Management of Adverse Events of Submucosal Endoscopy

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KEYWORDS

• ESD • POEM • Submucosal endoscopy • Complications • Dysplasia • Neoplasia

KEY POINTS

- Although generally safe and well tolerated, submucosal endoscopy carries a higher complication risk than most other endoscopic procedures. There are unique considerations in the recognition, management, and prevention of bleeding, perforation, and other complications in the context of submucosal procedures.
- Close monitoring for perforation is necessary during the procedure, especially if the muscularis propria is injured. However, perforations can generally be repaired with clips or endoscopic suturing, after which the procedure can continue.
- Electrocautery with the dissection knife is the first-line tool for small-volume bleeding; larger vessels may require hemostatic forceps.
- Preemptive coagulation of visible vessels in the endoscopic submucosal dissection of ulcer base may reduce the risk of delayed bleeding. Other potential tools being studied to prevent delayed bleeding include hemostatic sprays, over-the-scope clips, snares, and sheets of cultured cells.

INTRODUCTION

The advent of submucosal endoscopic interventions now allows endoscopists to perform procedures that previously necessitated surgical intervention. Despite the relatively recent introduction and evolution of submucosal and third space endoscopy, there is already sufficient evidence to support its efficacy and safety when performed by trained endoscopists in carefully selected patients. However, the learning curve of submucosal endoscopy remains steep, particularly in its initial stages, and the possibility of severe adverse events exists. Fortunately, most acute and delayed

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complications can be addressed endoscopically or nonprocedurally with medications and observation. The types of adverse events associated with submucosal endoscopy vary from those typically encountered during less invasive forms of endoscopy, so early recognition and management is paramount in patient and procedure outcomes.

In this article, we will review the spectrum of procedure-related adverse events relevant to submucosal endoscopy. The majority of experience and evidence in this area applies to endoscopic submucosal dissection (ESD), endoscopic mucosal resection, and perioral esophageal myotomy (POEM). Variations of these submucosal endoscopic procedures including G-POEM, Z-POEM, and STER are not specifically discussed but the adverse events herein can similarly occur in those procedures as well.

We categorize adverse events first by their time of presentation relative to the procedure, with certain events likely to occur during the procedure (immediate complications), and others more likely to occur in the following days to weeks (delayed complications; **Table 1**). For each major category of adverse event, we will discuss epidemiology and risk factors, characteristic presentations, immediate treatment recommendations, and recommendations for prevention. There are differences in the types of complications, degree of risk, and presentation of complications depending on the specific procedure being performed and the location within the gastrointestinal (GI) tract being intervened on. We will discuss those differences at a high level but subtle differences remain beyond the scope of this review.

Variability in how adverse events are assessed and categorized has previously hindered the study of the complications of endoscopy. There have been sustained efforts to develop more structured frameworks to categorize complications. In 2010, a working group of the American Society for Gastrointestinal Endoscopy developed a standardized lexicon to categorize endoscopic adverse events as mild, moderate, severe, or fatal.[1] More recently, the Adverse Events in GI Endoscopy (AGREE) classification published in 2022 divides adverse events into 5 grades based on the degree of postprocedural intervention needed to address the event.[2] With regards to POEM, publications have outlined clearer criteria for categories of complications, including insufflation-related adverse events, perforation, bleeding, postprocedural GERD, severe persistent pain, and aspiration pneumonia.[3] Further development and more widespread use of standardized classification systems for complications can aid in the continued study of the adverse events we discuss below and how to better prevent them.

Immediate Complications

Bleeding

Submucosal endoscopic procedures carry among the highest bleeding risk out of any endoscopic procedure.[4] The bleeding risk is greatest in gastric and duodenal submucosal procedures due to the high vascularity of those intestinal regions, with an incidence rate of 2.9% for major bleeding in gastric ESD.[5] Bile exposure in these areas may also increase bleeding risk.[6] Intraprocedural bleeding is less common but still occurs during esophageal and colonic submucosal endoscopy procedures.[7] In POEM, bleeding can happen at multiple stages of the procedure, from the initial mucosal incision through tunneling and myotomy.[3] Although small-volume bleeding is common, bleeding substantial enough to halt the procedure or cause shock is rare.[8,9]

Immediate intraprocedural bleeding should be self-evident, although the rate can vary from oozing to spurting to catastrophic hemorrhage. Nonetheless, even a small amount of bleeding should be addressed to prevent obscuring the field of view or delineation of the submucosal and muscle layers and extending procedure duration and increasing the risk of errors or other complications.

Table 1
Summary of common immediate and delayed complications with submucosal endoscopy

Immediate Complications		
Perforation	Bleeding	Aspiration
• Perforation risk is higher in esophageal or colonic procedures than in gastric procedures • CO_2 insufflation should be used for all submucosal endoscopy • Most perforations identified during the procedure can be closed with clips or endoscopic suturing before continuing with the procedure; postprocedural antibiotic therapy is recommended in case of perforation • Tension pneumothorax or pneumoperitoneum are rare but feared complications of perforation that require emergent decompression	• In ESD, preprocedural patient positioning should prioritizing placing the dissection site (in ESD) up relative to gravity, helping blood flow away from the work area • Electrocautery is the first-line tool to address bleeding but should not be overused to avoid causing perforation. Hemostatic forceps or clips can also be helpful in stemming bleeding • Urgent vascular interventional radiology or surgical consult may be needed in cases of severe hemorrhage but this is very rare • Low-dose aspirin is likely safe to continue for submucosal procedures, or with only minimal interruption. Other antiplatelet and anticoagulant medications should be held if possible	• Aspiration and resultant pneumonia can present more commonly on the left side following endoscopy • Avoiding excessive insufflation and considering intubation for proximal esophageal procedures can reduce risk of aspiration
Delayed Complications		
Stricture	Bleeding	Delayed Perforation
• Esophageal ESD, especially with resections involving more than three-fourths of the luminal circumference, has a high risk of postprocedural stricture • Prophylactic balloon dilations and intraprocedural steroid injections can reduce the risk of stricture	• Urgent repeat endoscopy is indicated in case of melena, hematochezia, or other evidence of bleeding following the procedure • Preventative hemostasis involving preemptive coagulation of visible vessels at the end of the procedure holds promise but more evidence is needed to definitively recommend it	• Pneumomediastinum and/or pneumoperitoneum are common postprocedural findings and may not represent complications • Chest/abdominal pain, nausea, and fevers in the postprocedural period should prompt workup for mediastinitis or peritonitis, which in most cases can be treated supportively with antibiotics

Most bleeding can be managed endoscopically and begins with the localization of the bleeding source. Ideally, the patient is already positioned such that the lesion is in an antigravity location, thus promoting contents including blood to pool away from the resection field. Water jet functions available in current generation endoscopes are helpful in rapidly clearing active bleeding to at least momentarily localize the site of bleeding. Underwater visualization can also be used to effectively localize the bleeding (**Fig. 1**). If the resection knife is equipped with an injection channel (manual or automated high-pressure), immediate injection of submucosal agent can provide tamponade effect to stop or reduce small volume bleeding, facilitate treatment, and protect against injury during subsequent electrocautery. If this is ineffective to slow the bleeding, injection of diluted epinephrine may be performed. Gentle tamponade using the side of the cap-fitted endoscope tip can also be helpful while exchanging accessories to administer therapy.

After localization, bleeding can be treated using a variety of electrocautery-based interventions. For example, smaller bleeds can be treated efficiently with coagulation using the knife. More brisk bleeding may require exchanging the knife for hemostatic forceps. These are used by grasping the bleeding vessel/region, gently retracting and then coagulating using "soft-coagulation" mode.[10] The endoscopist should be mindful not to overuse electrocautery because this can increase the risk of deep muscle injury and perforation. Through the scope, clips can also be used for hemostasis but are often considered a secondary measure due to their potential to impair visualization or accessibility and make subsequent dissection more difficult. If severe bleeding cannot be managed endoscopically, IR embolization or urgent surgical intervention may be needed.

Submucosal dissection should be undertaken with great care, with the endoscopist proactively identifying submucosal vessels to be treated prophylactically with electrocoagulation before dissecting (ie, "cutting") through the submucosa. If the identified vessel is large, hemostatic forceps as opposed to the knife can be used instead for the same prophylactic purpose (**Fig. 2**).[11] For smaller vessels, electrocautery using the dissection knife provides the benefit of sparing the endoscopist the time and effort of switching tools frequently. Red dichromatic imaging using a unique light spectrum on equipped endoscopes may be helpful in more easily identifying blood vessels during the procedure.[12]

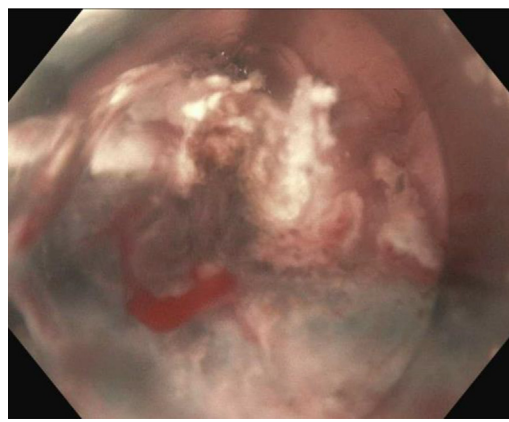

Fig. 1. Bleeding during submucosal dissection. Bleeding during submucosal dissection localized and treated underwater.

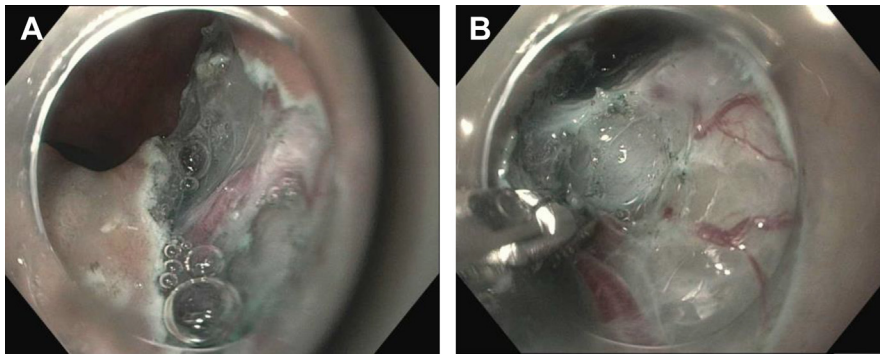

Fig. 2. Prophylactic coagulation of submucosal vessel. A medium-sized submucosal vessel encountered during submucosal dissection (*A*) and prophylactically treated with hemostatic forceps in soft coagulation mode (*B*).

Guidelines from Japan specific to ESD suggest it is acceptable to continue low-dose aspirin monotherapy during ESD, and other guidelines that apply to endoscopic procedures more broadly suggest the same.[13] More recent guidelines provide recommendations on the management of other antiplatelet and anticoagulant medications, depending on the risk of holding those medications. Heparin bridging for patients on warfarin is commonly done, although simply holding warfarin may be noninferior in thrombotic risk based on limited evidence. Overall, making definitive recommendations regarding specific management of nonaspirin antiplatelet agents or anticoagulants is difficult because the designs of past clinical trials in this area are heterogeneous.

Perforation

The incidence of perforation will vary widely depending on endoscopist skill level, difficulty of resection (size, position), intestinal region, procedure technique, and scope maneuverability. Generally, the risk of perforation is lowest in gastric ESD (particularly the distal stomach where the submucosa and muscularis propria is thicker) and thus most suitable for learners. At the opposite end of the spectrum, the duodenum represents the most technically difficult organ due to its thin wall layers and is generally reserved for experts. A recent large German study found perforation rates for ESD to be 2.6% in esophagus, 4.2% in stomach, and 14.1% in colon,[14] whereas meta-analyses have estimated the average perforation risk during ESD at 2.7% for gastric ESD and 4.8% for colonic ESD.[5,15] The risk of perforation into the mediastinum in POEM is low at less than 1%.[9] A small degree of pneumoperitoneum or subcutaneous emphysema during POEM is not uncommon and may not truly need to be considered an adverse event if not associated with tension physiology or other harmful effect.[16]

Large perforations may be directly visualized during the procedure with omentum and/or fat seen, whereas microperforations may only be evident as mediastinal or peritoneal free air palpated or seen on imaging after the procedure. Injury or breech of the muscularis propria should be vigilantly assessed during and at the end of the resection to recognize perforation early. In the esophagus, perforation can result in progressive pneumomediastinum causing compression of intraluminal space. Neck and chest wall crepitus can sometimes be palpated on the patient. Mediastinitis is a feared but an exceedingly rare adverse event. Pneumothorax can also occur, which in exceedingly rare occasions can progress to tension pneumothorax. Perforation in

the stomach, duodenum, or colon can cause pneumoperitoneum, which can evolve to tension pneumoperitoneum causing hemodynamic shock that becomes apparent during the procedure.

Endoscopy allows for early recognition of perforation, and provided the range of endoscopic management options, it is also the first-line treatment option. Thus, endoscopists should be trained and comfortable in closure techniques. Endoscopic management of perforation is reviewed in detail elsewhere in the collection. Briefly, closure will depend on the size of the defect and endoscopic accessibility. Through-the-scope clips offer closure of small defects without requiring exchange of the endoscope for setup of alternative closure devices and therefore should be the first consideration. They should be applied carefully without further injury to the muscularis propria or exacerbation of the perforation. Because clips can hinder further dissection, submucosal dissection may be continued in small-to-medium–sized perforations until there is sufficient space around defect to place a clip without entrapping or impairing dissection of the lesion. There are a wide variety of through the scope clips ranging in size (up to 16–17 mm), and selection will typically depend on institutional availability and endoscopist/assistant familiarity. For larger perforations, over-the-scope clips and endoscopic suturing devices are available but require removal of the endoscope. Of note, endoscopic suturing remains limited to a gastroscope length dual-channel therapeutic endoscope, and thus, advancement to the right colon may be challenging. Recently, a through-the-scope suturing device has been released compatible with colonoscope length endoscopes without need for endoscope removal (X-Tack, Apollo).

There exist unique considerations regarding closing perforations in the context of POEM. If a full-thickness perforation is made at the time of the initial mucosal incision (mucosotomy), through the scope clipping may not be sufficient, and suturing or an over-the-scope clip may be preferable.[9]

On recognition of perforation, IV antibiotics should be administered immediately with coverage of enteric organisms (anaerobes and broad gram-negative coverage). If a perforation is small and clipped successfully, the procedure can generally continue safely but the patient will need close postprocedure monitoring for evolving infection. Antibiotics should be continued and the patient should be kept NPO at least until any symptoms subside.

In the event of tension pneumoperitoneum intraprocedurally or postprocedure, emergent needle decompression (pneumoparacentesis) is required. A Veress needle can be used for this purpose.[9] However, pneumomediastinum and/or pneumoperitoneum are common incidental findings on postprocedural imaging, occurring in upward of 50% of cases in some studies of post-POEM patients without any impact on outcomes.[17] If tension pneumothorax were to occur, this requires emergent needle or tube thoracostomy and recruitment of help from pulmonology or anesthesiology colleagues may be necessary.

Endoscopist skill level and appropriate case selection are certainly key variables affecting the risk of perforation but can occur in expert hands as well. From a technical standpoint, endoscopists should avoid injury or breech of the muscularis propria layer by striving to preserve the deepest one-third of submucosa during dissection. Various devices and techniques have also been developed to facilitate safe submucosal dissection including insulated tip knives, scissor knives, and countertraction techniques. There should be a low threshold to consider these when difficult portions of dissection are encountered. Other strategies related to perforation include intubation (owing to positive intrathoracic pressure), which reduces the risk of significant pneumomediastinum, and CO_2 insufflation rather than air because CO_2 can be resorbed relatively rapidly from body cavities. Insufflation CO_2 flow rate should be reduced to

the lowest effective setting once perforation is suspected to minimize pneumoperitoneum.[8] Particular care to using minimal CO_2 insufflation flow should be taken when in the submucosal tunnel during POEM.[9] Bleeding should be controlled as discussed earlier to maintain exposure and avoid inadvertence injury. For colonic ESD, poor bowel preparation predisposes patients to poor outcomes in the event of a perforation due to peritoneal contamination, and therefore should only be pursued in the setting of a high-quality preparation.

Although concern is generally for perforation into the space outside of the organ, with POEM, there is also the potential for mucosal perforation from the submucosal tunnel into the gastroesophageal lumen. In a large study reviewing more than 1800 patients who underwent POEM, 2.8% experienced inadvertent mucosectomy.[18] Closure of these defects can be performed with clips or endoscopic suturing. There is not sufficient data to advocate for one of these means over the other, with the choice being influenced by the size of the perforation.[8] Generally, in the hands of experienced operators, mucosal perforations can be addressed fully during the procedure without long-term sequelae.

Aspiration Pneumonia

Aspiration pneumonia is manifest by hypoxia, sepsis, dyspnea, and or productive cough or sputum. Because GI endoscopy patients are often positioned on their left side, aspiration more often affects the left lung, as opposed to more general contexts when the right lung is at greater risk.[19] Prompt initiation or broadening of antibiotics with enteric (GNR and anaerobe) coverage should occur. To prevent aspiration pneumonia, patients undergoing procedures of higher aspiration risk (eg, proximal esophageal ESD) may benefit from intubation. Moreover, for upper GI procedures, excessive air insufflation should be avoided. A "flexible overtube" (Sumitomo Bakelite) has also been suggested to lower the risk of aspiration pneumonia.

Delayed Complications

Stricture

Gastrointestinal stricture is of greatest concern in esophageal ESD. However, stricture can occur in other locations especially with large near or fully circumferential resections. Involvement of a greater circumference of the esophagus is a significant predictor of stricture risk, with the risk markedly elevated in resections greater than 75% circumference (**Fig. 3**).[20] A case-control study of 134 patients with and without stricture after esophageal ESD found that 75% circumferential tumor involvement was associated with refractory stricture with an adjusted odds ratio of 5.49.[21] These manifest themselves based on region, such as dysphagia in the esophagus or constipation in the colon (**Fig. 4**). Stricture formation can have a major impact on quality of life and prevention and management is important. As with most benign strictures, balloon dilations are first-line treatment, with serial dilations usually being required until resolution of symptoms.

There have been significant efforts to prevent stricture formation. Intraprocedural injection of steroids (generally triamcinolone injected into the resection or ulcer base) may be effective in reducing stricture and the frequency of postprocedural balloon dilations.[6] Care must be taken not to inject into the muscularis propria, which can cause abscess formation or perforation. Oral prednisolone moderately reduced stricture rate but the dose of prednisolone trialed was very high.[22] Prophylactic balloon dilations early in the postresection period (theoretically before significant fibrosis has occurred), for example, 3 to 4 days after ESD, can be performed. Other investigational things

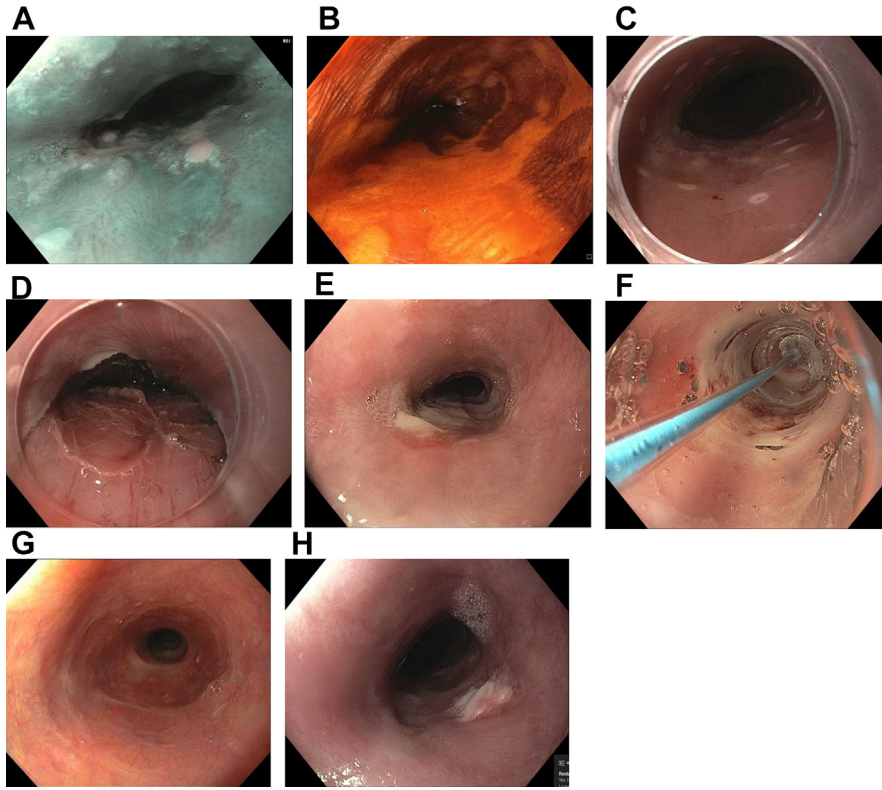

Fig. 3. Esophageal stricture following esophageal ESD. Appearance of esophageal squamous cell carcinoma on NBI (*A*), Lugol's stain (*B*), and white light endoscopy after marking (*C*). ESD was performed of a 7-cm length region that was nearly circumferential (*D*). Three weeks following ESD, an esophageal stricture formed (*E*), and was serially dilated (*F, G*) with eventual intralesional steroid injection resulting in durable stricture improvement and tolerance to solid foods (*H*). (*Courtesy of* Amrita Sethi, MD, MASGE, NYSGEF, New York, NY.)

include dissolving stents, antifibrotic medications, polyglycolic acid sheets, or cultured oral mucosal cells in sheets.[23]

Bleeding

Delayed bleeding occurs much less commonly compared with intraprocedural bleeding. There is significant variability in estimates of delayed bleeding due to lack of consistency in how delayed bleeding is defined, diagnosed, and quantified in the literature, although the AGREE adverse event classification may help standardize the assessment in future studies.[2,24] The rate has been estimated at between 2% and 16% following ESD, with antithrombotic medication therapy and resected specimen size greater than 40 mm being the predominant risk factors for delayed bleeding.[7,25,26] In terms of organ-specific risk, meta-analyses have estimated the risk of delayed major bleeding at 3.6% with gastric ESD and 4.0% for colonic ESD.[5,15] Other factors that may increase the risk of delayed bleeding include prolonged procedure time and chronic hemodialysis.[7] In POEM, delayed bleeding into the submucosal tunnel occurs generally less than 1% of cases, rarely requiring repeat endoscopy for treatment.[9,27,28]

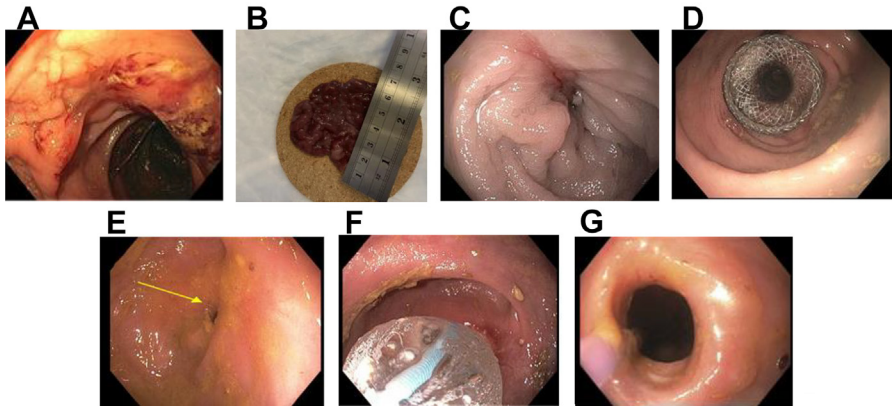

Fig. 4. Rectal stricture following ESD. A 5-cm rectal lesion (*A*) resected by ESD (*B*). The patient returned with constipation 2 months and later and was to have a rectal stricture (*C*). This was treated initially with a fully covered metal stent for 3 months (*D*). However 2 months later the stricture recurred (*E*) and was then treated with aggressive serial balloon dilation (*F*) resulting in durable endoscopic and clinical improvement (*G*). (*Courtesy of* Amrita Sethi, MD, MASGE, NYSGEF, New York, NY.)

Delayed bleeding can present with hematemesis, melena, hematochezia, shock, or a significant hemoglobin drop without another causative explanation depending on the site and severity of bleeding. Vague symptoms including abdominal pain and nausea can sometimes herald the early phase of delayed bleeding. The greatest risk of delayed bleeding is within 24 hours of the procedure.[7] In early Japanese studies, most delayed bleeding occurred while patients were still hospitalized, with only approximately 1 in 5 instances occurring after discharge.[24] However, in the United States, patients typically have a shorter postprocedure length of stay, and so by definition, the risk of delayed bleeding after hospital discharge may be higher.[29,30]

The mainstay of management for delayed bleeding after adequate resuscitation is repeat endoscopy. In most cases, standard tools to treat bleeding ulcer such as epinephrine injection, hemostatic clips, and or electrocautery can be used. To avoid perforation, excessive use of electrocautery on the ESD ulcer base should be avoided but hemostatic forceps may be carefully applied to visible vessels. Generally, delayed bleeding is not catastrophic and responds well to endoscopic interventions, making the need for interventional radiology or surgical intervention is rare.[25] In the event of catastrophic bleeding, or bleeding that cannot be sufficiently addressed by endoscopic means, urgent surgery or embolization should be pursued promptly.

Second-look endoscopy has been proposed as a means to identify patients with bleeding or who may be at high risk of delayed bleeding after ESD. However, data in this area has generally shown no significant benefit of second-look endoscopy.[31,32] Some groups have theorized that second-look endoscopy could offer benefit if performed more selectively in patients with risk factors for increased bleeding risk.[26]

Medical optimization may lower the risk of bleeding. Proton pump inhibitor (PPI) therapy is often used after submucosal procedures in the upper GI tract, although there is insufficient evidence to recommend a specific agent or course.[6] Many centers use between 2 weeks and 2 months of PPI therapy for gastric and distal esophageal submucosal endoscopic procedures. Studies to date are mixed in the degree of benefit PPIs offer, and other more recent studies support the use of lower dose intermittent PPI dosing as noninferior to daily high-dose use.[33] H2 receptor blockers have

also been used to reduce the risk of delayed bleeding. However, although there is heterogeneity in results, there is some evidence to suggest PPIs are more effective overall than H2 receptor blockers in reducing bleeding risk.[7] In the authors' view, the risk–benefit profile based on current data favors a course of PPI therapy following gastric and distal esophageal procedures, although more data are needed in this area. Early evidence on the potassium-competitive acid blocking medication vonaprazan, including from phase II clinical trials, suggests that this emerging medication class could be more effective than PPIs in prevention of delayed bleeding following gastric ESD.[34,35] Preprocedural gastric lavage has been theorized as a means to reduce the risk of delayed bleeding, under the hypothesis that bacterial growth in the stomach due to frequent concomitant PPI use may increase the risk of infection and bleeding in the ulcer base.[36] However, there is insufficient evidence to recommend this practice.

Preventative hemostasis is a concept that many experts in the field have suggested as a means to reduce the risk of postprocedural bleeding. It involves the preemptive coagulation of nonbleeding visible vessels in the postdissection ulcer base in ESD. An early retrospective study suggested a benefit of preventative coagulation using forceps.[37] However, the benefits of this preventative coagulation must be weighed against the increased risk of perforation with increased coagulation exposure.[7] Small studies have demonstrated promise in the use of endoscopic Doppler probe ultrasonography to better identify at-risk vessels in the postdissection ulcer base.[7] A suggested alternative to preventative electrocoagulation is the search, coagulation, and clipping (SCC) method. Per the developers of this method, it involves "observing the ulcer floor, identifying blood vessels, and cauterizing and clipping respective blood vessels." A retrospective study of the method compared with standard preventative electrocoagulation suggested a reduced risk of delayed bleeding with the SCC method.[38]

There are ongoing efforts to explore other novel tools and techniques to reduce the risk of delayed bleeding.[6] Most attempt to address the fact that prolonged exposure of the dissection ulcer base to the harsh environment of the gastrointestinal lumen is a major contributing factor to delayed bleeding. A recent pilot study of endoscopic suturing of the mucosal defect in gastric ESD suggested a reduced risk of delayed bleeding after the procedure.[39] However, a single-center retrospective study of a strategy using the endoloop and endoclips for closure after gastric ESD showed no benefit.[40] Some groups have explored the use of polyglycolic acid, a biodegradable material used in surgical settings, in combination with fibrin glue to coat the base of ESD dissection ulcers.[41] A systematic review of the current body of evidence suggested a decreased risk of bleeding, including in patients on antithrombotic agents, although the effect may be attenuated in patients with larger sized mucosal defects after dissection.[42]

Applied hemostatic chemicals are another category of therapies indicated to reduce the risk of delayed bleeding in submucosal procedures. The synthetic hemostatic gel PuraStat can be applied using a dedicated catheter compatible with most endoscopes, and dries transparently to allow the proceduralist to assess the ulcer base or other area to which the compound is applied.[43] A single-center randomized control trial found a reduced need for thermocoagulation and improved wound healing (assessed endoscopically 4 weeks after the primary procedure) in the PuraStat group with equivalent rates of delayed bleeding, as compared with the control group where only thermocoagulation could be used.[44] Other applied chemicals including Hemospray have utility in addressing delayed bleeding during follow-up endoscopy but are less useful as a preventative measure during ESD because they are opaque and would obscure the field of view.[45]

Other potential means to reduce the risk of delayed bleeding include over-the-scope clips, snares, or applied sheets of cultured cells, to treat the ESD ulcer base. There is not yet enough clinical evidence to quantify the benefit or to definitively advocate for one of these possibilities over the others. However, overall these efforts represent one of the most potentially fruitful areas for future clinical studies to target.

Delayed Perforation

Delayed perforation is relatively uncommon as most perforations occur or are apparent during the procedure warranting real-time closure. Meta-analyses have estimated the rate of delayed perforation in gastric ESD at only 0.039%.[15]

Despite its rarity, delayed perforation should be kept in mind as a potential cause of postprocedural decompensation due to the potential for serious downstream complications. Peritonitis can result if the defect was incompletely closed, ineffective (eg, premature clip dislodgment), or unrecognized and left untreated. Delayed perforation can manifest as abdominal pain and/or sepsis. The risk decreases as time from procedure increases but there can be especially delayed presentations if the cause is dehiscence/clips dislodgment. In the esophagus, delayed perforation can manifest as chest pain, sepsis/fever, and XR or computed tomographic (CT) can show free air, with CT having higher sensitivity for mediastinal free air. Rapid surgical evaluation is warranted and multidisciplinary formulation of a plan is critical. Depending on the severity of symptoms, repeat endoscopy may be an option to close the defect. However, in the case of severe clinical deterioration, rapid surgical intervention may be necessary. Methods to prevent delayed perforation are similar to those for preventing and/or addressing acute perforation.

Pneumothorax is a relatively uncommon delayed complication of POEM and, if small, can be managed nonprocedurally because the air will be absorbed over time. Any respiratory compromise or tension physiology necessitates the placement of a thoracostomy tube. The same principles apply for postprocedural pleural effusion, in that small collections can be observed while collections large enough to cause symptoms merit thoracostomy tube placement.

SUMMARY

There is justifiable enthusiasm toward the broader adoption of submucosal endoscopy and familiarizing gastrointestinal proceduralists with its unique spectrum of complications will be essential. As with any procedure, factors such as appropriate case selection, preprocedure preparation, sufficient provider skill/experience, preventative measures are the best means to reduce the risk of complications. Fortunately, most complications can be prevented or managed endoscopically, especially when recognized early. Ongoing efforts are anticipated to further enhance the safety and performance of submucosal endoscopy.

CLINICS CARE POINTS

- Orient the endoscopic submucosal dissection site up relative to gravity to allow fluid and blood to flow away from the work area and improve visualization.
- In cases of intraprocedural bleeding, balance the use of electocautery to neutralize bleeding but avoid excessive perforation risk; hemostatic forceps may be better suited to larger bleeding vessels than knife electrocautery.

- For most submucosal procedures, low-dose aspirin is safe to continue without interruption or with only minimal interruption, although other antiplatelet agents and anticoagulants should be held if possible.
- Use CO_2 rather than air for insufflation to reduce the negative downstream complications of perforation if incurred.
- Maintain a high degree of suspicion for tension pneumothorax, pneumoperitoneum, and/or mediastinitis (depending on location of procedure) because these may require urgent procedural intervention. Similarly, maintain a high degree of suspicion for infections in these compartments following the procedure, especially if a visible perforation occurred during the procedure.
- To reduce the risk of aspiration during esophageal submucosal procedures, avoid excessive insufflation and consider planned intubation.

DISCLOSURE

The authors have nothing to disclose.

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