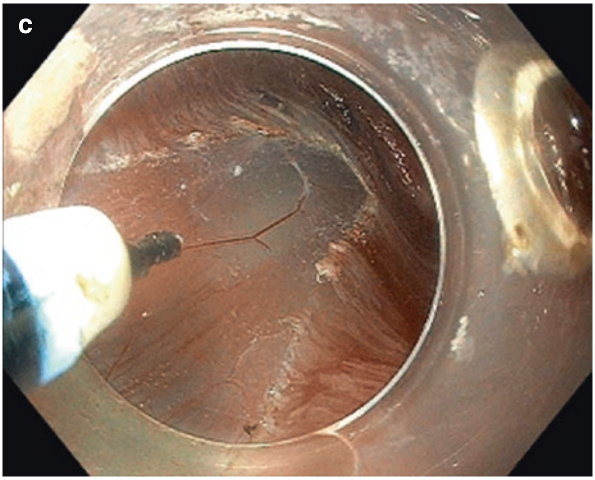


Fig. 7.7 Anterior POEM with inadvertent muscle splitting in the distal esophagus during submucosal tunnel dissection. (**a**) Demonstrates circular muscle fibers at 7 o' clock position (where normally the mucosa and submucosa forming the roof of the tunnel should be seen in an anterior POEM) in addition to the 2 o' clock position (which is the expected location of the circular muscle fibers in an anterior POEM). This can also be seen in (**b**) (i.e. circular muscle fibers at both 2 o' clock and 7 o' clock positions) as the endoscope is withdrawn in an attempt to identify the area of the dissection where the inadvertent muscle splitting commenced. (**c**) Illustrates recovery from this pitfall as the split fibers have been incised and the proper dissection plane in the submucosa has been re-established

Fig. 7.7 (continued)



demonstrated in the first half of Video 7.2. After correction of this pitfall, the second half of the video illustrates resumption and completion of the anterior POEM myotomy including full-thickness muscle dissection along the high-risk location posterior to the pericardial sac (discussed below).

A number of POEM submucosal dissection pitfalls relate to bleeding. Acute bleeding can be classified as minor—usually resulting from inadvertently or inexpertly divided veins and very small caliber submillimeter arteries in the esophageal body—or major, usually resulting from accidental injury or inadequate coagulation of large arteries in the 1–2 mm range which are generally encountered in the cardia and represent branches of the left gastric artery that penetrate through the muscularis propria and arborize to supply the overlying mucosa and submucosa. The best approach to intraprocedural bleeding is prevention by identification of vessels and pre-emptive coagulation. Submucosal dissection, particularly in the area of the cardia, should be performed with short superficial swipes of the knife that ensure that the bundle of submucosal fibers being cut does not harbor undetected vessels. For this reason, it is important to avoid injection solutions that are too dark due to excessive blue dye and may prevent visualization of submucosal vessels. Treatment of bleeding is inferior to prevention for a number of reasons: (1) Even if successfully controlled, bleeding episodes can result in significant prolongation of the procedure time, since identification of the bleeding vessels and effective treatment can be quite time-consuming. (2) Copious bleeding can stain the submucosa red, which can make submucosal tunnel dissection substantially harder since the usually pink/tan underside of the mucosa and submucosal vessels do not appear distinct from one another (Fig. 7.8). (3) Multiple poorly targeted coagulation efforts resulting from the suboptimal visibility conditions of an active bleed can result in mucosal thermal injury or deep injury to the muscle and adjacent structures or at a minimum heavily coagulated, contracted, or even charred tissue. This hinders progress since the submucosa needs to be carefully dissected before a clean submucosal dissection plane can be re-established.

The endoscopist needs to distinguish arteries from veins since even small arteries generally require more coagulation treatment with graspers rather than simply using

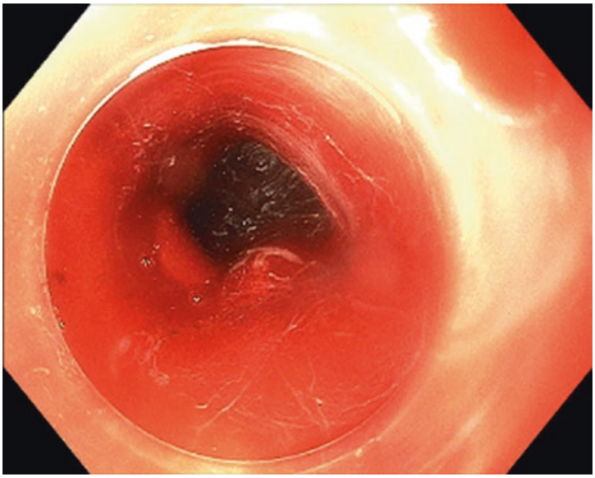


Fig. 7.8 Clot and extensive red staining of the submucosa after a large arterial bleed that required several minutes to identify and control. *Red* staining of the submucosa hinders proper identification of the submucosal dissection plane and identification of vessels within the submucosa that should be avoided or pre-emptively coagulated, thus predisposing to further intraprocedural bleeds until a clean unstained submucosal plane can be recovered distally as the tunnel is extended

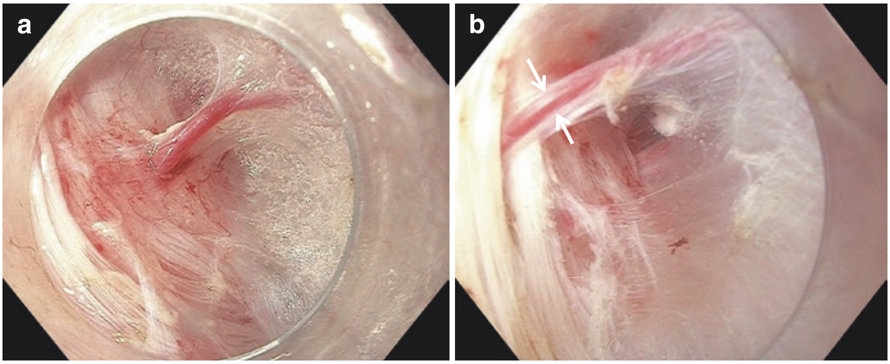


Fig. 7.9 (**a**) Illustration of a penetrating vein, larger, cylindrical bulging, soft, compressible with deeper red color. (**b**) Illustration of a penetrating artery which is smaller, flatter, firmer, often with visible pulsatile flow and *paler red color* often with *pale white borders*, annotated with *white arrows* here (an appearance caused by the thick muscular wall)

the tip of the endo-knife (which conversely is adequate for all but the largest veins when properly applied). Figure 7.9 illustrates the differences in the appearance of veins (generally larger, more cylindrical, more compressible with a deeper red color than arteries) and arteries (smaller, flatter, paler, sometimes with detectable pulsations, and with well delineated pale white borders representing their thicker muscular wall). Proper coagulation technique using the tip of the knife (Fig. 7.10) involves first heating the vessel indirectly by addressing the submucosa surrounding it and only proceeding with the division of the vessel once it has been desiccated and its lumen obviously

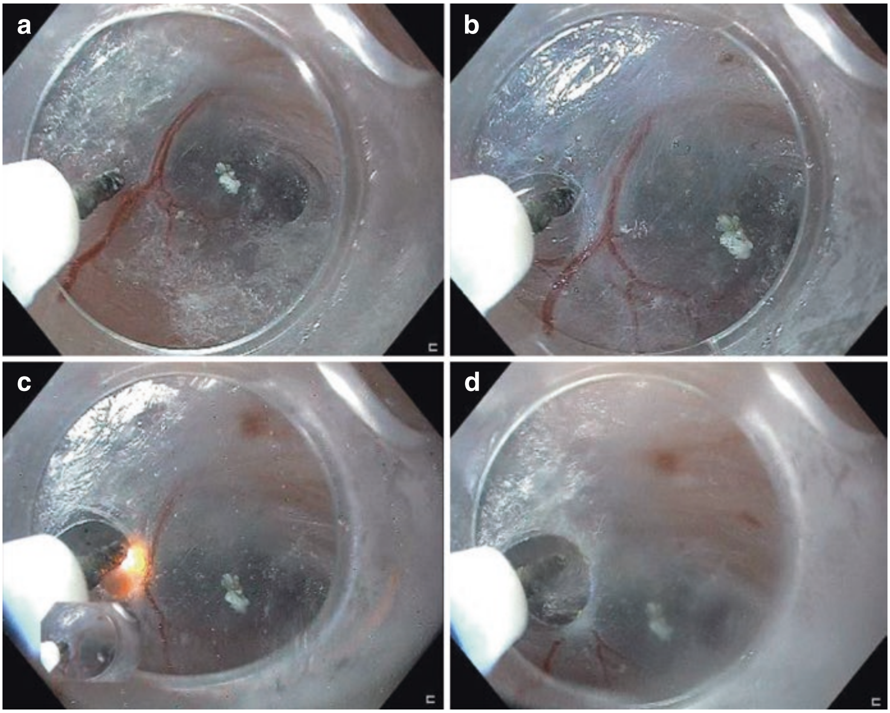


Fig. 7.10 Proper coagulation technique using the tip of the knife. (**a**) The submucosa surrounding the vessel is injected (**b**) A small incision is made with the knife in the submucosa next to the vessel (**c**) Electrosurgical energy is delivered to the vessel initially indirectly by targeting the submucosa surrounding it (**d**) Direct energy to the vessel to effect division of the vessel is only applied once the vessel has been desiccated and its lumen obliterated

obliterated. This avoids the potential for electrosurgical energy applied directly to the vessel, resulting in the division of the vessel prior to luminal sealing. A coagulation grasper should be used rather than the tip of the knife in the case of arteries (including the large arteries in the cardia), where the rapid luminal flow results in a powerful heat sink effect that can only be overcome by using a grasper to coapt the walls and disrupt blood flow prior to coagulation. A coagulation grasper should also be used for vessels under tension being stretched between their origin at the muscle layer and their insertion in the mucosa by the presence of the endoscope and insufflation within the emerging submucosal tunnel. In such vessels under tension, attempted coagulation with the tip of the knife may result in tearing of the vessel as soon as the structural integrity of its wall is weakened but prior to effective sealing of the lumen of the vessel. In fact, veins under such tension are fragile enough that injudicious use of suction via the endoscope can injure them and cause bleeding emphasizing the importance of gentle suction within the tunnel (unlike the customary use of suction in traditional luminal endoscopy [41]. Proper pre-emptive coagulation technique with the coagulation grasper (Fig. 7.11, Video 7.3) involves skeletonizing the entire circumference of a large vessel or multiple vessels within a vascular bundle. They can be grasped followed by extensive coagulation using a coagulation current algorithm that minimizes spread, and avoiding mucosal injury. The coagulation should be continued until impedance sharply

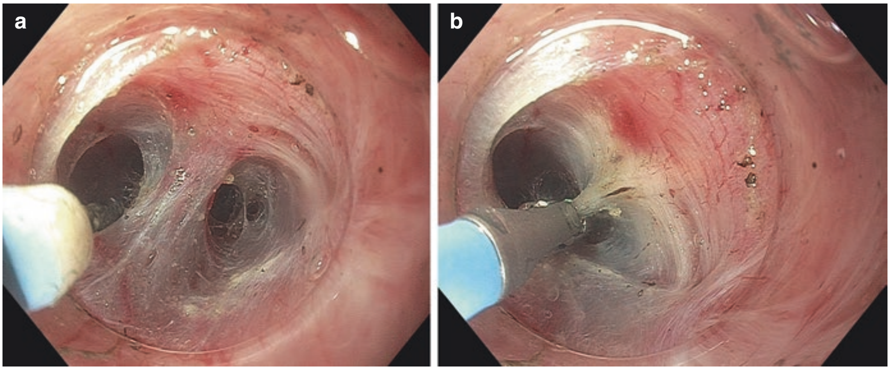


Fig. 7.11 Proper technique for coagulation of larger vessels or vascular bundles. (**a**) A vascular bundle containing at least three penetrating vessels has been "skeletonized" using careful dissection with the knife (blunt dissection using the tip of the forceps can also be used to skeletonize vessels as shown in the accompanying video). (**b**) The isolated vascular bundle is grasped and coagulated with a coagulating forceps

rises and energy delivery sharply drops indicating tissue desiccation. Only then can the vessel be safely divided to proceed with tunnel dissection.

Massive pulsatile bleeding from an accidentally divided penetrating branch of the left gastric artery can result in substantial hemorrhage. Such events require immediate intervention since the tunnel may rapidly fill with blood, eliminating visibility and thus the ability to identify and effectively treat the source of the bleeding (Fig. 7.12). A coagulation grasper should be immediately available. We use the hot biopsy forceps rather than the Olympus coag-graspers for this type of predicament since the thinner caliber and larger jaws of the hot forceps allow for better suction of blood and irrigation of fluid and less need for precision placement of the jaws compared to other devices. Tamponade of the bleeding by exerting pressure with the tip of the endoscope should be applied before proceeding with definitive coagulation. Once the grasper is applied, irrigation should be employed to clean the site and ensure that the flow of blood has been arrested. If this is not the case, suction should be applied to remove fluid mixed with blood that may obscure visualization. Suction should be combined with insufflation and avoidance of excessive irrigation while the grasper is readjusted. Another useful technique involves placing a sticker on the shaft of the coagulation grasper that marks the proper length of insertion to the tip of the endoscope, which allows much faster insertion of the grasper since the operator is less concerned about overshooting with the grasper insertion and causing further injury. We also note that there may be a higher density of large cardia vessels when POEM is performed anteriorly (2 o' clock orientation) rather than posteriorly (6 o' clock orientation) which may shift the desired route for POEM to a posterior course [41].

Mucosal flap injury is usually a minor technical error that can be corrected by clip placement [42]. However, occasionally, mucosal perforations can be very challenging to close and may subject the patient to a risk of leakage with resultant severe morbidity. Such challenging perforations are usually located in the difficult area of the GE junction and cardia, in a background of devitalized tissue due to extensive coagulation (e.g. secondary to hemostatic maneuvers), and/or tissue with little resiliency due to malnutrition, comorbidities, prior Botox injections, or extensive fibrosis

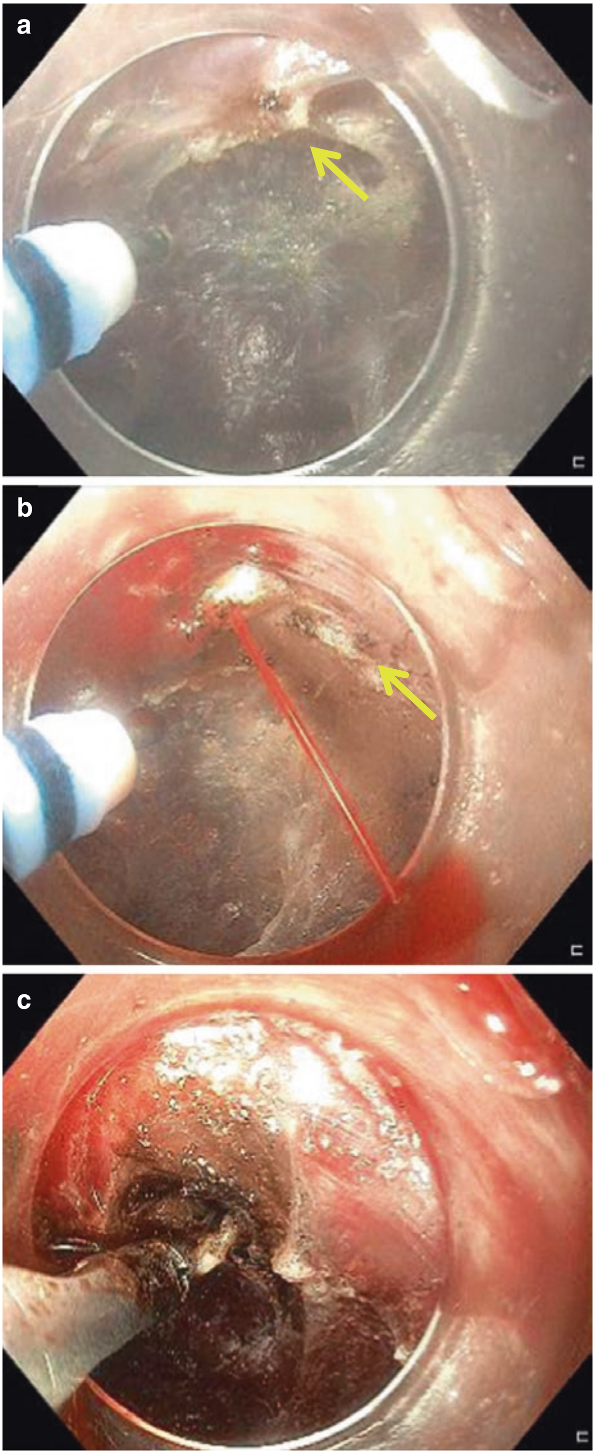


Fig. 7.12 Pulsatile bleeding from inadvertent injury to the wall of a penetrating artery expeditiously coagulated. (**a**) A penetrating artery (yellow arrow) is difficult to identify in this case due to partial coagulation of its wall giving it a similar white color to surrounding partially coagulated muscle (**b**) Pulsatile bleeding from inadverent injury to wall of this undetected penetrating artery (**c**) The hot biopsy forceps is used to expeditiousy coagulated the artery in order to avoid accumulation of blood that may eliminate visibility and hinder endoscopic coagulation efforts

due to other causes such as prior biopsies taken aggressively. This devitalized and/or delicate tissue is difficult to approximate and tears when clip placement is attempted, thus enlarging the defect. Furthermore, such defects tend to enlarge with continued insufflation (since closure is often deferred until the end of the procedure). We have reported on the use of endoscopic suturing (Overstitch, Apollo Endosurgery Austin, TX) for such challenging perforations in the GEJ and cardia (Fig. 7.13). We believe suturing to be the most robust and secure closure method for this scenario [43]. Others from China, where endoscopic suturing is not available, have reported using fibrin glue [44] or stent placement [45] to seal such defects.

Inoue et al. recently speculated that the anterior approach that has commonly been advocated may result in more accidental mucosotomies than the posterior approach due to a wider path of knife movement during the myotomy portion resulting in mucosal injury [41]. Since we have varied our approach between posterior and anterior orientation over our 7 year POEM experience, we have observed differences between the two techniques including a potentially higher rate of mucosal injuries when an anterior approach was followed. We attributed this to the closer proximity of the dissecting knife to the mucosa in the anterior approach (due to the knife exiting at 7 o' clock position in Olympus gastroscopes and the mucosa being

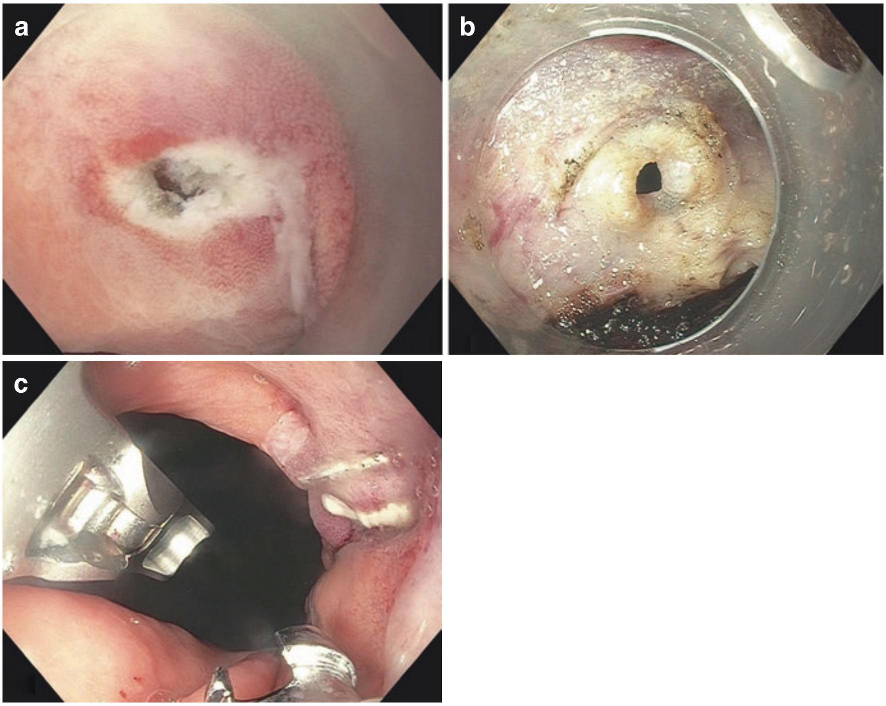


Fig. 7.13 Inadvertent mucosal perforation just distal to the Z-line at the GE junction in an anterior POEM (a POEM orientation that, as discussed in the text, may be more prone to such injuries). This location can be challenging for clip application, and attempts at clip placement can result in tearing of the mucosal flap with enlargement of the defect. (**a**) Demonstrates the defect from the luminal side, whereas (**b**) shows the defect from the submucosal tunnel side. (**c**) Shows effective closure using endoscopic suturing (the metallic t-tag and white plastic cinch at the two ends of the suture can both be seen on the right side of the image)

located at 6 o' clock position during anterior POEM compared to 12 o' clock position in posterior POEM) (Fig. 7.14). Our group is completing a single-center randomized study comparing anterior and posterior orientation and we recently presented data from a comparison of anterior and posterior POEMs in our single-operator series using data from a prospectively maintained database [46]. In this study, we analyzed all POEMs performed at our center from 10/2009 to 10/2015, 248 consecutive POEMs (120 anterior, 128 posterior), all successfully completed, with no aborted POEMs or surgical conversions. No learning curve bias was expected as we performed a similar percentage of anterior POEMs in the first 3 years of our series (48/91, 53%), as in the last 2 years (72/157 46%). There were no differences in efficacy or significant adverse events, but it should be noted that there was paucity of such events in our series with no leaks, no tunnel bleeds, and no surgical/IR interventions or aborted POEMs. There were more accidental

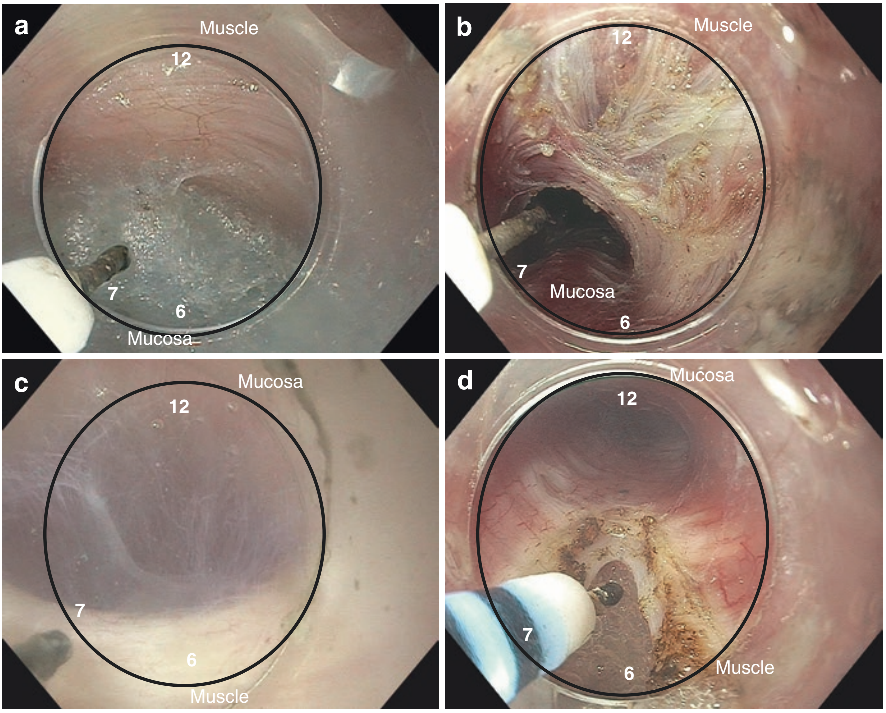


Fig. 7.14 (**a**, **b**) Illustration of knife position relative to the mucosa and muscularis in an anterior POEM during tunnel dissection (**a**) and myotomy (**b**). (**c**, **d**) Illustration of knife position relative to the mucosal and muscularis in a posterior POEM during tunnel dissection (**c**) and myotomy (**d**). The knife is much closer to the mucosa in anterior POEM (possibly resulting in higher rates of mucosal injury). In posterior POEM, the myotomy is on the same side of the tunnel as the knife and endoscope, possibly resulting in faster myotomy by forward advancement of endoscope and knife and minimal if any lateral movement of the knife. In contrast, in anterior POEM, incising the muscle at 2 o' clock position, the diametrically opposed position to that of the endoscope and knife (exiting the endoscope at 7 o' clock position) can only be done by interrupted lateral cuts hooking and cutting individual muscle bundles which result in large lateral swings of the knife from the muscle at 2 o' clock position to the knife's neutral position at 7 o' clock, very close to the mucosa which may suffer "countercoup" injuries

mucosal injuries (defined as any visible injury including even minor nontransmural blanching) (29% vs 23%) following 284 POEMs (mucosal injuries in 42/131, 32% of anterior POEMs vs 33/153, 22% posterior POEMs, $P = 0.046$). Posterior approach for POEM was significantly faster overall (97 min A, 79 min P, $P = 0.0007$) including a faster closure (Suturing $n = 177$, clips $n = 71$) (9.6 min A, 7.9 min P, $P = 0.02$). More patients had pain, requiring narcotics in posterior POEM (17% A vs 27% P, $P = 0.007$). We discuss this issue further on the myotomy section below. There was a trend for less acid exposure in anterior POEM: +BRAVO studies 21/58 (36%) A vs 29/58 (50%) P, $P = 0.13$, reflux esophagitis 22/57 (38%) A vs 33/60 (55%) P, $P = 0.076$. In summary, based on the preceding discussion, a posterior approach may result in encountering fewer high-risk vessels in the cardia and result in less mucosal injuries with additional benefit including a faster procedure.

A final important pitfall in submucosal tunnel dissection involves inadequate extension of the tunnel onto the cardia. This may represent one of the most important contributors to a failed POEM. Extension of the tunnel into the cardia is the most challenging part of the submucosal tunnel dissection as it entails dissecting through the narrow submucosal space of the high-pressure zone of the LES (which may also be quite fibrotic in previously treated or biopsied patients) and then extending the tunnel into the submucosal space of the cardia which is rich in high-risk large penetrating arteries as noted above. Therefore, operators early in their experience should emphasize adequate extension of the tunnel onto the cardia. Surgical studies have suggested extending the myotomy to the cardia by 2–3 cm is important for clinical efficacy [47]. In a recent small study, extension of the POEM myotomy 2 cm onto the cardia resulted in a small but significant augmentation of LES distensibility as measured intraoperatively with the Endoflip device, but further lengthening of the myotomy to 3 cm past the esophagogastric junction did not increase distensibility further [48]. Indicators that can be used to ensure adequate extension of the tunnel onto the cardia have been covered in other POEM publications including review papers such as the POEM NOSCAR white paper [42] and the International POEM survey [1] as well as step-by-step videos (VJGIEN video) [34]. Table 7.1 lists these indicators. Figure 7.15 illustrates the indicators that require recognition of endosopic signs and landmarks that can be subtle at times.

Table 7.1 Indicators identifying gastroesophageal junction

1	Insertion depth of the endoscope measured from the incisors
2	Marked narrowing of the submucosal space with resistance to endoscope advancement at the level of the LES followed by a prompt expansion of the submucosal space in the cardia with easier dissection (see Fig. 7.15c)
3	Large caliber vessels in the submucosa of the gastric cardia (penetrating branches of the left gastric artery emerging from the muscularis propria and arborizing to supply the mucosa) (see Fig. 7.15d)
4	Venules with segmental spindle shaped fusiform dilations (so called “spindle veins”) (see Fig. 7.15a)
5	Palisading vessels seen on the under-surface of the mucosal flap (see Fig. 7.15b)
6	Short aberrant extraneous-longitudinal muscle bundles located on the inner (luminal) side of the circular muscle layer at the GE junction (see Fig. 7.15e)
7	Blue dye staining of the gastric cardia mucosa seen on retroflexed luminal view (see Fig. 7.15f)

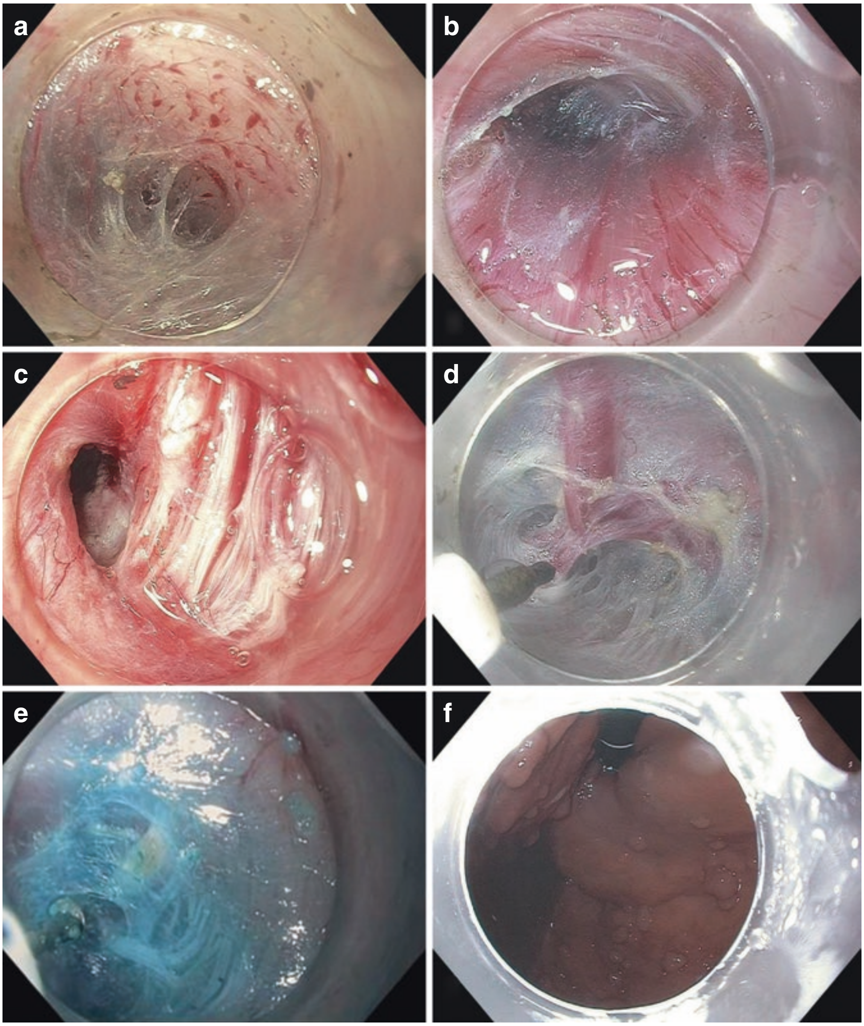


Fig. 7.15 Indicators used to confirm adequate extension of the submucosal tunnel to the cardia. (**a**) "Spindle" veins on the surface of the muscularis propria in the area of the GEJ. (**b**) Pallisading vessels in the GEJ mucosa (these are only visible if the submucosa on the underside of the mucosal flap has been extensively dissected which is generally not the case, since dissection preferably should be performed as close to the muscle as possible to avoid mucosal injury). (**c**) Prominent lower esophageal sphincter impeding scope progress and resulting in constricted submucosal space. This is best appreciated in patients with hypertensive sphincters (**d**). Once the tunnel is successfully extended over the sphincter and into the cardia, the constriction of the submucosal space at the LES is followed by expansion of the submucosal space making tunnelling easier again but more risky, given the presence of a high density of large vessels. The expansive submucosal space and large vessels signify that the tunnel has reached the cardia (**e**). Bundle(s) of aberrant inner longitudinal muscle fibers running in the submucosa, few cm in length, inserting into the circular muscle on their proximal and distal ends are encountered just proximal to the GE junction in some patients (**f**). Adequate extension of the tunnel into the cardia can be confirmed by retroflexing the endoscope in the lumen of the stomach and noting raised edematous mucosa at the tunnel terminus resulting from the submucosal injectate used during tunnel dissection. In patients with thick mucosa and submucosa, this sign may not be easy to visualize, particularly in posterior POEM where the tunnel terminus lies largely behind the shaft of the retroflexed scope

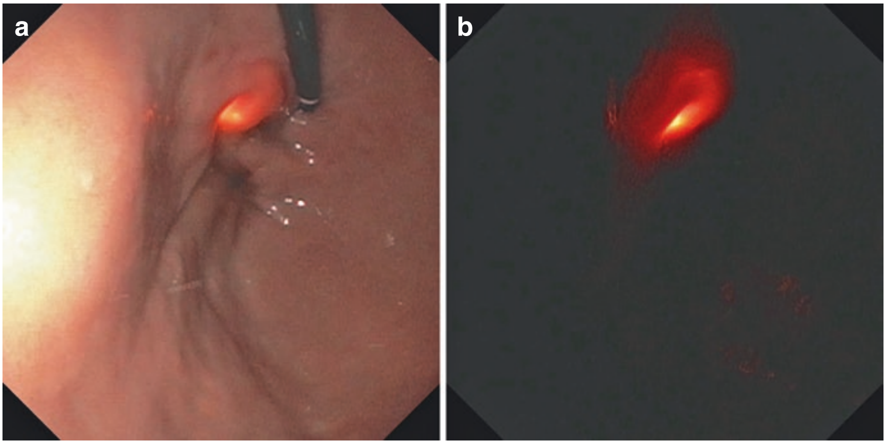


Fig. 7.16 Transillumination technique to confirm adequate extension of the submucosal tunnel to the cardia. (**a**) A second small-caliber transnasal endoscope is inserted next to the gastroscope and retroflexed in the proximal stomach to detect transilluminated light from the tip of the gastroscope located within the submucosal tunnel at the tunnel terminus which allows precise determination of the extent of the tunnel in the cardia. Here, the technique confirmed adequate extension of the tunnel in this posterior POEM (at least 2–3 cm extension in the cardia). (**b**) This image demonstrates transillumination detected with the light of the transnasal endoscope in the stomach turned off for illustration purposes

It should be noted that two adjunctive techniques have been described to ensure adequate extension into the cardia when this may remain in doubt despite use of the indicators listed. This may occur with operators early in their learning curve or in challenging patients such as those with sigmoid esophagus where anatomical landmarks can become obscured. One of these techniques involves fluoroscopy with a metallic marker used to mark the GE junction either intracorporeally (endoclip) or extracorporeally (e.g. paper clip) [49]. Another technique involves the use of two endoscopes. The gastroscope used for the POEM is inserted to the tunnel terminus, while a second small-caliber endoscope is inserted transnasally next to the gastroscope and retroflexed in the proximal stomach to detect transillumination from the gastroscope which allows precise determination of the extent of the tunnel (Fig. 7.16). This technique was originally described in a 2013 publication [50] with its utility confirmed more recently in a small randomized trial [51].

Myotomy

The myotomy is optimally initiated at least 2 cm distal to the distal extent of the tunnel opening to decrease the risk of leak, should dehiscence of the closure occur. This is important since centers using clips for closure and performing routine second-look endoscopy at 24–48 h after POEM have anecdotally reported frequent loss of clips and occasional partial dehiscence of the mucosal edges without leak. The absence of leak in these situations is attributed to independent sealing of the tunnel by mucosal flap adherence to the muscle proximal to the myotomy.

There is no consensus at present regarding full-thickness versus circular layer myotomy. Proponents of circular layer myotomy offer as the main rationale for this technique possible increased safety. Preservation of the longitudinal layer by the operator may be less likely to cause injury to adjacent organs. Proponents of full-thickness myotomy argue that this procedure is a more faithful endoscopic version of the full-thickness myotomy performed during a surgical Heller myotomy, and therefore would be expected to have the excellent long-term efficacy results of that procedure. The only current data comparing these techniques consist of a large retrospective study from the Shanghai group comparing their initial circular-layer only POEMs to later full-thickness myotomy POEMs [52]. They demonstrated equivalent outcomes except for a shorter procedure duration in the full-thickness myotomy group. However, these results may be confounded by a possible learning curve effect, given the retrospective methodology utilized. It should be noted that the positions of the two myotomy "schools" may be less entrenched than one might imagine, since operators that favor circular-only myotomy tend to inadvertently mechanically disrupt the insubstantial longitudinal layer in areas of the esophageal body during endoscope movements, and at the area of the GEJ they often perform full-thickness myotomy due to a complicated multidirectional bundle orientation as the two layers of the esophagus fuse with the three muscle layers of the stomach. Conversely, operators that favor full-thickness myotomy often start the myotomy in the esophageal body with a circular-only myotomy, since the utility of any myotomy in the esophageal body is uncertain in achalasia type I/II patients [48] and, in addition to the risk of injuring adjacent organs, full-thickness myotomy in the esophageal body may increase the likelihood of formation of diverticula through the weakened myotomized wall.

During anterior myotomy, one needs to be particularly mindful of the pericardial sac extending from approximately 30 to 35 cm from the incisors and "bulging" intraluminally (as illustrated in Fig. 7.17 and the second half of Video 7.2), which makes it particularly prone to injury or irritation during an anterior myotomy. Injury to the pericardial sac leading to tension capnopericardium has been reported [53]. We also know via personal communication of a case from a center early in their

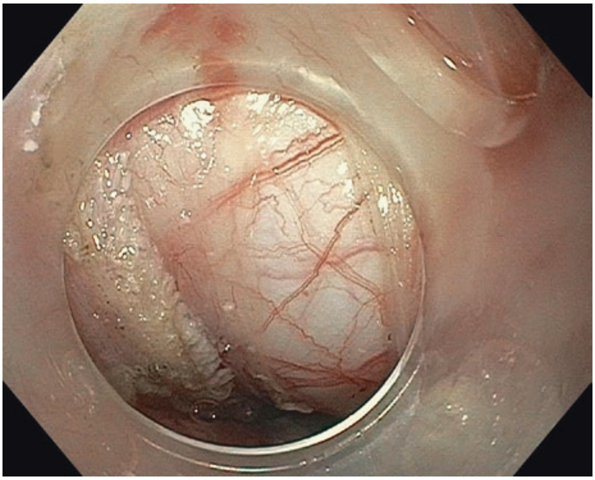


Fig. 7.17 The left atrium covered by pericardium (whitish bulging structure with dense network of superficial vessels) seen protruding through the edges of the full thickness myotomy incision in anterior POEM. Careful myotomy technique is required to avoid injury to the pericardium that can result in capnopericardium and possible tamponade and cardiac irritation that may increase the incidence of atrial arrhythmias

POEM learning curve of delayed post-POEM presentation with severe mediastinal sepsis requiring emergency thoracic surgery revealing an esophago-pericardial fistula. Despite the young age and good general health of this patient, this was a near-fatal event resulting in prolonged SICU stay and overall admission of 2–3 months. We are also aware of an adverse event from a moderate volume center consisting of tension capnopericardium due to inadvertent air insufflation treated with drain placement. Atrial fibrillation has also been reported [54] and, as is the case in traditional thoracic surgery, it is not uncommon to observe tachycardia after POEM or arrhythmias such as atrial tachycardia or atrial fibrillation (which can represent a de novo episode self-limited to the perioperative period as in the cited case report or a paroxysmal episode in the setting of known paroxysmal atrial fibrillation). Therefore, one might suggest that an anterior myotomy should be "paired" with a partial thickness myotomy in an effort to avoid any contact with the pericardium.

As noted above in the submucosal tunnel section, it has been speculated that there may be more accidental mucosal injuries during anterior POEM compared to posterior POEM [41]. We confirmed this in our recent retrospective comparison of anterior and posterior myotomy [46] summarized in the submucosal tunnel section. This is likely due to the closer proximity of the knife to the mucosa during submucosal tunnel dissection in the anterior orientation (where the mucosa is located at 6 o' clock position very close to the location of the knife at 7 o' clock position) (Fig. 7.14). Furthermore, during anterior myotomy, the location of the muscle to be cut at the 1–2 o' clock position (opposite the location of the endoscope, which, due to gravity lies on the mucosal flap, and opposite to the location of the knife at 7 o' clock position) results in interrupted muscle dissection, as individual fibers need to be hooked and cut with large excursions of the knife from 12 o' clock to 7 o' clock position that may cause opposing injury to the mucosal flap. In contrast, during posterior myotomy, gravity causes the knife to sit within the emerging myotomy groove and thus dissect the muscle straight-ahead in the continuous linear fashion. Furthermore, the knife and muscle are located at 6–7 o' clock position away from the mucosa located at 1–2 o' clock position (Fig. 7.14). For these reasons, injury to the mucosa is less likely. In posterior POEM, one needs to be mindful of potential injury to the posterior trunk of the vagus nerve which can often be seen through the transparent esophageal adventitia and pleura when a full-thickness myotomy is performed (Fig. 7.18) (the anterior vagus nerve due to its deeper and more lateral location cannot usually be identified during "anterior" POEM). Irritation to the vagus nerve which carries sensory afferent fibers may account for the higher rate of immediate perioperative pain found in our study in posterior POEM vs anterior POEM [46]. It should be emphasized however that this finding is not of major clinical significance as the pain is mild, controlled with few administrations of low doses of analgesics, and resolves within 12–24 h. However, more significant injury to the vagus may result in gastroparesis, diarrhea, and other motility disturbances. Due to the overall apparent increased safety of posterior POEM (less risk of pericardial injury or mucosal injury) as well as faster procedure times [46], and potentially improved LES disruption by cutting sling fibers rather than the mainly shorter weaker clasp fibers cut during anterior myotomy [46], posterior POEM appears to incorporate some anatomical advantages.

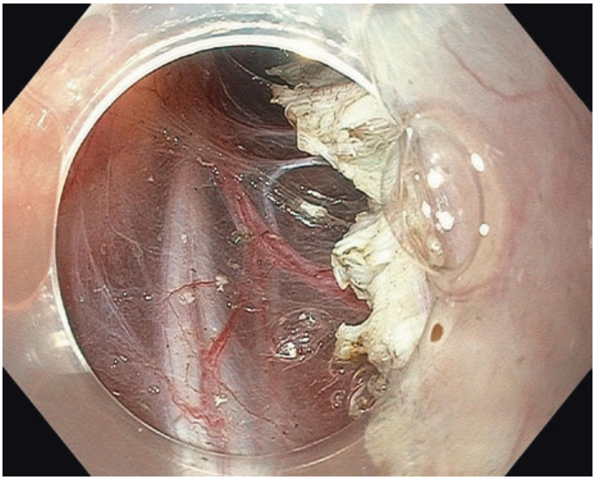


Fig. 7.18 Posterior trunk of the vagus nerve. In this posterior full-thickness POEM, the posterior trunk of the vagus nerve is seen through the transparent adventitia of the esophagus as a white shiny linear structure running parallel to the esophagus and dividing into multiple branches in the area of the cardia

Another common myotomy pitfall involves inadequate extension of the myotomy in the esophageal body in patients with spastic achalasia (Chicago type 3) or spastic disorders involving the esophageal body such as DES and jackhammer. These patients require a long esophageal body myotomy (exact length is guided by manometric data and endoscopic evidence of spasm but can range from 16 to 26 cm in our experience) in order to myotomize the long spastic segment along the distal two-thirds of the esophagus. Such a "long" myotomy is essential to relieve dysphagia and particularly pain which is often a dominant symptom in these patients. Inadequate extension of the myotomy in the esophageal body has been reported as a cause of residual symptoms in patients with spastic disorders [3] and can be diagnosed by high-resolution manometry demonstrating a residual spastic segment proximal to the myotomized segment (Fig. 7.19). This scenario has been successfully addressed with a second POEM targeting this proximal spastic segment [3]. Avoiding this pitfall hinges on having access to high-quality HRM studies that can allow differentiation of a spastic disorder requiring long myotomy such as type III achalasia from type I and II and also access to expert HRM interpretation to determine the length of esophageal body myotomy required in spastic patients. However, it should be noted that even among motility experts there can be substantial interobserver variability in HRM interpretation. For example, in a recent multicenter trial that included expert centers, there was only "moderate" agreement in the HRM diagnosis of type I, II, and III achalasia (kappa value of 0.48, 0.60, and 0.56, respectively) [55]. Therefore, it behooves the POEM operator to develop experience in HRM interpretation and to use complementary information from endoscopy, barium esophagram, and clinical history to maximize diagnostic accuracy and minimize the probability of performing a myotomy of inadequate length in patients with spastic disorders.

A final pitfall involving the "extent of myotomy" involves patients with esophageal spastic disorders such as jackhammer or nutcracker esophagus that (unlike achalasia patients) demonstrate normal LES relaxation on manometric evaluation. Initially, many POEM operators eschewed extension of the myotomy through the

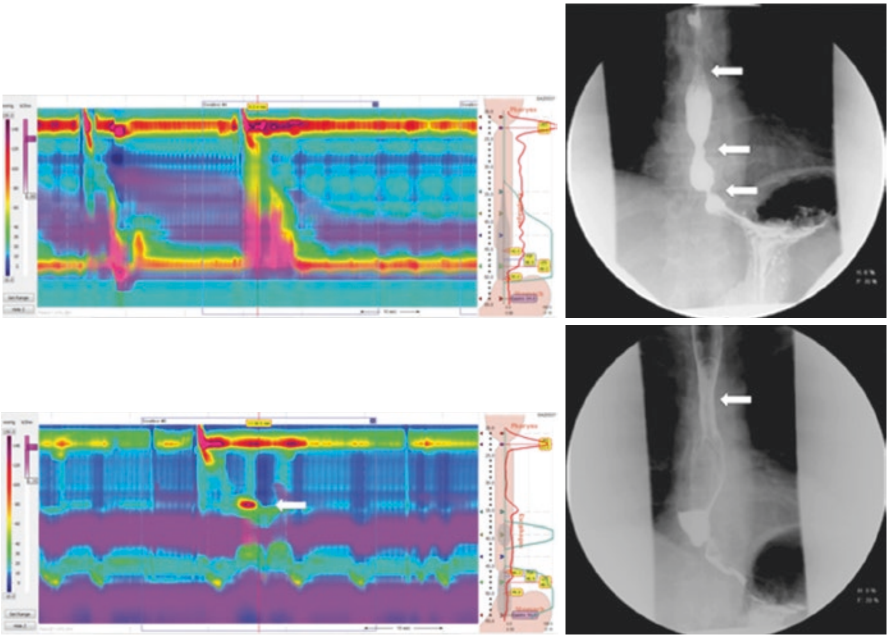


Fig. 7.19 Illustration of the pitfall of inadequate proximal extension of the myotomy in spastic patients. This patient with Chicago classificaiton type III (spastic) achalasia underwent POEM with a 15 cm "long" myotomy which proved not long enough as he had a residual 3 cm proximal spastic segment on post-POEM HRM and barium esophagram causing persistent discomfort. The patient declined a second POEM to extend the myotomy proximally and opted for pharmacological management with antispasmodics

LES and cardia in these patients. The rationale was that, since the LES relaxes normally in these disorders, performing LES myotomy may have no therapeutic benefit and may in fact subject the patient to acid reflux, which, apart from resulting in GERD and possible sequelae such as Barrett's esophagus and strictures, may also exacerbate the underlying spastic disorder. It gradually became apparent, however, that performing esophageal myotomy without concomitant LES myotomy in these patients may result in suboptimal outcomes. It appears that the substantial weakening or virtual obliteration of peristalsis by the esophageal body myotomy results in poor emptying unless the LES is also proportionately weakened by extending the myotomy through the LES. In Fig. 7.20, we present a case of LES-sparing POEM in a jackhammer patient that illustrates this point.

Unlike immediate bleeding which most frequently occurs during dissection of the submucosal tunnel and was addressed in the earlier section of this chapter, delayed bleeding has been reported to usually occur from vessels at the cut muscular edges "because of an abundance of blood vessels and collateral circulation in the muscle layers of the esophagus" [56]. In our experience, the vessels encountered during myotomy include small vessels intercalated between the muscle bundles and large vessels (mostly veins, but also few scattered arteries) running transversely in the space between the esophageal muscle and mediastinal pleura. The vessels are

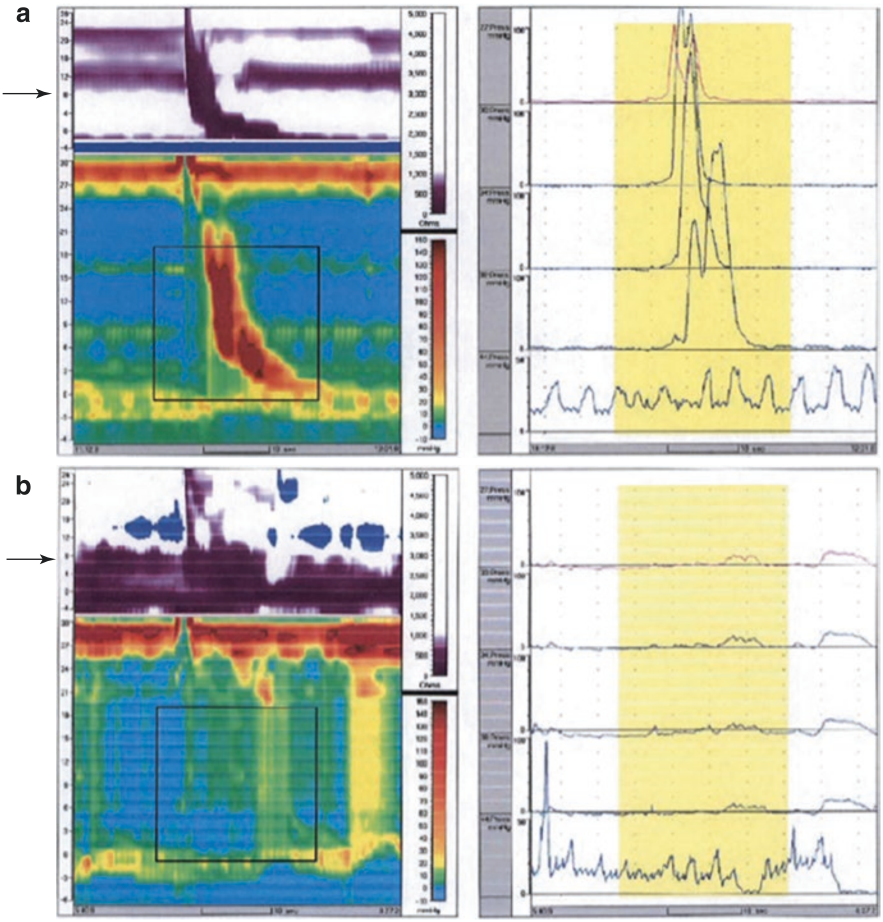


Fig. 7.20 This figure illustrates the potential pitfalls of POEM, particularly POEM without LES myotomy, to treat spastic disorders with intact peristalsis and normal LES relaxation. This patient with jackhammer esophagus underwent POEM with preservation of the LES. On the pre-POEM HRM (**a**), classic jackhammer features are present with high-amplitude peristaltic contractions extending from the LES to 21 cm proximal to the LES (see scale on left of HRM plot) which were causing severe pain, moderate dysphagia, and rare regurgitation. The patient had minimal response to pharmacological therapy and was referred for POEM. We performed POEM with long esophageal body myotomy of 21 cm and no incision of the LES since it demonstrated normal relaxation on HRM. On the post-POEM HRM (**b**), the patient has essentially abolished peristasls with only minimal pressurization waves. Note the poor emptying noted on the post-POEM impedance graph compared to the pre-POEM impedance graph (*white arrows*). Residual fluid (denoted by *purple color* on the impedance graph) remains in the esophagus after POEM, whereas there was prompt and complete clearance of fluid prior to POEM. After the POEM, even though the patient's pain symptoms improved dramatically, dysphagia and regurgitation worsened slightly. A second POEM was performed with LES myotomy which improved but did not normalize emptying with moderate improvement in dysphagia and regurgitation

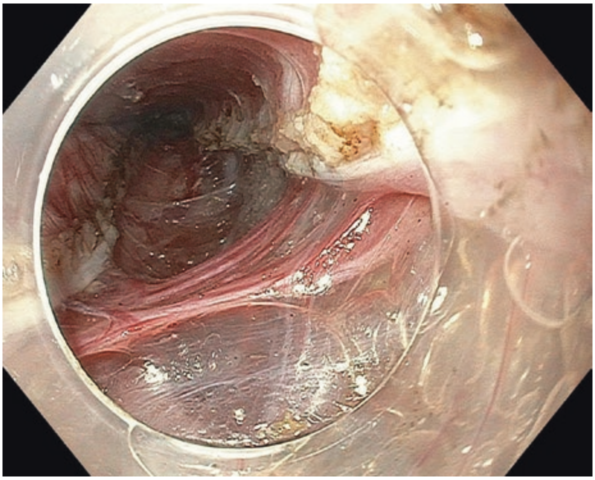


Fig. 7.21 The vascular plexus deep to the muscularis propria layer exposed during POEM with full-thickness posterior myotomy. This plexus consists of a “ladder” of transvserse arteries and veins located between the esophageal wall and mediastinal pleura

largely adherent to the esophageal wall and thus often divided during full-thickness myotomy. The density of the small intramuscular vessels can be variable, whereas the deeper vessels forming a plexus in the form of a “ladder” in the bed of a full-thickness myotomy is a reliable finding that needs to be considered during the myotomy (Fig. 7.21). Bleeding from the small intramuscular vessels can be easily controlled by short pulses of a coagulation current using the tip of the knife. If a high density of such vessels is encountered, increasing the coagulation effect in the current used for the myotomy (e.g. by using a higher “effect” setting on the commonly used Endocut Q program in the ERBE VIO generator) can effectively coagulate these vessels as the myotomy is being performed. Bleeding from the larger, transverse, submuscular vessels can be riskier to control since extensive irrigation is ill-advised in an exposed mediastinum, and coagulation will by necessity involve some current escape to the underlying mediastinal pleura and other adjacent structures such as the pericardium and pleura potentially injuring these structures. Therefore, prevention of bleeding from these deeper vessels is the optimal strategy. Identification of the vessels as the muscle bundles are being hooked prior to cutting is optimal since, if such vessels are detected, the myotomy can be performed with high coagulation (e.g. with spray coagulation on the VIO 300 D generator) or a plane for the knife can be found between the vessels and the muscle thus avoiding division of these vessels altogether. It should be noted that identification of such vessels (as well as other structures deep to the muscle to be cut) is not possible when myotomy is performed in distal to proximal fashion as has been advocated by some operators [57].

Closure of the Submucosal Tunnel

Although in the majority of cases tunnel closure is uneventful, in a small percentage of cases closure can be difficult. This situation can be very stressful for the endoscopist given the critical role of tunnel closure in preventing leakage and the potentially life-threatening adverse events such as mediastinitis, empyema, and abscess formation.

Advance planning is essential in avoiding closure pitfalls. As noted above in the "Site and Orientation Selection" section, it is important to pick a site away from potential submucosal fibrosis. It is also important to avoid creating the opening of the tunnel in an area of esophageal angulation or next to the spine in an area where the spine severely indents the esophagus. An angulation of the esophagus can be easily overcome for the purpose of making the initial incision by creating a large submucosal injection. However, at the time of closure with submucosal lifting no longer present, the operator may discover that what appeared as a minor lumen indenting fold or angulation at the time of tunnel initiation after a generous submucosal injection now presents a major obstacle to clip or suture placement. Applying clips or even sutures may be very challenging if the incision is placed along the downsloping mucosa draped over the right side of a prominent spine impression. Again, the potential adverse impact on closure may not be appreciated when the initial incision is made since a large submucosal injection can elevate the mucosa and submucosa well above the prominent spine impression. However, at the time of closure without the assistance of a lifted mucosa and submucosa, the firm concave protruding bone under a downsloping everted left edge of the tunnel entry site makes it difficult to apply clips and even sutures. Also, as briefly alluded to above in the "Submucosal Tunnel Dissection" section, forceful blunt insertion of the endoscope can result in tearing of the insertion site creating a much larger defect than the one initially created (Fig. 7.6). Finally, again as briefly mentioned above, submucosal dissection closer to the mucosa rather than muscularis propria during tunnel initiation can result in thin mucosal edges without significant underlying submucosa (which is much stronger structurally).This can also occur in cases of severe fibrosis and malnutrition with resultant paucity of submucosal tissue. Finally, thick mucosal edges resulting from chronic inflammation due to long-standing disease and severe food stasis can be difficult to approximate with the usual endoscopic clips. In this scenario, use of larger over-the-scope clips (OTSC) has been reported [58]. Endoscopic suturing using the only such device currently available in the United States (Overstitch, Apollo Endosurgery, Austin, TX) can also be effective in this situation. We have used endoscopic suturing routinely and exclusively for POEM tunnel closure for the past 4 years (including over 200 POEMs) and have published a retrospective comparison of the two techniques [59]. We collected and analyzed data on our first 62 consecutive POEMs closed with clips and the subsequent 61 consecutive POEMs closed with sutures. To avoid learning curve bias from early cases, we compared the most recent 25 consecutive closures in each group with regard to cost, procedure time, and adverse events. There were no significant differences in closure time (8.8 min for endoclips and 10.1 min with OverStitch), cost ($916 versus $818), and hospital stay (1.9 days versus 1.7 days). The Portland group also conducted a smaller retrospective case-controlled study evaluating closure with hemostatic clips versus endoscopic suturing [60]. Out of the 124 POEM cases that were assessed, endoscopic suturing was employed in only 10 (8%). Five of these cases were selected for the study and were matched to five cases where conventional clips were used. Median closure time was significantly shorter for the endoscopic clip group (16 ± 12 min) as compared to the suturing group (33 ± 11 min),

$p = 0.044$. The very long median closure time for endoscopic suturing is not explained and was the main reason for a cost advantage when endoscopic clips were used (the device costs were similar with the OR time difference accounting for most of the cost difference according to the authors). The authors concluded that endoscopic suturing seems best suited for cases of difficult mucosotomy closure. Special situations are occasionally encountered. When attempting to close very thin devitalized mucosal edges that tear even with attempted interrupted suture placement or very large linear defects as can be caused by extensive tearing in a narrow-lumen esophagus where suturing may occlude the lumen, neither clips nor suture closure is optimal. In these situations, third-line methods may need to be applied such as fibrin glue [44] or stent placement [45]. Such methods provide less reliable closure and should be accompanied by longer observation under NPO status, intravenous antibiotics, and radiographic leak assessments similar to the management of contained esophageal leaks.

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