



Adverse events associated with EGD and EGD-related techniques

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This document is intended to educate readers on the rates and predictors of adverse events (AEs) in patients who undergo EGD and EGD-related techniques. Our goal is to assist endoscopists in providing accurate, evidence-based, and up-to-date information on the rates of AEs to patients, caretakers, and trainees. The information provided should not be construed as encouraging or discouraging any particular treatment or technique. Clinical decision-making in any specific case involves a personalized and thorough analysis of the patient's condition, available courses of action, local expertise, and the patient's values and preferences. Therefore, certain clinical considerations could lead an endoscopist to take a course of action that varies from the guidance in this document. This document is an update of a previous guideline prepared by the Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) in 2013.¹

EGD or upper GI endoscopy is one of the most commonly performed GI procedures, with annual volumes exceeding 7.4 million in the United States.² Accurate estimates of the AE rates associated with the performance of EGD are difficult to summarize because of several limitations encountered in source data. Such limitations include variability in data collection and outcome definitions, inconsistent follow-up periods, and reliance on self-reporting, among others.³ Despite these limitations, diagnostic EGD has generally been considered a safe procedure.³ However, because of increasing patient complexity and constant evolution in therapeutic endoscopic techniques, contemporary updates to estimates of risk associated with EGD are necessary. This document

provides a review of commonly encountered potential AEs associated with EGD and EGD-related techniques.

METHODS

A comprehensive electronic database search was executed with the help of an expert medical librarian. The search was designed to capture AEs associated with diagnostic EGD with or without biopsy sampling, EGD with management of foreign body impaction, EGD with dilation and/or stent placement, EGD with hemostasis, and EGD with placement of percutaneous gastric or enteral access. Other therapeutic maneuvers including EMR, endoscopic submucosal dissection,⁴ radiofrequency ablation,⁵ endoscopic suturing, peroral endoscopic myotomy,⁶ antireflux endoscopy, and bariatric endoscopy⁷ were not intended to be captured in this review, because of relative novelty of and/or widespread lack of familiarity with the technique or because of discussion in detail of the technique(s) in more relevant ASGE documents.

An electronic search was performed in PubMed and MEDLINE (Ovid) for English-language citations of prospective, retrospective, and relevant studies published from 1966 to January 7, 2021 using the search methods detailed in [Appendix 1](#) (available online at www.giejournal.org). In addition, we solicited expert endoscopists for any relevant studies published up to and beyond this date. All citations initially identified were imported into Covidence (Covidence, Melbourne, Australia), and all duplicates were removed. In parallel, bibliographies of selected citations were searched, ad hoc supplementary PubMed database searches were performed, and experts

TABLE 1. Summary of estimated common adverse event ranges for EGD, based on results from relevant studies

EGD type	Bleeding	Perforation	Infection	Other	Risk factors for adverse events
Diagnostic	<.1% ⁹	<.01% ^{9,19}	<.3% ^{22,23}	Cardiopulmonary: <.1% ^{9,28-32}	Bleeding: age ≥65 y ⁹ Infection: preceding hospitalization, preceding endoscopy, lower facility procedural volume ²² Cardiopulmonary: age ≥65 y, obesity, hypertension, diabetes, coronary artery disease, recent acute myocardial infarction ^{9,33-36}
Management of foreign body or food impaction	2.6% ⁴³	.4%-3.3% ^{41,43,45-48}	Aspiration pneumonia: 1.8%-6.0% ^{42,43}	Cardiopulmonary: 1.5%-4.4% ^{39,41}	Bleeding: no use of cap-assisted technique ⁴⁴ Perforation: esophageal location, longer time from impaction to EGD, foreign body size, bone ^{41,45,47}
Dilation	Esophageal: .1%-0.7% ^{57,58,60,75,77} Gastroduodenal: 0.7%-7.0% ⁶¹⁻⁶³ Postsurgical: .1%-1.5% ^{55,64,65}	Esophageal: .1%-.7% ^{57,58,66,67} Pneumatic: 2.0%-5.0% ⁷¹⁻⁷⁴ Gastroduodenal: 1.5%-1.8% ^{61,63} Postsurgical: .5%-2.3% ^{55,64,65}	Not reported	Not applicable	Bleeding: male sex, Barrett's esophagus, malignancy, caustic strictures ^{57,61} Perforation: male sex, age ≥70 y, head and neck malignancy, corrosive injury ^{57,66-70}
Stent placement	Esophageal: 1.3%-3.7% ^{77,78} Gastroduodenal: .8%-1.5% ^{83,84}	Esophageal: .9%-1.2% ^{77,78,85} Gastroduodenal: 1.2%-1.4% ^{82,87}	Aspiration pneumonia: .5%-2.5% ^{78,87}	Esophageal: 4.1%-12.2% (migration, cancer), ^{77,78} 28.6% (migration, benign), ⁸⁰ 2.4%-12.4% (occlusion) ^{77,78} Gastroduodenal: 4.3% (migration), ⁸³ 12.6% (occlusion) ^{82,83}	Stent migration: covered stents, ⁷⁹ stent for benign disease ⁸⁰ Stent occlusion: uncovered stents ⁸²
Hemostasis or prophylaxis of bleeding	1.4% (with gluing) ¹⁰⁰	Not reported	Aspiration pneumonia (with balloon tamponade): 11.2% ¹⁰⁴	Fever (with gluing): 35.0% ¹⁰¹ Stent migration (with variceal bleed): 23.8% ¹⁰⁴ Dysphagia or chest pain (with endoscopic band ligation): 6.0%-23.0% ¹⁰⁴	Not reported
PEG or percutaneous endoscopic jejunostomy	PEG: .6%-2.6% ^{112,113,116,117} Percutaneous endoscopic jejunostomy: .0%-2.4% ^{114,115}	PEG: .2%-.8% ^{117,119-121}	Site infection: 1.7%-3.4% ^{117,119-121} Aspiration pneumonia: 1.7% ^{115,119}	Fever: 3.5% ¹¹⁹	Bleeding: obesity, diabetes ^{118,119} Cellulitis: obesity ^{118,119}

were consulted for any potential studies not identified by the electronic strategy.

Studies were considered for inclusion if they reported the rates of any AE(s) during or after performance of EGD. Studies were generally considered for inclusion based on design, in the descending order of strength of evidence: systematic review and meta-analyses, randomized controlled trials, prospective observational studies, retrospective observational studies, and case series or reports, with study size, study quality, and publication date factoring into the decision. In the first

round of screening, an author (N.C.-P.) screened titles and abstracts and assigned studies to a designation of “possibly include” or “exclude” considering the above criteria. Any abstract labeled with the decision to possibly include was included in the second round. After the title and abstract screen, we made the decision on whether to cite studies included in the second round in the final review document based on the above criteria. Data on AEs were then extracted from the full-text studies selected for inclusion and presented according to each EGD-related procedure type.

RESULTS

The electronic search yielded 4623 initial citations after removal of duplicates. A review of the evidence for each major AE type is provided below, with a summary of AE rates provided in Table 1. Predictors of AEs were also synthesized and reported wherever possible.

DIAGNOSTIC EGD

Bleeding

Clinically significant bleeding according to the ASGE lexicon (defined as a hemoglobin drop >2 g/dL and/or evidence of hematemesis, melena, or hematochezia)⁸ is rare after diagnostic EGD either with or without biopsy sampling. In a 2021 nationwide retrospective claims data analysis of over 380,000 patients who underwent diagnostic EGD, bleeding requiring emergency department visit or inpatient stay occurred at a rate of 80 in 100,000 patients within 30 days of the index procedure.⁹

A potential etiology is Mallory-Weiss tears caused by either direct trauma from the endoscope or retching during the procedure.¹⁰ The subgroup of patients aged ≥ 65 years has been correlated with an increased risk of bleeding (.05% vs .17%, $P < .001$).⁹ Although intraprocedural bleeding has been observed in up to 2% to 6% of patients undergoing EGD while on continued antithrombotic therapy,^{11,12} this outcome is generally believed to be of limited clinical significance given that it does not usually alter a patient's clinical trajectory.¹¹ Importantly, the available body of evidence suggests no significant differences in clinically relevant delayed bleeding between patients undergoing diagnostic EGD who do or do not take antithrombotic agents.¹¹⁻¹⁵ Also of note, in patients taking antithrombotic agents at baseline, available evidence suggests no differences in clinically significant bleeding outcomes when EGD (with or without biopsy sampling) is performed after appropriate periprocedural cessation of these agents¹⁶ versus when they are continued leading up to and after the procedure.^{11,17,18} Based on these and other data, the ASGE guideline on management of antithrombotic agents concludes that there is a low overall risk of bleeding during diagnostic EGD with or without biopsy sampling in patients on all antithrombotic medication.¹⁶

Perforation

Perforation is an extremely rare AE of diagnostic EGD. In the same nationwide retrospective claims-based analysis of over 380,000 patients having undergone diagnostic EGD, perforation occurred at a rate of 1 in 25,000.⁹ Similarly, in a 2018 retrospective analysis of over 13,000 EGDs with biopsy sampling, no perforations occurred within 30 days of the index procedure.¹⁹ These contemporary estimates are similar in magnitude but even more encouraging than prior estimates of perforation risk

ranging between 1 in 2500 and 1 in 11,000³ that were based on considerably older studies.^{20,21}

Infection

In the most comprehensive study assessing the risk of clinically significant infection after EGD, a 2018 claims-based analysis of over 870,000 EGDs performed across 6 states reported unplanned emergency department visits or hospital admissions for infection within 7 days of the index procedure in .3% of patients.²² Of these, respiratory infections including aspiration pneumonia were most common, occurring in .16% of patients.²² The rate of bacteremia after EGD was 1 in 1500, whereas rates of GI and genitourinary infections were both less than 1 in 2000.²² Endocarditis after EGD was also noted to occur at a rate of 1 in 140,000 patients in this study,²² with rare cases having previously been reported.²³

Prior hospitalization, prior endoscopy (compared with noninvasive screening mammography or prostate cancer screening), and lower facility procedural volumes each independently predicted higher rates of infection.²² Although the risk of endoscope-to-patient infectious transmission has become an increasing concern for duodenoscopes and linear echoendoscopes because of their designs, among other factors,^{24,25} EGD procedures are not believed to carry a high risk of this AE.^{26,7}

Cardiopulmonary AEs

As mentioned in earlier the ASGE guidelines, cardiopulmonary AEs include hypoxia, hypotension, cardiac dysrhythmia, and aspiration.²⁷ Despite efforts to standardize reporting of cardiopulmonary AEs with endoscopy, few studies use these definitions.⁸ Transient episodes of hypoxia or hypotension may not be reported because they are not considered clinically significant. Although physiologic variations in response to diagnostic EGD, sedation, and/or anesthesia are usually mild and transient, the rate of serious cardiopulmonary AEs during or after EGD is low. In a nationwide retrospective claims-based analysis of over 380,000 patients undergoing diagnostic EGD, acute myocardial infarction and congestive heart failure occurred at rates of 1 in 2300 and 1 in 6700 patients, respectively, within 30 days of the index procedure.⁹ In a single-center retrospective analysis of 31,441 diagnostic EGDs, cardiorespiratory arrest (defined as requiring chest compressions) occurred at a rate of 1 in 2200 patients.²⁸ In a 2019 retrospective study including over 87,000 procedures with patients under conscious sedation, intraprocedural hypoxia, defined as any oxygen saturation $<90\%$, occurred in .08% of patients.²⁹ However, the clinical significance of isolated transient oxygen desaturations during endoscopy is uncertain. Although aspiration pneumonia is always of concern during diagnostic or therapeutic EGD, evidence assessing the rate of aspiration events is scarce outside of studies assessing

acute GI bleeding.³⁰ Air embolism is a rare but potentially fatal AE of EGD that has been described and warrants awareness,^{31,32} especially if air (rather than carbon dioxide) insufflation is used intraprocedurally.

Predictors of periendoscopic cardiopulmonary AEs are as follows:

- Age ≥ 65 years.⁹
- Obesity.^{33,34}
- Hypertension.³⁴
- Diabetes.³⁴
- Coronary artery disease,^{9,34} in particular, EGD performed within 30 days of an acute myocardial infarction is associated with increased cardiopulmonary AEs of 1% to 8%, with most AEs being transient and/or mild.³⁵
- Higher American Society of Anesthesiologists scores, which have been correlated with greater risk of serious AEs after EGD, with odds ratios (ORs) of 1.54 (95% confidence interval [CI], 1.31-1.82), 3.90 (95% CI, 3.27-4.64), and 12.02 (95% CI, 9.62-15.01) for scores of II, III, and IV/V, respectively.³⁶
- Monitored anesthesia care, which has been correlated with a higher risk (.09% vs 0%, $P < .05$) of cardiorespiratory arrest compared with conscious sedation, although this may be confounded by patient selection.²⁸

Although obstructive sleep apnea has been postulated to be associated with a higher risk of cardiopulmonary AEs, a meta-analysis of over 3000 patients did not demonstrate this as a risk factor.³⁷ The addition of capnography to standard monitoring has been shown to significantly reduce the incidence of clinically significant hypoxemia (OR, .53; 95% CI, .35-.81) in a meta-analysis including 3088 patients.³⁸ Endoscopists and anesthesiologists should be aware of these risk factors when performing EGD and should counsel their patients accordingly.

EGD WITH MANAGEMENT OF FOREIGN BODY AND/OR IMPACTION

Overview

GI foreign bodies and/or impactions frequently require urgent or emergent EGD.³⁹ Given that obstructions and impactions occur most often at sites of angulation or narrowing,³⁹ mucosal tears, ulcerations, and/or full-thickness perforations resulting from the ingested foreign body itself are all possible. They are, in fact, more common than AEs attributable to the performance of EGD, occurring in up to 15% of cases.^{40,41} Aspiration and respiratory compromise are also possible. Therefore, a thorough clinical evaluation for signs of any evidence of respiratory compromise is crucial before attempting to perform upper endoscopy. Furthermore, care should be taken during endoscopic evaluation and management of impactions, given that 80% of presenting patients will have an underlying lesion or condition such as a ring, eosinophilic esophagitis (EoE), strictures (benign or malignant), or a mass.⁴²

Bleeding

In a large retrospective analysis of over 900 patients with ingested foreign bodies, the rate of bleeding was 2.6%, with almost all of these being self-limited.⁴³ In this study, the use of a through-the-scope instrument (rather than using the push technique, in which gentle central pressure is applied to a soft bolus in the absence of significant resistance to displace it distally) was associated with a higher rate of periprocedural AEs, including bleeding.⁴³ However, this may possibly be a reflection of larger foreign bodies requiring the use of such instruments. In a recent multicenter randomized trial of 342 patients with food bolus impactions, the use of a soft, oblique, cap-assisted approach was associated with a significantly lower risk of mucosal tears and bleeding compared with a conventional approach (.0% vs 7.6%).⁴⁴

Perforation

The risk of perforation during endoscopic management of impactions or obstructions appears to be highest in the esophagus compared with the stomach or small intestine.⁴¹ Several retrospective studies reported rates of perforation from .4% to 3.3%.^{41,43,45-48}

Several procedure-related variables have been associated with a higher overall risk of perforation in this population:

- Increasing time between presentation and endoscopic management^{45,47}: Although the optimal timing for performing EGD on these patients has not been well established, EGD within 24 hours of presentation should be considered when the site of the bolus is suspected to be esophageal.
- Larger (≥ 3 cm) foreign body size.⁴⁷
- Presence of an ingested bone.⁴⁷
- Use of an endoscopic instrument to retrieve or extract a bolus⁴³: however, other studies demonstrate the equivalence of instrument-assisted techniques to the push technique as described above, and selection bias may play a role in interpreting these data^{46,48}; hence, an optimal strategy is not well established.
- Use of an overtube can very rarely cause perforation at the level of the hypopharynx, cricopharyngeus, or esophagus.^{49,50}

Infection

Aspiration pneumonia is the most common infectious AE related to EGD performed for management of a foreign body or impaction. In a retrospective cohort of 173 patients, the combined incidence of immediate and delayed aspiration pneumonia was over 6% (4.6% immediate, 1.7% delayed).⁴² In a large retrospective series of over 900 patients, the incidence of delayed aspiration pneumonia was 1.8%.⁴³ In a separate multicenter study of 214 patients, the risk was shown to be similar, at 3%.⁴¹ However, it should be noted that in this study, 24% of

patients underwent endotracheal intubation before the EGD, which has been associated with a greater risk of pneumonia in a meta-analysis considering emergent EGD for other indications.⁵¹ Although endotracheal intubation is often performed before EGD to prevent aspiration in this patient population, the effectiveness of this practice in reducing rates of aspiration pneumonia has not yet been well characterized.

Cardiopulmonary AEs

Cardiovascular and respiratory AEs occurred in 1.5% and 2.9%, respectively, of 200 patients undergoing EGD for foreign body impaction³⁷; however, it is unclear what proportion of patients received endotracheal intubation. In a retrospective series from 2011 to 2014 where endotracheal intubation was performed before EGD in 24% of cases, cardiopulmonary AEs occurred in 4.4% of patients who are believed to be sicker patients requiring intubation.⁴¹ This is the only study that reported the rate of intubation, and it suggests that intubation may not be a prerequisite in this patient population. European guidelines recommend intubation in uncooperative patients or those at high risk of aspiration, such as proximal esophageal locations of a foreign body, food bolus impaction, and a known full stomach.⁵² However, given the paucity of available evidence describing AEs in this population and their predictors, the impact of endotracheal intubation on the incidence of cardiopulmonary AEs in patients undergoing EGD for foreign body impaction is uncertain.

EGD with Dilation

Dilation during EGD has become more common over time, likely because of the increasing prevalence of GERD, EoE, and endoscopic bariatric surgeries that can result in stenosis and stricture formation.^{2,53-56}

Bleeding

Esophageal dilation. The true rate of bleeding after EGD with esophageal dilation is difficult to accurately assess given important differences in definitions and methods of ascertainment of this outcome between studies but overall is very low. In a large, recent, claims-based study of over 160,000 EGDs with esophageal dilation, clinically significant bleeding, defined according to the International Classification of Diseases codes, occurred in .07% of patients.⁵⁷ For comparison, a meta-analysis of randomized trials that included 461 patients reported an overall bleeding rate of .7%,⁵⁸ confirming that study methodology is likely a factor in determining bleeding rates. Factors associated with higher bleeding risk after esophageal dilation include male sex, Barrett's esophagus, and esophageal malignancy.⁵⁷ The choice of dilator (balloon vs bougie) has not been shown to predict the risk of bleeding in patients undergoing dilation of benign esophageal strictures.⁵⁸ Studies assessing esophageal

dilation in patients with EoE have reported similar rates of bleeding to those without EoE. In 2 separate meta-analyses assessing outcomes of esophageal dilations in adults and children with EoE, bleeding occurred after .03% and .05% of procedures.^{59,60}

Gastroduodenal dilation. Balloon dilation of benign gastroduodenal strictures because of inflammatory conditions such as Crohn's disease or peptic ulcer disease is also routinely performed. In a single-center analysis of 264 patients treated with dilation for benign gastric outlet obstruction, self-limited bleeding occurred in 7.7% of patients, but none of these events was deemed clinically significant because they did not lead to increased hospitalizations or requirements for blood transfusion.⁶¹ Similarly, in a study of 89 balloon dilations of the pylorus in patients with delayed gastric emptying after esophagectomy, no clinically significant episodes of bleeding were reported.⁶² A meta-analysis of 141 EGDs with balloon dilation of gastroduodenal strictures in the setting of Crohn's disease reported a 2.1% bleeding rate.⁶³ Self-limited bleeding has been shown to occur more commonly in patients undergoing dilation for caustic strictures compared with peptic strictures (13.1% vs 2.8%).⁶¹

Postsurgical stricture dilation. Endoscopic dilation is an established therapy in the management of anastomotic strictures after bariatric or other surgery. A meta-analysis of 21 studies including 896 patients undergoing dilation for post Roux-en-Y gastrojejunostomy anastomotic strictures demonstrated a very low overall bleeding rate of .1%.⁵⁵ In a 2020 meta-analysis including 18 studies of 426 patients undergoing endoscopic balloon dilation of gastric stenosis after sleeve gastrectomy, the clinically significant bleeding rate was .5%.⁶⁴ The presence of a presumed ischemic segment has been shown to predict higher rates of bleeding.⁶⁵

Perforation

Esophageal dilation. The overall rate of esophageal perforation after dilation ranges from .09% to .7%.^{57,58} In a nationwide study of over 160,000 esophageal dilations, perforation occurred in .09% of patients.⁵⁷ A meta-analysis of 5 randomized controlled trials including 461 patients undergoing endoscopic dilation of benign esophageal strictures demonstrated a perforation rate of .7%, demonstrating a 10-fold difference in the rate of this outcome depending on the study methodology used.⁵⁸ In a study identifying over 169,000 esophageal stricture dilations using the National Inpatient Sample database of hospital discharges, perforation occurred at a rate of .5%.⁶⁶ A separate single-center retrospective analysis of over 2000 bougie and balloon dilations reported a perforation rate of .5%.⁶⁷

Potential risk factors for perforation are as follows:

- Male sex.⁵⁷
- Age ≥ 70 years,⁵⁷ although the associations of both age and sex could be confounded by disease status.

- Distal esophageal location and smaller initial stricture diameter under 10 mm, which have been inconsistently associated with a higher risk of perforation.^{67,68}
- Dilation of malignant strictures, which portends a higher risk of perforation compared with benign strictures (.9% vs .5%).⁶⁶ Furthermore, patients experiencing this outcome also experience higher rates of in-hospital mortality (3.1% vs 1.4%).⁶⁶
- Presence of head and neck cancer.⁶⁹
- Dilation of strictures caused by corrosive injury, which may be associated with a greater risk of perforation based on limited evidence (5.6%-36.4%).⁷⁰
- Pneumatic dilation for achalasia, which has been associated with a higher perforation risk of 2% to 5%,⁷¹⁻⁷⁴ with this risk being more common at the initial dilation session and when using a 35-mm versus 30-mm balloon.⁷¹

In contrast, no clear associations have been elucidated between dilator size, compliance with the “rule of 3” (using a maximum of 3 dilator sizes, including the starting dilator, in a single session),⁶⁷ or dilator type (balloon vs bougie).⁵⁸ Similarly, pooled perforation rates in patients with EoE undergoing esophageal dilation range between .4% and .9% in several meta-analyses, indicating no significantly increased risk in this population compared with those without EoE.^{59,60,75}

Gastroduodenal dilation. In a meta-analysis of 11 studies of EGD with balloon dilation of gastroduodenal strictures in the setting of Crohn’s disease, a perforation risk of 1.5% was reported.⁶³ In a review of 111 patients who underwent endoscopic balloon dilation of caustic injury–induced gastric outlet obstruction, perforation occurred in 1.8% of patients.⁷⁶

Postsurgical stricture dilation. A meta-analysis of 21 studies including 896 patients undergoing endoscopic dilation for gastrojejunal anastomotic strictures after Roux-en-Y gastric bypass surgery reported a perforation rate of 2.3%, but only .9% required surgical intervention.⁵⁵ The presence of an ischemic segment or a fistula has been associated with a higher risk of perforation.⁶⁵ In a meta-analysis of 18 studies of 426 patients undergoing endoscopic balloon dilation of gastric stenosis complicating sleeve gastrectomy, the overall perforation rate was .5%.⁶⁴

EGD WITH STENT PLACEMENT

Bleeding

Esophageal stent placement. Palliative stent placement for advanced esophageal malignancy has been shown to have a relatively higher risk of bleeding. In a multicenter cohort study of self-expanding metal stent (SEMS) insertion for inoperable malignant esophageal strictures, bleeding occurred in 3.7% of patients.⁷⁷ In a separate study of 442 patients who underwent SEMS placement for similar indications, bleeding occurred in 1.3% of patients.⁷⁸ In a 2020 meta-analysis of 231 patients that

compared fully covered to partially covered SEMS insertion for palliation in esophageal cancer, the bleeding risk was the same for both stent types.⁷⁹ In a meta-analysis including 444 patients with stents placed for benign indications, the risk of bleeding was 1.8%.⁸⁰

Gastroduodenal stent placement. Malignant gastric outlet obstruction has historically been managed with endoscopic SEMS placement.^{81,82} A meta-analysis of 19 studies including 1281 patients undergoing SEMS placement for malignant gastric outlet obstruction reported an overall bleeding rate of 4.1%, with clinically significant bleeding requiring intervention occurring in .8% of patients.⁸³ Similarly, in a multicenter study of 202 patients having received duodenal stent placement for malignant gastroduodenal obstruction, bleeding occurred in 3% of patients, although half of these episodes were self-limited.⁸⁴ Bleeding appears to be more common in patients treated with partially covered stents.⁸³

Perforation

Esophageal stent placement. In a recent meta-analysis of palliative esophageal stent placement without fluoroscopy in 1778 patients from 17 studies, the pooled perforation rate was 1.2%, indicating the safety of this approach.⁸⁵ In the same study, retrosternal chest pain was found to be the most common AE reported (10.4%). In a retrospective review of 442 patients undergoing SEMS placement for dysphagia because of unresectable esophageal cancer, perforation occurred in .9% of patients.⁷⁸ This rate is similar to that reported in a separate multicenter cohort study of SEMS placement for malignant esophageal stricture (1.2%).⁷⁷ In the meta-analysis of 444 patients receiving esophageal stent placement for benign indications, chest pain was reported in 6.5% and perforation in 4.4%.⁸⁰ In a meta-analysis comparing esophageal stents with other therapies for inoperable malignant strictures, a tracheoesophageal fistula was reported in 4.5% to 5.6% patients in 2 cohorts.⁸⁶

Gastroduodenal stent placement. Pooled data from the recent ASGE guideline reviewing the role of endoscopy in management of gastroduodenal obstruction including covered and uncovered stents show a perforation rate of 13 in 944 (1.3%).⁸² In a retrospective review of 219 patients undergoing SEMS placement for gastroduodenal outlet obstruction, perforation occurred in 1.4% of patients.⁸⁷ In a meta-analysis of 19 studies including 1281 patients undergoing SEMS placement for malignant gastric outlet obstruction, perforation occurred in 1.2% of patients.⁸³ The rate of perforation after stent placement of gastroduodenal stenosis is comparable between partially covered and uncovered metal stents.⁸³

Stent migration

When placing an indwelling luminal stent, an additional consideration for endoscopists and patients is the risk of

stent migration. This AE can occur with variable frequency depending on both the indication for the procedure and the location of the stent. In cases of SEMs placement for benign esophageal strictures, fistulae, and leaks, the rate of stent migration has been reported at 40% to 50% in multiple single-center studies assessing both fully and partially covered SEMs.^{88,89} An overall migration rate of 28.6% was reported in a meta-analysis of 444 patients treated with esophageal stents for benign indications.⁸⁰ Conversely, when placed for the management of malignant esophageal strictures, the risk of partially covered and fully covered SEMs migration was considerably lower, ranging from 4.1% in a large retrospective study⁷⁸ to 12.2% in a multicenter prospective study.⁷⁷ In the case of SEMs placement for malignant gastric outlet obstruction, the pooled risk of migration was reported at 4.3% in a meta-analysis of over 1200 patients.⁸³

The risk of stent migration out of the esophagus can be mitigated through-the-scope or over-the-scope through various anchoring techniques.^{90,91} Chief among these is fixation with endoscopic suturing; in a meta-analysis of 212 patients undergoing suturing of SEMs placed for several indications including strictures, leaks, and fistulae, the migration rate was reported to be 15.9%.⁹² Importantly, in the setting of malignant esophageal strictures, the risk of migration was demonstrated to be no different between fully covered and partially covered metal stents in a 2020 meta-analysis including over 200 patients.⁷⁹ The risk of stent migration in the case of malignant gastric outlet obstruction has been demonstrated to be higher when partially covered (vs uncovered) stents are deployed.⁸³

Stent occlusion

The risk of stent occlusion similarly depends on the indication for the procedure, design of the stent, and location of the stent. Occlusion is possible both because of tissue ingrowth of an uncovered metal stent and from occlusion by ingested food. When performed for the management of malignant esophageal strictures, SEMs insertion was complicated by tissue overgrowth and by food impaction in 8.5% and 2.4% of patients, respectively, in a multicenter prospective study.⁷⁷ This was similar to a reported risk of tissue overgrowth of 12.4% in a large retrospective study of over 400 patients undergoing stent placement for the same indication.⁷⁸ In the case of SEMs placement for malignant gastric outlet obstruction, the pooled risk of occlusion was reported at 12.6% in a meta-analysis of over 1200 patients.⁸³ This was confirmed in the recent ASGE guideline on management of gastroduodenal obstruction that found occlusion of 4.1% with covered SEMs versus 25.2% with uncovered SEMs.⁸²

Infection

Infectious AEs of EGD with stent placement mostly relate to aspiration. In a single-center retrospective review

of 442 patients undergoing SEMs placement for dysphagia because of esophageal cancer, pneumonia occurred in 2.5% of patients.⁷⁸ In a review of 219 patients undergoing SEMs placement for malignant gastric outlet obstruction, pneumonia occurred in .5% of patients.⁸⁷

EGD WITH HEMOSTASIS OR PROPHYLAXIS OF BLEEDING

Summary of AEs

Hemostasis for active nonvariceal upper GI bleeding. AEs associated with hemostasis of nonvariceal bleeding are heterogeneously defined and inconsistently reported in the literature and are therefore difficult to categorize and synthesize. A network meta-analysis of endoscopic therapies for high-risk bleeding peptic ulcers demonstrated that both epinephrine plus mechanical therapy and epinephrine plus thermal therapy demonstrated better AE profiles compared with epinephrine monotherapy or sclerosant injection, while significantly decreasing the odds of rebleeding (OR, .19 [95% CI, .07-.52] and .30 [95% CI, .10-.91], respectively).⁹³ AEs from this overall group of treatments (injection, mechanical modalities, thermal modalities) include low risks of bleeding and perforation.^{93,94}

The use of monopolar hemostatic forceps with soft coagulation, a relatively newer approach in the treatment of active peptic ulcer bleeding, appears to have a similar AE rate compared with the traditional therapies listed above from a 2020 meta-analysis including 6 studies.⁹⁵ The rate of AEs directly associated with the use of TC-325 hemostatic powder, more commonly known as Hemospray (Cook Medical, Winston-Salem, NC, USA), in the management of nonmalignant upper GI bleeding was reported to be .7% in a large meta-analysis of over 1900 patients,⁹⁶ including self-limited abdominal pain. Similarly, low AE rates have been associated with its use in upper GI bleeding from GI malignant etiologies.⁹⁷

Over-the-scope clip devices are another tool for the management of active nonvariceal bleeding. In a meta-analysis of 769 patients, only .3% experienced AEs.⁹⁸ In another review of 1519 procedures using over-the-scope clips, overall over-the-scope clip-related AEs were reported in 1.7% of patients, with .6% of these requiring surgical intervention.⁹⁹ These AEs included luminal obstruction and clip maldeployment.

Hemostasis of active variceal bleeding. AEs associated with hemostasis of variceal bleeding are similarly difficult to synthesize given heterogeneous definitions and inconsistent reporting. The rate of intraprocedural bleeding with injection of glue into gastric varices was reported to be 1.4% in a large, single-center, retrospective analysis of 628 procedures.¹⁰⁰ Fever is a common AE after cyanoacrylate injection, occurring in 35.0% of patients,¹⁰¹ and subjective chest pain and dysphagia are also

potential AEs.¹⁰² Infectious AEs are rare but possible with either approach,¹⁰³ but it is difficult to attribute these to endoscopic interventions as opposed to severe underlying medical comorbidities of some patients (eg, in cases of spontaneous bacterial peritonitis or sepsis). In a meta-analysis of 23 studies involving balloon tamponade (570 patients) or esophageal stenting (188 patients) as bridge therapies to temporize refractory variceal bleeding, the overall major AE rate for balloon tamponade was 20.4%, whereas there was a high risk of migration of 23.8% with the stenting approach.¹⁰⁴ In the same meta-analysis, balloon tamponade for active variceal bleeding was shown to result in bronchopulmonary aspiration and pneumonia in 11.2% of cases.¹⁰⁴ A meta-analysis of 14 randomized studies and 1236 patients with active esophageal variceal bleeding comparing endoscopic variceal ligation and endoscopic sclerotherapy found a lower rate of AEs in the ligation group (relative risk [RR], .28; 95% CI, .13-.58).¹⁰⁵

Prophylaxis or treatment of nonbleeding nonvariceal lesions. A systematic review and meta-analysis of 24 studies comparing effectiveness and safety of radiofrequency ablation and argon plasma coagulation in the treatment of gastric antral vascular ectasia revealed that radiofrequency ablation resulted in significantly fewer and less severe AEs as compared with argon plasma coagulation (1.9% vs 5.1%, respectively).¹⁰⁶ These most commonly consisted of bleeding ulcers that developed after therapy.¹⁰⁶ A meta-analysis of 11 studies assessing endoscopic band ligation for gastric antral vascular ectasia showed that AEs occurred after 10.9% of procedures, with a rebleeding rate of 9.0%.¹⁰⁷ AEs included postbanding bleeding ulcers, fever, and subjective abdominal pain.¹⁰⁸

Prophylaxis of nonbleeding varices. A 2019 Cochrane review of studies assessing endoscopic band ligation in the prophylaxis of esophageal variceal bleeding reported a low overall rate of AEs related to this procedure, including dysphagia in 6% to 22% of patients, chest pain in 8% to 23% of patients, self-limited fever in 3% to 11% of patients, and retrosternal burning in up to 40% of patients.¹⁰⁹ The endoscopic injection of cyanoacrylate or other glue into gastric varices has resulted in distant embolic events according to multiple case reports.^{110,111} Performing glue injection, with or without concomitant coiling, under EUS guidance may help mitigate these risks but is not a prerequisite.⁸¹

EGD WITH GASTROSTOMY OR JEJUNOSTOMY TUBE PLACEMENT

Bleeding

Clinically significant bleeding after PEG tube placement has been reported to occur in between .6% and 1.2% of cases¹¹² and is of variable clinical significance, almost always minor and self-limited in nature. A 2020 meta-analysis of 320 PEG patients demonstrated a .9% rate of

minor bleeding associated with PEG tube insertion.¹¹³ Similar rates of bleeding have been reported for percutaneous endoscopic jejunostomy (PEJ) procedures, with a reported rate of 2.4% in a single-center 10-year cohort of 83 patients¹¹⁴ and no bleeding events in a separate series of 59 cases.¹¹⁵

A meta-analysis of 11 studies including 6233 patients undergoing PEG tube placement while on antiplatelet therapy reported a bleeding rate of 2.67%.¹¹⁶ Conversely, a large retrospective analysis of 1613 consecutive PEG tube placements, of which 95.5% of patients received some form of uninterrupted periprocedural antithrombotic therapy, the rate of bleeding requiring transfusion or intervention was .39%,¹¹⁷ suggesting that bleeding risk is likely similar to patients on no antithrombotic therapy. The ASGE guideline on the management of antithrombotic agents for endoscopy describes both PEG and PEJ as high-risk procedures overall and recognizes that aspirin alone does not portend an increased risk of bleeding.¹⁹

Risk factors associated with a higher risk of bleeding after PEG placement are as follows:

- Active dual antiplatelet therapy or full anticoagulation.¹⁹
- Obesity: In a single-center analysis of 67 obese patients who underwent PEG placement, hemoperitoneum occurred in 3.4% of cases, with patient weight of >250 pounds being shown to predict the overall risk of AEs with an OR of 3.86 (95% CI, 1.02-14.57).¹¹⁸
- Diabetes mellitus.¹¹⁹

It is also noteworthy that the insertion of PEG tubes is associated with a lower risk of bleeding compared with insertion of gastrostomy tubes using interventional radiology techniques. A study of over 184,000 patients undergoing gastrostomy tube placement showed an increased risk of bleeding with interventional radiology-placed PEG tubes (OR, 1.84; 95% CI, 1.26-2.68; $P = .002$) compared with endoscopically placed tubes.¹²⁰ In a nationwide sample of over 33,000 patients, interventional radiology-placed PEG tubes had a higher risk of bleeding (OR, 1.47; 95% CI, 1.18-1.83; $P < .01$).¹²¹

Perforation

In a recent series of 1613 patients undergoing PEG placement, uncontained gastric perforation was reported in .2% of patients, resulting in sepsis and subsequent mortality in all.¹¹⁷ Similarly, in a multicenter retrospective study of 1625 patients, peritonitis occurred in .8% of patients.¹¹⁹ Perforation of the transverse colon is another major potential AE. This was reported in .2% in the large inpatient cohort and in .12% in a nationwide cohort.^{120,121} There was a higher risk for interventional radiology-guided PEG placement versus endoscopic PEG (OR, 1.90; 95% CI, 1.26-2.86).¹²⁰ Although evidence is scarce, PEJ procedures may carry a higher risk of perforation, with this event mostly observed at the time of traction tube removal and/or exchange.^{114,122} Transhepatic placement of PEG tubes is an exceedingly rare AE.¹²³

Infection

Most infections related to PEG or PEJ tube placement are superficial site infections that commonly respond to short treatment courses with antibiotics. In a series of 1613 patients undergoing PEG tube placement, superficial site infection was reported in 2.1% of patients.¹¹⁷ It was reported as .9% in a large inpatient cohort.¹²⁰ In a multicenter study of 1625 patients, the most common infectious AEs were fever without evident infection in 3.5% of patients, peristomal infection in 3.4% of patients, and aspiration pneumonia in 1.5% of patients.¹¹⁹ In this study, multivariable logistic regression demonstrated that the administration of periprocedural prophylactic antibiotics was associated with a reduction in the incidence of fever (OR, .58; 95% CI, .38-.88).¹¹⁹ In a single-center series of 59 cases of direct PEJ tube placement, 3.4% of patients experienced infectious AEs, including 1.7% of patients with aspiration pneumonia and 1.7% of patients with exit site infections.¹¹⁵ Obese patients are at a higher risk of cellulitis, with this AE occurring in 8.5% of patients with a body mass index of 30 kg/m² or higher.¹¹⁸ The ASGE recommends antibiotic prophylaxis before both PEG and PEJ procedures.¹²⁴

Two systematic reviews showed a .32% to .56% risk of tumor seeding when the pull technique was used.^{125,126} Hence, in this cohort, a direct push technique for placement is preferable when possible.

FUTURE DIRECTIONS

This document highlights several important areas within the field of EGD for which further high-quality research is needed to improve the strength of recommendations for future EGD-related guidelines. Below is a brief outline of these specific areas.

- **Predictors of AEs.** Limited evidence is available regarding patient- and procedure-level predictors of AEs for routine EGD as well as more advanced EGD-guided techniques (Table 1). Dedicated efforts to reliably elucidate these independent predictors (ideally using prospective population-level cohort studies and clinical trials) are needed, especially for newer and/or evolving techniques and commonly used medications such as antithrombotic agents.
- **Data on AEs for novel EGD-guided procedures.** More data, ideally in the form of randomized controlled trials and prospective observational studies, are needed to formally elucidate the AE rates and predictors of AEs for several novel EGD-guided procedures not described within this document, including Zenker's diverticulectomy, antireflux endoscopy, and robotic-assisted endoscopy.
- **Implications for training.** Data are scarce on both the learning curves and trainee-related AE profiles associated with most EGD-guided procedures described in this document. Data describing ideal procedural vol-

umes and optimal training methods for these techniques as well as AEs associated with training are urgently needed.

CONCLUSION

Routine EGD with or without biopsy sampling is well established as a safe and effective procedure. Although several AEs are associated with routine EGD, their overall incidence is low. Additional interventional EGD-guided techniques are increasingly used as alternatives to surgical, radiologic, and other endoscopic approaches to managing GI disease and may be associated with higher AE rates compared with routine EGD. Endoscopists performing EGD-guided procedures should be aware of associated AE rates and their risk factors to optimize the informed consent process and patient selection.

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Abbreviations: AE, adverse event; ASGE, American Society for Gastrointestinal Endoscopy; CI, confidence interval; EoE, eosinophilic esophagitis; PEJ, percutaneous endoscopic jejunostomy; SEMS, self-expanding metal stent.

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APPENDIX 1

MEDLINE (OVID) search strategy

Database: Ovid MEDLINE ALL

Search Date: January 7, 2021

Number of results: 4603

1. exp endoscopy, digestive system/ and exp upper gastrointestinal tract/ 19,597
2. (oesophagogastroduodenoscop* or esophagogastroduodenoscop* or gastroscop*).tw,kf. 11,767
3. (oesophageo-gastro-duodenoscop* or esophageo-gastro-duodenoscop* or gastro-scop*).tw,kf. 4
4. ((upper adj2 gastro*) and endoscop*).tw,kf. 11,747
5. ((upper adj2 GI) and endoscop*).tw,kf. 2390
6. egd.tw,kf. 2391
7. or/1-6 41,381
8. ((adverse or dangerous or harmful or indirect or injurious or secondary or side or undesirable) adj1 (complication* or consequence* or effect* or event* or impact* or outcome* or reaction*)).tw,kf. or exp "drug-related side effects and adverse reactions"/ or ae.fs. 2,325,892
9. 7 and 8 7199
10. limit 9 to english language 6280
11. (addresses or biography or case reports or comment or directory or editorial or festschrift or interview or lectures or legal cases or legislation or letter or news or newspaper article or patient education handout or popular works or congresses or consensus development conference or consensus development conference, nih or practice guideline).pt. not (exp animals/ not exp humans/) 4,179,901
12. 10 not 11 4603