Communication from the ASGE Standards of Practice Committee

GUIDELINE

ASGE American Society for Gastrointestinal Endoscopy

Adverse events associated with EUS and EUS-guided procedures

Prepared: ASGE STANDARDS OF PRACTICE COMMITTEE

Nauzer Forbes, MD, MSc,[1,2] Nayantara Coelho-Prabhu, MD, FASGE,[3] Mohammad A. Al-Haddad, MD, FASGE,[4] Richard S. Kwon, MD,[5] Stuart K. Amateau, MD, PhD, FASGE,[6] James L. Buxbaum, MD, FASGE,[7] Audrey H. Calderwood, MD, MS, FASGE,[8] Sherif E. Elhanafi, MD,[9] Larissa L. Fujii-Lau, MD,[10] Divyanshoo R. Kohli, MD,[11] Swati Pawa, MD, FASGE,[12] Andrew C. Storm, MD,[3] Nirav C. Thosani, MD, MHA,[13] Bashar J. Qumseya, MD, MPH, FASGE[14] (ASGE Standards of Practice Committee Chair)

This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

This document is intended to educate readers on the rates and predictors of adverse events in adult patients who undergo endoscopic ultrasound (EUS). Our goal is to assist endoscopists in providing accurate, evidence-based, and up-to-date information on the rates of adverse events 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 in 2013.[1]

EUS has become a frequently used diagnostic and therapeutic modality used by endoscopists in the United States and throughout the world. Yearly use of EUS in the United States has consistently increased, supplanting the volume of ERCPs performed.[2] Indications for EUS are broad and include the diagnosis and staging of GI and non-GI malignancies, assessment of pancreatobiliary targets, and sampling and drainage of cystic structures. In addition, several EUS-guided procedures have become widely accepted in recent years, including management of pancreatic fluid collections (PFCs), EUS-guided biliary and gallbladder drainage (EUS-BD and EUS-GD, respectively), celiac plexus blockade and neurolysis (CPB/CPN), variceal management, and EUS-guided gastroenterostomy (EUS-GE) or enteroenterostomy.

Given the associated skill profile including technical proficiency, image recognition, and cognitive skills, additional training beyond a GI fellowship is generally required to perform EUS safely. To optimize the overall quality of EUS procedures, evidence-based indicators specific to the performance of EUS have been established.[3] The adverse event (AE) profile specifically associated with the performance of EUS must similarly be considered separately from those associated with other luminal endoscopic procedures. This document summarizes available evidence on AEs associated with EUS and EUS-guided procedures in adult patients.

METHODS

A comprehensive electronic database search was executed in conjunction with an expert healthcare librarian (M.V.) and was composed of 5 parts, each designed to capture specific AEs associated with (1) routine EUS with or without FNA or fine-needle biopsy sampling (FNB), (2) EUS with PFC management, (3) EUS-BD and EUS-GD, (4) EUS with CPB or CPN, and (5) other EUS-guided techniques including variceal management and EUS-GE. AEs related to sedation and/or anesthesia, which are not specific to EUS, were not reviewed in this document. An English-language search, whose full details are provided in Appendix 1 (available online at www.giejournal.org), was performed in PubMed, MEDLINE (Ovid), MEDLINE (EBSCO), the Excerpta Medica Database, Web of Science, the Cochrane Central Registry of Controlled Trials, and the Cumulative Index of Nursing and Allied Health Literature for citations published between January 1, 2000 to December 7, 2020 (deemed a suitable search period to reflect contemporary experiences with EUS). All citations initially identified were imported into DistillerSR (Evidence Partners, Ottawa, Ontario, Canada), and all duplicates were removed. In parallel, bibliographies of selected citations were searched, ad hoc supplementary PubMed database searches were performed, and experts were consulted for any potential studies not identified by the electronic strategy.

Given that this document was not designed to answer any specific comparative questions but rather to update the state of knowledge on EUS-associated AEs, specific screening eligibility criteria were not required to be met for a study to be considered for inclusion. This decision was made given the variable amounts and quality of evidence available describing each separate EUS-guided technique. However, studies were generally considered for inclusion based on design in the descending order of the following: meta-analyses, randomized controlled trials (RCTs), prospective observational studies, retrospective observational studies, and case series or reports, with study size, study quality, and study recency factoring into the decision.

In the first round of screening, we 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 the citation resulted in the study being 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 EUS-guided procedure type.

RESULTS

Of 3619 initial citations identified from the electronic search, 1284 were for routine EUS, 556 for EUS with drainage and/or stenting of PFCs, 623 for EUS-BD and EUS-GD, 475 for EUS with CPB or CPN, and 681 for EUS-guided variceal management, EUS-GE, and other miscellaneous and novel EUS-guided procedures. A review of the evidence for each major AE type is provided below, with an overview of estimated AE rates provided in Table 1. Predictors of overall and/or specific AEs were also considered and reported wherever possible.

ROUTINE EUS

Perforation

Luminal perforation associated with routine EUS is a rare occurrence. Because of a relatively rigid echoendoscope tip and that intubation is frequently performed with an oblique view, the incidence of upper EUS-associated cervical esophageal perforation has been reported at higher rates than that associated with EGD,[4] although direct comparative studies are unavailable. Gastric, duodenal, and rectal perforations have also been reported at higher rates than with EGD or colonoscopy, possibly because of the larger size of echoendoscopes combined with the requirement for frequent transluminal scanning and positioning of the echoendoscope within often narrowed or deformed lumens, although there is no direct evidence to support this theory. The duodenum is at particular risk for perforation (especially with an oblique-viewing echoendoscope) given a relatively thin bowel wall, sharp angulation that exists between the first and second duodenal portions, and the potential presence of luminal deformities associated with benign or malignant pancreatobiliary structures being examined.

A 2011 meta-analysis reported a pooled perforation rate of .02% for EUS with FNA among over 10,900 patients.[5] A 2021 population-based retrospective study including over 4300 patients undergoing EUS reported a .05% overall perforation rate.[6] In a 2020 retrospective study of over 13,000 patients, gastric and duodenal perforations occurred at a rate of .06% and were more common with linear (vs radial) echoendoscopes.[7] In the same study, esophageal perforation occurred in .02% of all EUS procedures, both events occurring with radial echoendoscopes.[7] Conversely, a 2009 prospective study including over 4800 EUS procedures reported an esophageal perforation rate of .06%, all occurring with linear endoscopes.[8] In a national survey, endosonographers self-reported esophageal perforation rates of .03% in a large sample of over 43,000 procedures. EUS-associated perforation is widely variable in terms of its severity, although most patients recover fully after either endoscopic or surgical management.[7,9] Overall, there is no clear association between echoendoscope type and perforation risk.

The following factors have been independently associated with higher perforation rates during EUS[7,9-11]: trainee involvement, operator inexperience, advanced patient age, history of difficult esophageal intubation, presence of esophageal malignancy, or cervical spine osteophytes. Endoscopists should be aware of these risk factors when performing EUS and should counsel their patients accordingly on the risk of perforation.

Hemorrhage

Hemorrhage is also associated with diagnostic and therapeutic EUS and is most commonly observed when either FNA or FNB is performed. Bleeding can occur in the GI lumen, intraperitoneally, retroperitoneally, or into the structure being targeted such as a cyst or visceral organ, and can present immediately (intra- or periprocedurally) or in a delayed fashion. Estimates of the true rate of bleeding associated with EUS-FNA/FNB are difficult to characterize because of inconsistent outcome definitions and a relative paucity of high-quality prospective studies. Clinically significant bleeding according to the American Society for Gastrointestinal Endoscopy (ASGE) lexicon (defined as a hemoglobin drop >2 g/dL and/or evidence of hematemesis, melena, or hematochezia)[12] is rare after routine EUS-FNA/FNB. Most commonly, bleeding after FNA/FNB is self-limited and does not require endoscopic or other intervention.

A 2011 meta-analysis reported a pooled bleeding rate of .13% in over 10,900 patients undergoing EUS with FNA,[5] whereas a 2017 meta-analysis of over 5100 patients undergoing EUS with FNA specifically of pancreatic cystic lesions reported a pooled bleeding rate of .69%.[13] Both analyses considered all types of bleeding, including mild self-

TABLE 1. Summary of estimated common adverse event ranges for EUS-guided procedures

EUS-guided procedure type	Perforation (%)	Hemorrhage (%)	Infection (%)	Other/specific (%)	Risk factors for adverse events
Routine EUS (with or without FNA/fine-needle biopsy sampling)	.02-.08[5-9]	.13-.69*,[5,7,10,13,14]	.4-1.7%†,[13,31,111]	Pancreatitis: .44-.92‡,[5,13]	Perforation[7,9-11]: trainee involvement, operator inexperience, older patient, history of difficult esophageal intubation, presence of esophageal malignancy, cervical spine osteophytes Hemorrhage[15-21]: antiplatelets, anticoagulants, low-molecular-weight heparins, lower GI FNA/fine-needle biopsy sampling, fiducial placement Infection[29,32]: sampling of pancreatic cyst or mediastinum Pancreatitis[33]: fiducial placement
Pancreatic fluid collection management	0-5[44,47,51,53,112]	1-12[47,51-53,55]	0-24[44-47,56]	Stent migration: 0-20[44,46,47,53,60] Stent occlusion: 0-17.7[44,46,47,62]	Perforation[45]: subsequent necrosectomy Perforation, hemorrhage[43,55]: lumen-apposing metal stent insertion Infection[57]: larger pancreatic fluid collection size
EUS-guided biliary drainage	0-3.1[68-70]	0-8.3[68-70,72]	Not reported	Stent migration: 2.7[65] Stent occlusion: 0-14.3[68-70]	Not well studied
EUS-guided gallbladder drainage	1.2[71]	1.3-8.3[73-75]	Not reported	Stent migration: 0-2.7[73-75] Stent occlusion: 0-10.4[73-75]	Not well studied
Celiac plexus blockade and celiac plexus neurolysis	Similar to routine EUS	Similar to routine EUS	Similar to routine EUS	Diarrhea: 0-28[80-83] Hypotension: 2-5[79] Inebriation (celiac plexus neurolysis): 0-14[80,83] Abdominal pain: 2-4[79]	Not well studied
Variceal management	Not reported	7.0[95]	1.6-2.5[94,97,100]	Abdominal pain: 3.2-12.5[96-99] Embolism: 5.6[95]	Not well studied
EUS-guided gastroenterostomy	7-10[103-106]	3.8[105]	Not reported	Stent occlusion: 4.2[104]	Not well studied

*Bleeding of variable clinical significance.
†When sampling of pancreatic cystic lesion was performed.
‡When sampling of pancreatic duct, cyst, or mass was performed.

limited bleeding, in the calculation of these overall rates. These rates have been largely supported by more contemporary studies as well. For instance, a 2020 retrospective study reported a significant bleeding risk of 0.18% after routine EUS-FNA/FNB in over 1600 patients.[10] A separate 2020 retrospective study reported a bleeding rate of .13% associated with routine FNA in over 3000 procedures, with all events classified as mild and therefore of uncertain clinical significance.[7] A 2014 retrospective study of over 3000 patients undergoing EUS-FNA of pancreatic masses reported a clinically significant bleeding rate of .23%.[14]

Neither the number of passes nor the needle gauge appear to be associated with the incidence of bleeding after FNA.[13] Higher rates of bleeding have been reported in patients on antiplatelet and/or anticoagulant medications[15-17] or prophylactic doses of low-molecular-weight heparins,[18] procedures performed in the lower GI tract compared with the upper GI tract,[19] and placement of fiducials to guide radiation therapy in cases of pancreatic cancer.[20,21] Furthermore, sampling of the liver has been associated with bleeding and/or subcapsular hematoma in .6% to .9% of patients.[22,23] According to current ASGE guidance, EUS with FNA/FNB is considered high risk for bleeding and should be performed in patients on anticoagulation or antithrombotic agents only after careful consideration of both the indication for the procedure and the medical indication for the underlying anticoagulation medication(s).[24] The decision to interrupt any antiplatelet and/or anticoagulant agents should carefully incorporate the subsequent risk of thrombotic events and may benefit from a multidisciplinary review.

Infection

Incidental bacteremia has been reported as an AE after routine EUS, occurring in 0% to 5.8% of patients in 3 separate prospective studies.[25-27] None of the patients in any of these studies ultimately developed sepsis or had their clinical course altered as a result of the incidental bacteremia,[25-27] and therefore the clinical significance of EUS-associated bacteremia has been questioned. Although the microbiologic environment of the lower GI tract is distinct and might theoretically predispose to a higher risk of bacteremia, rates of bacteremia do not appear to be higher than those encountered after EUS of the upper GI tract.[28] EUS-guided sampling of mediastinal cysts has been associated with infection, including mediastinitis, although reliable estimates are unavailable.[29] Endoscopists and patients should be aware of the high morbidity and potential mortality associated with mediastinitis before FNA is contemplated.[29] If FNA is performed for this indication, we suggest antibiotic prophylaxis when targeting mediastinal cystic lesions.[30]

Sampling of pancreatic and mediastinal cystic lesions puts patients at a somewhat higher risk of symptomatic infection compared with sampling of solid lesions. A 2017 meta-analysis of 40 studies assessed 5124 patients undergoing EUS-FNA of pancreatic cystic lesions and reported a pooled infection rate of .4%.[13] More recent data from a 2020 RCT of 226 patients undergoing EUS-FNA of pancreatic cystic lesions demonstrated low and statistically similar rates of infection (.4% and .9%) in those receiving antibiotics versus those receiving placebo, respectively.[31] A subsequent 2021 meta-analysis including 6 studies (the above RCT plus 5 observational studies) and 1683 patients reported similar results, with infection rates of .4% and .9% in patients with FNA of pancreatic cysts receiving and not receiving antibiotics, respectively (odds ratio, .54; 95% confidence interval [CI], .16-1.82).[32] Updated searches applying the electronic strategy used by this meta-analysis through June 13, 2021 resulted in no new citations assessing this question. Therefore, we conclude that sufficient data are lacking at this time to change our existing recommendation for prophylactic antibiotics in these patients.[30]

Pancreatitis

Pancreatitis is also a possible AE after FNA/FNB of pancreatic ducts, cysts, or masses. A 2017 meta-analysis assessing over 5100 patients having undergone FNA/FNB of pancreatic cystic lesions reported a pancreatitis rate of .92% across 40 studies.[13] A 2011 meta-analysis reported a pancreatitis rate of .44% among over 8200 patients having undergone FNA/FNB of any pancreatic structure.[5] Of note, 91.7% of cases were classified as either mild or moderate.[5] Two recent studies reported the rate of post-FNA pancreatitis to be .32% and .44%.[6,7]

There is some evidence to suggest that the risk of pancreatitis (of up to 3.1%[33]) may be higher in patients undergoing EUS for fiducial placement for pancreatic cancer, but these estimates are limited by study size and methodology. No other risk factors have been identified otherwise. Unlike ERCP, the use of nonsteroidal anti-inflammatory drugs to prevent post-FNA/FNB pancreatitis has not been studied, primarily because of low event rates that have thus far precluded adequately powered prospective studies. It is hypothesized but not proven that traversing the main pancreatic duct during FNA/FNB increases the risk of pancreatitis.

Needle tract seeding

Given that EUS-FNA/FNB often involves sampling of malignant or premalignant lesions, there is a theoretical concern that these cells can be seeded through the needle tract into the peritoneal or other cavities. This AE has thus far only been reported in the form of case reports, making an overall estimate of incidence difficult to determine. A 2020 narrative review referenced 29 independent case reports on needle tract seeding after EUS-FNA/FNB.[34] Needle tract seeding has been reported with various target lesions including pancreatic cancer and mediastinal lymphadenopathy, with needles of all sizes, and with as few as 1 pass.[34] Time to recognition of needle tract seeding is widely variable, ranging from several days to several months.[34]

The location of the sampled lesion can theoretically alter the risk of seeding. For instance, transduodenal sampling of pancreatic head lesions can be inconsequential if the needle tract is subsequently removed during pancreaticoduodenectomy. In comparison, transperitoneal sampling of pancreatic body or tail lesions (or hilar or intrahepatic cholangiocarcinoma) could theoretically increase the risk. In cases of cholangiocarcinoma in particular, needle tract seeding can result in a patient becoming ineligible for liver transplantation, and therefore EUS-guided sampling of suspected cholangiocarcinoma should be avoided in patients who are potential transplant candidates.

PFC MANAGEMENT

Overview

EUS-guided transmural drainage of PFCs through either the stomach or duodenum has been shown to be a safe and effective technique, with success rates of over 90% and less morbidity compared with percutaneous/radiologic or surgical decompression.[35-40] Several types of stents can be used to drain PFCs, including plastic stents (PSs), fully covered self-expandable metal stents (SEMSs), and lumen-apposing metal stents (LAMSs). For walled-off necrosis (WON) specifically, LAMSs make endoscopic debridement of necrotic material possible directly through the stent, which has been associated with fewer endoscopic sessions necessary to achieve PFC resolution compared with PSs.[41,42] The overall AE rates associated with EUS-guided PFC drainage were reported at 19.1% and 22.4% for LAMS- and PS-assisted drainage, respectively, in a 2021 meta-analysis of 1691 patients.[43]

Perforation

By definition, EUS-guided transmural stenting creates a controlled perforation; however, the risk of uncontrolled iatrogenic perforation is considerably higher with therapeutic EUS-guided procedures (including PFC drainage) than with routine diagnostic EUS. For EUS-guided drainage of PFCs including pseudocysts and WONs, the overall perforation rate was reported at 1.8% in a recent meta-analysis that included 900 patients.[43] However, in a 2020 large cohort study of LAMSs for PFC drainage in 328 patients across 15 international centers that was not included in the above meta-analysis, no perforations were reported,[44] suggesting the possible effect of growing experience and comfort levels with this technique over time. Delayed perforation (occurring and/or diagnosed after completion of the index procedure) is also a possible AE after PFC drainage and is often related to stent dislodgement, with the overall risk increasing with subsequent endoscopic necrosectomy.[45] Although perforation rates by stent type have varied between available studies,[46-50] the use of LAMSs was associated with higher odds of perforation in the drainage of WON compared with PSs in a 2021 meta-analysis, although the CI was quite wide (odds ratio, 7.10; 95% CI, 1.22-41.30).[43]

Hemorrhage

With EUS-guided PFC drainage, the bleeding risk is considerably higher than with routine EUS, with reported rates ranging between 1% to 12%.[47,51-53] A 2021 meta-analysis reported a pooled bleeding rate of 5.3%.[43] The higher intraprocedural bleeding rate can be readily explained given the insertion of a transmural stent across the GI lumen into the PFC.

Delayed bleeding is more commonly encountered with LAMS insertion compared with PS insertion.[54] In fact, higher than expected rates of bleeding with LAMSs resulted in a protocol amendment in a seminal randomized trial, with a final bleeding rate of 9.7% in the LAMS group compared with 3.4% in the PS group.[46,54] Bleeding can occur because of direct trauma, injury to nearby blood vessels, or pseudoaneurysm formation.[46] A recent meta-analysis of over 1700 patients demonstrated higher pooled rates of bleeding with LAMSs (10.7%) compared with SEMSs (4.3%), with a risk ratio of 6.70 (95% CI, 1.77-36.27), and a nonsignificant trend toward higher bleeding rates with LAMS compared with PS (5.0%), with a risk ratio of 2.67 (95% CI, .71-9.28).[55]

To mitigate the risk of bleeding, several recommendations have been proposed, including the appropriate periprocedural management of anticoagulation as per current ASGE guidance.[24] Prompt cross-sectional imaging to track PFC resolution after LAMSs has also been proposed, as has the removal of LAMSs within 3 to 5 weeks if possible to avoid impingement on adjacent intra-abdominal vascular structures after relatively rapid PFC decompression[54]; however, prospective data are required to reliably determine the optimal timing of stent removal.

Infection

Infection after PFC drainage is most often associated with stent occlusion, which is more common with WON than with pseudocysts. Secondary infection of PFCs has a widely variable incidence of between 0% and 24%,[44-47,56] with larger PFC size an established risk factor.[57] A 2019 meta-analysis demonstrated pooled poststent infection rates of 5.4% for metal stents (SEMSs or LAMSs) and 13.2% for PSs, although the risk ratio did not suggest a significant difference between the groups ($P = .13$).[58] When LAMSs are used for PFC drainage, the placement of PSs through the LAMS lumen has been reported to decrease the risk of global AEs related to LAMSs, which includes potentially decreasing infections.[59]

Stent migration

Spontaneous stent migration is also possible after EUS-guided PFC drainage. Subsequent interventions such as endoscopic necrosectomy through an existing stent increase this risk. In a 2020 study of 333 procedures at 15 centers, stent migration was reported at 6.6%, with a mean time to diagnosis of 45 days.[44] Overall, early and late migration rates have jointly been reported to occur in between 0% and 20% of PFC drainage cases.[46,47,53,60]

Stent occlusion

Stent occlusion from either GI contents or debris from a necrotic collection is also possible after PFC drainage and is a risk factor for the development of secondary infection of the PFC cavity (see above). The incidence of stent occlusion is widely variable but more common with drainage of WON compared with drainage of simple pseudocysts. A recent large retrospective study of 328 patients reported a LAMS occlusion rate of 17.7%, with over 90% of these requiring unplanned repeat endoscopic intervention for resolution.[44] A recent RCT of 387 patients undergoing WON drainage reported a higher rate of occlusion with SEMSs (10.2%) compared with LAMSs (5.9%).[61] Other studies have reported stent occlusion rates ranging between 0% and 10.2%,[46,47,62] with higher rates of occlusion and secondary infection reported with PSs over LAMSs.[47] More details on stent occlusion are discussed in the ASGE guideline on the role of endoscopy in the diagnosis and treatment of inflammatory PFCs.[63]

EUS-BD AND EUS-GD

EUS-guided direct transmural biliary access (EUS-BD technique) has historically been used as a rescue technique in the setting of failed ERCP[64] but has more recently become increasingly common as a primary decompressive modality in the setting of malignant distal obstruction.[65] EUS-BD is possible via choledochoduodenostomy or hepatogastrostomy.[66,67] A recent meta-analysis reported a clinical success rate of 91.2% with EUS-BD when used as a primary modality in the decompression of malignant distal biliary obstruction.[65]

The data on AEs of this technique as a primary modality are somewhat limited because the technique is quite new. Perforation is rare and is reported to occur in 0% to 3.1% of patients in RCTs for primary decompression of malignant distal biliary obstruction.[68-70] The perforation rate with EUS-GD has been reported at 1.2% in 1 cohort study.[71] No clinically significant bleeding resulting in unplanned healthcare use was reported in 3 separate RCTs of EUS-BD versus ERCP for primary decompression of malignant distal biliary obstruction.[68-70] In a recent large retrospective study of 195 patients in which the bleeding rate after EUS-BD was reported at 3.6%, patients receiving antiplatelet and/or anticoagulant therapy were no more likely to experience bleeding than patients not receiving these medications.[72] The bleeding risk appears to be somewhat higher with EUS-GD, reported to range between 1.3% and 8.3%.[73-75] A recent meta-analysis of patients undergoing EUS-BD as a primary treatment modality for malignant distal biliary obstruction reported the pooled stent migration rate to be 2.7%, which was comparable with the migration rate associated with ERCP for the same indication.[65]

Bile peritonitis secondary to leakage has also been described with the EUS-BD technique, with an estimated pooled rate of 2.2% in a 2019 meta-analysis of patients undergoing decompression for malignant distal biliary obstruction.[65] Occlusion from GI contents is also possible after EUS-BD, with reported rates ranging between 0% and 14.3% in RCTs comparing this technique with ERCP in the primary decompression of malignant distal biliary obstruction.[68-70] Rates of stent occlusion are similar for EUS-GD, ranging between 0% and 10.4%.[73-75]

CPB OR CPN

For patients with chronic abdominal pain, analgesia can be achieved using CPB or CPN. Various image-guided modalities have been used to deliver targeted CPB and CPN, including EUS. The most common indication for CPB and CPN is chronic abdominal pain originating from pancreatic cancer or chronic pancreatitis.[76,77] CPB involves the injection of a long-lasting local anesthetic and steroid into the celiac ganglia or the adjacent celiac plexus, whereas CPN involves the injection of alcohol or any agent that results in ablation of the nerve fibers. In addition to the AEs related to the use of a needle, as seen in routine EUS-FNA/FNB, there are AEs specific to celiac plexus therapy.

Self-limited diarrhea from increased parasympathetic tone is a possible AE after CPB or CPN.[78] A 2014 review of over 1100 patients from 20 studies reported transient diarrhea in 2% of patients after EUS-CPB and 10% of patients after EUS-CPN.[79] The incidence of transient diarrhea is widely variable, ranging from 0% to 28% even in RCTs assessing CPN.[80-83] Hypotension from sympathetic blockade is also possible after EUS-CPB/CPN, although variability in outcome definitions contribute to variations in its incidence. In a 2014 review, hypotension occurred in 2% of patients after EUS-CPB and 5% of patients after EUS-CPN.[79]

Subjective inebriation, an inconsistently defined entity associated with transient loss of cognition and/or inhibition, is also possible after EUS-CPN, but its true incidence is also difficult to ascertain given inconsistencies in outcome definitions and measurement. Nevertheless, some degree of inebriation after EUS-CPN has been reported in 0% to 14% of patients in RCTs.[80,83] Self-limited exacerbation of a patient's baseline abdominal pain or severe pain is another possible AE after either CPB or CPB, occurring at rates of 2% after EUS-CPB and 4% after EUS-CPN.[79] This may be related to activation of the pain pathway in the celiac ganglion. Patients should be advised on the risks of the above AEs. Adequate intravenous hydration before and after EUS-CPB/CPN could mitigate the relatively rare risk of transient hypotension and/or orthostasis and should be considered in all patients, despite the lack of prospective evidence to inform this practice.

There are also numerous reported severe AEs associated with EUS-guided CPN and CPB that, although documented only in case reports, have the potential to result in devastating patient morbidity. Retroperitoneal abscess formation and empyema have both been reported after CPB and CPN.[84-86] Ischemia and necrosis of vascular structures and/or intraperitoneal organs have also been reported, sometimes resulting in death.[87,88] Although it was hoped that paraplegia would be avoided with the anterior EUS approach compared with the posterior radiologic approach, paraplegia has also been reported after EUS-CPN and has been attributed to infarction of the anterior spinal cord because of compromised blood flow in the artery of Adamkiewicz.[89,90] Case reports have also described transient paralysis because of reversible arterial spasm after the performance of CPN.[91,92]

EUS-GUIDED VARICEAL MANAGEMENT

EUS-guided angiotherapy of gastric varices has gained considerable traction over the past 2 decades. Compared with non–EUS-guided endoscopic management, EUS-guided therapy affords the advantage of being able to directly visualize the injection of coils and/or cyanoacrylate into selected varices. A 2020 meta-analysis of 11 studies reported a pooled overall AE rate of 14% with EUS-guided variceal therapy, with a significant difference demonstrated between AE rates for cyanoacrylate injection alone (21%) and cyanoacrylate injection with coiling (10%).[93] Of note, some input data informing these pooled AE rates were derived from studies in which overall AE rates were reported per patient over multiple EUS sessions, making these rates more challenging to interpret.[94] A separate 2020 meta-analysis included 23 studies and reported a pooled distant embolism rate of 5.6% (including pulmonary embolism) and a pooled periprocedural and early recurrent bleeding rate (within 120 hours) of 7.0%.[95] Other common AEs associated with this technique include self-limited abdominal pain in 3.2% to 12.5% of procedures,[96-99] self-limited fever in 3.3% to 4.7% of procedures,[97,99] and bacteremia of uncertain clinical significance in 1.6% to 2.5% of procedures.[94,97,100]

EUS-GE AND ENTEROENTEROSTOMY

EUS has rapidly become a viable alternative to percutaneous, surgical, or other endoscopic approaches for palliation through decompressive therapy for patients with gastric outlet or small-bowel obstruction, regardless of the etiology. EUS-GE and enteroenterostomy both use placement of a LAMS from the stomach or small bowel to the bowel distal to the obstruction. A 2021 meta-analysis of 5 studies assessing 659 patients reported a pooled overall AE rate of 10.7% with EUS-GE, with a major AE rate of 3.7%.[101] A 2020 meta-analysis of 12 studies assessing 285 patients reported a similar pooled overall AE rate of 12%.[102] The most common associated AE is stent maldeployment into the peritoneum resulting in perforation, occurring in up to 6.8% to 10% of procedures.[103-106] This outcome varies in terms of severity, often managed endoscopically and other times requiring surgical intervention and rarely leading to mortality.[103,105] Other common AEs associated with EUS-GE include stent occlusion because of ingrowth, reported in 4.2% of procedures,[104] and bleeding, reported in 3.8% of procedures.[105]

NOVEL EUS-GUIDED PROCEDURES

The ongoing development of novel EUS-guided procedures continues to evolve at a rapid pace. Given this, there are several EUS-guided techniques for which widespread experience and reliable estimates of AE rates are both lacking to date, including, but are not limited to, EUS-guided transgastric ERCP[107] and EUS-directed transenteric ERCP,[108] EUS-guided radiofrequency ablation of pancreatic lesions,[109] and EUS-guided portal pressure gradient measurement.[110] As the experience level with these novel techniques (and others) continues to grow and higher-quality data are acquired, more reliable estimates of AE incidence will become available.

FUTURE DIRECTIONS

This document highlights several important areas within the field of EUS for which further high-quality research is needed to bolster the strength of recommendations for future EUS-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 EUS and more advanced EUS-guided techniques (Table 1). Dedicated efforts to reliably elucidate these independent predictors (ideally through prospective population-level cohort studies and clinical trials) are needed, especially for newer techniques.
- *Antibiotic prophylaxis for pancreatic cyst drainage.* The question of whether antibiotic prophylaxis is required for those undergoing pancreatic cyst drainage is highly relevant. Current ASGE guidance recommends routinely administering antibiotic prophylaxis in this population,[30] with newer evidence suggesting a limited benefit to this practice. However, given that most contemporary studies assessing this question are observational and retrospective, further evidence from RCTs is needed before reversing current guidance, especially given the established side effect profile of antibiotics and concerns around antibiotic resistance.
- *Effectiveness, AEs, and cost-effectiveness of interventions by stent type.* High-quality evidence regarding the use of LAMSs in multiple EUS-guided procedures is emerging. Given that LAMSs represent a relatively new class of device (compared with PSs and SEMSs), it is imperative that high-quality prospective comparative data (both on efficacy from RCTs and on effectiveness from real-world observational studies) are sought and subsequently used to inform cost-effectiveness models, especially related to PFC drainage. Collectively, these data are essential to guide evidence-based practice.
- *Data on AEs for novel EUS-guided procedures.* More data, ideally in the form of RCTs and prospective observational studies, are needed to formally elucidate the AE rates and predictors of AEs for the novel EUS-guided procedures described above, including EUS-guided transgastric ERCP and EUS-directed transenteric ERCP, EUS-guided radiofrequency ablation of pancreatic lesions, and EUS-guided portal pressure gradient measurement.
- *Implications for training.* Data are scarce on both the learning curves and trainee-related AE profiles associated with most EUS-guided procedures described in this document. Data describing required procedural volumes and optimal training methods for these

techniques as well as AEs associated with training are urgently needed.

CONCLUSION

Routine EUS with or without FNA/FNB is well established as a safe and effective procedure. Although several AEs are associated with routine EUS, their overall incidence is low. Interventional EUS-guided techniques are becoming increasingly established as alternatives to surgical, radiologic, and other endoscopic approaches and are associated with higher AE rates compared with routine EUS. Endoscopists performing EUS-guided procedures should be aware of associated AE rates and their risk factors to optimize the informed consent process and improve intraprocedural techniques.

DISCLOSURE

The following authors disclosed financial relationships: N. Forbes: Consultant for Boston Scientific Corporation, Pentax Medical, and Pendopharm Inc; speaker for Pentax Medical; research support from Pentax Medical. N. Coelho-Prabhu: Food and beverage comensation from Boston Scientific Corporation. M. A. Al-Haddad: Grant recipient, research/teaching support, and food and beverage compensation from Boston Scientific Corporation. R. S. Kwon: Travel compensation from C2 Therapeutics, Inc; food and beverage compensation from Covidien LP. S. K. Amateau: Consultant for Boston Scientific Corporation, Olympus America Inc, Cook Medical LLC, Endo-Therapeutics, Hemostasis LLC, Merit Medical Systems Inc, and Steris Corporation; travel compensation from Boston Scientific Corporation and Olympus America Inc; food and beverage from Boston Scientific Corporation, Olympus America Inc, and Cook Medical LLC. J. L. Buxbaum: Consultant for Olympus America Inc, Boston Scientific Corporation, Eagle Pharmaceuticals, Inc, and Cook Incorporated; grant recipient from Olympus America Inc and Medtronic USA, Inc; travel and food and beverage compensation from Olympus America Inc, Boston Scientific Corporation, Covidien LP, and AbbVie, Inc. S. E. Elhanafi: Food and beverage compensation from Gilead Sciences, Inc, Pfizer Inc, Salix Pharmaceuticals, Olympus America Inc, Lumendi LLC, and Covidien LP. L. L. Fujii-Lau: Grant recipient from Cook Medical LLC; travel compensation from Ovesco; food and beverage compensation from Covidien LP and Boston Scientific Corporation. D. R. Kohli: Grant recipient from Olympus Corporation of the Americas; food and beverage compensation from Boston Scientific Corporation. S. Pawa: Educational support from Alexion Pharmaceuticals, Inc; food and beverage compensation from Cook Medical LLC. A. C. Storm: Consultant for Apollo Endo Surgery US Inc, Endo-TAGSS, and Enterasense; travel compensation from Apollo Endo Surgery US Inc; food and beverage compensation from Apollo Endo Surgery US Inc and Boston Scientific Corporation; receives data/safety monitoring from Erbe USA Inc and GI Dynamics; research support Boston Scientific Corporation. N. C. Thosani: Consultant for Boston Scientific Corporation, TaeWoong Medical, and Pentax of America, Inc; travel compensation from Boston Scientific Corporation and Pentax of America, Inc; food and beverage compensation from Boston Scientific Corporation, Pentax of America, Inc, Endogastric Solutions, AbbVie, Inc and Covidien LP; research support from Pentax of America, Inc and Endogastric Solutions; royalties from UpToDate; speaker for AbbVie, Inc; advisory board for ColubrisMX Inc. B. J, Qumseya: Food and beverage compensation from Boston Scientific Corporation and GlaxoSmithKline, LLC. All other authors disclosed no financial relationships.

ACKNOWLEDGMENTS

We acknowledge and are grateful for the contribution of Marcus Vaska, MLIS, who helped design and perform the electronic search strategies for this document, as well as Dr Ashley Faulx, Dr Ajay Pal Singh, Dr Tiffany Chua, and Dr Jenifer Lightdale for their review of this document.

REFERENCES

1. Early DS, Acosta RD, Chandrasekhara V, et al. Adverse events associated with EUS and EUS with FNA. Gastrointest Endosc 2013;77:839-43.
2. Peery AF, Crockett SD, Murphy CC, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2018. Gastroenterology 2019;156:254-72.
3. Wani S, Wallace MB, Cohen J, et al. Quality indicators for EUS. Am J Gastroenterol 2015;110:102-13.
4. Ben-Menachem T, Decker GA, Early DS, et al. Adverse events of upper GI endoscopy. Gastrointest Endosc 2012;76:707-18.
5. Wang KX, Ben QW, Jin ZD, et al. Assessment of morbidity and mortality associated with EUS-guided FNA: a systematic review. Gastrointest Endosc 2011;73:283-90.
6. Razik R, James P, Khan R, et al. Risk of adverse events associated with upper and lower endoscopic ultrasound: a population-based cohort study. Endosc Int Open 2021;9:E1427-34.
7. Marchetti G, Ricardo VD, Ardengh AO, et al. Adverse events and mortality: comparative analysis between diagnostic and interventional endoscopic ultrasound. Scand J Gastroenterol 2020;55:995-1001.
8. Eloubeidi MA, Tamhane A, Lopes TL, et al. Cervical esophageal perforations at the time of endoscopic ultrasound: a prospective evaluation of frequency, outcomes, and patient management. Am J Gastroenterol 2009;104:53-6.
9. Das A, Sivak MV Jr, Chak A. Cervical esophageal perforation during EUS: a national survey. Gastrointest Endosc 2001;53:599-602.
10. Khan U, Abunassar M, Chatterjee A, et al. Advanced endoscopy trainee involvement early in EUS training may be associated with an increased risk of adverse events. J Can Assoc Gastroenterol 2020;3:83-90.
11. Mortensen MB, Fristrup C, Holm FS, et al. Prospective evaluation of patient tolerability, satisfaction with patient information, and complications in endoscopic ultrasonography. Endoscopy 2005;37:146-53.

12. Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc 2010;71:446-54.
13. Zhu H, Jiang F, Zhu J, et al. Assessment of morbidity and mortality associated with endoscopic ultrasound-guided fine-needle aspiration for pancreatic cystic lesions: a systematic review and meta-analysis. Dig Endosc 2017;29:667-75.
14. Hamada T, Yasunaga H, Nakai Y, et al. Severe bleeding and perforation are rare complications of endoscopic ultrasound-guided fine needle aspiration for pancreatic masses: an analysis of 3,090 patients from 212 hospitals. Gut Liver 2014;8:215-8.
15. Inoue T, Okumura F, Sano H, et al. Bleeding risk of endoscopic ultrasound-guided fine-needle aspiration in patients undergoing antithrombotic therapy. Dig Endosc 2017;29:91-6.
16. Kawakubo K, Yane K, Eto K, et al. A prospective multicenter study evaluating bleeding risk after endoscopic ultrasound-guided fine needle aspiration in patients prescribed antithrombotic agents. Gut Liver 2018;12:353-9.
17. Nagata N, Yasunaga H, Matsui H, et al. Therapeutic endoscopy-related GI bleeding and thromboembolic events in patients using warfarin or direct oral anticoagulants: results from a large nationwide database analysis. Gut 2018;67:1805-12.
18. Kien-Fong Vu C, Chang F, Doig L, et al. A prospective control study of the safety and cellular yield of EUS-guided FNA or Trucut biopsy in patients taking aspirin, nonsteroidal anti-inflammatory drugs, or prophylactic low molecular weight heparin. Gastrointest Endosc 2006;63:808-13.
19. Levy MJ, Abu Dayyeh BK, Fujii LL, et al. Prospective evaluation of adverse events following lower gastrointestinal tract EUS FNA. Am J Gastroenterol 2014;109:676-85.
20. Park WG, Yan BM, Schellenberg D, et al. EUS-guided gold fiducial insertion for image-guided radiation therapy of pancreatic cancer: 50 successful cases without fluoroscopy. Gastrointest Endosc 2010;71:513-8.
21. Dhadham GC, Hoffe S, Harris CL, et al. Endoscopic ultrasound-guided fiducial marker placement for image-guided radiation therapy without fluoroscopy: safety and technical feasibility. Endosc Int Open 2016;4:E378-82.
22. Nieto J, Khaleel H, Challita Y, et al. EUS-guided fine-needle core liver biopsy sampling using a novel 19-gauge needle with modified 1-pass, 1 actuation wet suction technique. Gastrointest Endosc 2018;87:469-75.
23. Diehl DL, Johal AS, Khara HS, et al. Endoscopic ultrasound-guided liver biopsy: a multicenter experience. Endosc Int Open 2015;3:E210-5.
24. Acosta RD, Abraham NS, Chandrasekhara V, et al. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc 2016;83:3-16.
25. Levy MJ, Norton ID, Wiersema MJ, et al. Prospective risk assessment of bacteremia and other infectious complications in patients undergoing EUS-guided FNA. Gastrointest Endosc 2003;57:672-8.
26. Barawi M, Gottlieb K, Cunha B, et al. A prospective evaluation of the incidence of bacteremia associated with EUS-guided fine-needle aspiration. Gastrointest Endosc 2001;53:189-92.
27. Janssen J, König K, Knop-Hammad V, et al. Frequency of bacteremia after linear EUS of the upper GI tract with and without FNA. Gastrointest Endosc 2004;59:339-44.
28. Levy MJ, Norton ID, Clain JE, et al. Prospective study of bacteremia and complications With EUS FNA of rectal and perirectal lesions. Clin Gastroenterol Hepatol 2007;5:684-9.
29. Diehl DL, Cheruvattath R, Facktor MA, et al. Infection after endoscopic ultrasound-guided aspiration of mediastinal cysts. Interact Cardiovasc Thorac Surg 2010;10:338-40.
30. Khashab MA, Chithadi KV, Acosta RD, et al. Antibiotic prophylaxis for GI endoscopy. Gastrointest Endosc 2015;81:81-9.
31. Colán-Hernández J, Sendino O, Loras C, et al. Antibiotic prophylaxis is not required for endoscopic ultrasonography-guided fine-needle aspiration of pancreatic cystic lesions, based on a randomized trial. Gastroenterology 2020;158:1642-9.
32. Palomera-Tejeda E, Shah H, Attar BM, et al. Prophylactic antibiotics do not prevent infectious complications of endoscopic ultrasound fine-needle aspiration of pancreatic cysts: a systematic review and meta-analysis. Pancreas 2021;50:667-72.
33. Choi JH, Seo DW, Park DH, et al. Fiducial placement for stereotactic body radiation therapy under only endoscopic ultrasonography guidance in pancreatic and hepatic malignancy: practical feasibility and safety. Gut Liver 2014;8:88-93.
34. Mizuide M, Ryozawa S, Fujita A, et al. Complications of endoscopic ultrasound-guided fine needle aspiration: a narrative review. Diagnostics (Basel) 2020;10:964.
35. Shah RJ, Shah JN, Waxman I, et al. Safety and efficacy of endoscopic ultrasound-guided drainage of pancreatic fluid collections with lumen-apposing covered self-expanding metal stents. Clin Gastroenterol Hepatol 2015;13:747-52.
36. Varadarajulu S, Bang JY, Phadnis MA, et al. Endoscopic transmural drainage of peripancreatic fluid collections: outcomes and predictors of treatment success in 211 consecutive patients. J Gastrointest Surg 2011;15:2080-8.
37. Akshintala VS, Saxena P, Zaheer A, et al. A comparative evaluation of outcomes of endoscopic versus percutaneous drainage for symptomatic pancreatic pseudocysts. Gastrointest Endosc 2014;79:921-8; quiz 983.e2, 983.e5.
38. van Santvoort HC, Besselink MG, Bakker OJ, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med 2010;362:1491-502.
39. van Brunschot S, van Grinsven J, van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. Lancet 2018;391:51-8.
40. Hollemans RA, Bakker OJ, Boermeester MA, et al. Superiority of step-up approach vs open necrosectomy in long-term follow-up of patients with necrotizing pancreatitis. Gastroenterology 2019;156:1016-26.
41. Abu Dayyeh BK, Mukewar S, Majumder S, et al. Large-caliber metal stents versus plastic stents for the management of pancreatic walled-off necrosis. Gastrointest Endosc 2018;87:141-9.
42. Mukai S, Itoi T, Baron TH, et al. Endoscopic ultrasound-guided placement of plastic vs. biflanged metal stents for therapy of walled-off necrosis: a retrospective single-center series. Endoscopy 2015;47:47-55.
43. Lyu Y, Li T, Wang B, et al. Comparison between lumen-apposing metal stents and plastic stents in endoscopic ultrasound-guided drainage of pancreatic fluid collection: a meta-analysis and systematic review. Pancreas 2021;50:571-8.
44. Fugazza A, Sethi A, Trindade AJ, et al. International multicenter comprehensive analysis of adverse events associated with lumen-apposing metal stent placement for pancreatic fluid collection drainage. Gastrointest Endosc 2020;91:574-83.
45. Sharaiha RZ, Tyberg A, Khashab MA, et al. Endoscopic therapy with lumen-apposing metal stents is safe and effective for patients with pancreatic walled-off necrosis. Clin Gastroenterol Hepatol 2016;14:1797-803.
46. Bang JY, Navaneethan U, Hasan MK, et al. Non-superiority of lumen-apposing metal stents over plastic stents for drainage of walled-off necrosis in a randomised trial. Gut 2019;68:1200-9.
47. Yang J, Chen YI, Friedland S, et al. Lumen-apposing stents versus plastic stents in the management of pancreatic pseudocysts: a large, comparative, international, multicenter study. Endoscopy 2019;51:1035-43.
48. Lang GD, Fritz C, Bhat T, et al. EUS-guided drainage of peripancreatic fluid collections with lumen-apposing metal stents and plastic double-pigtail stents: comparison of efficacy and adverse event rates. Gastrointest Endosc 2018;87:150-7.
49. Kayal A, Taghizadeh N, Ishikawa T, et al. Endosonography-guided transmural drainage of pancreatic fluid collections: comparative outcomes by stent type. Surg Endosc 2021;35:2698-708.

50. Siddiqui AA, Kowalski TE, Loren DE, et al. Fully covered self-expanding metal stents versus lumen-apposing fully covered self-expanding metal stent versus plastic stents for endoscopic drainage of pancreatic walled-off necrosis: clinical outcomes and success. Gastrointest Endosc 2017;85:758-65.
51. Adler DG, Shah J, Nieto J, et al. Placement of lumen-apposing metal stents to drain pseudocysts and walled-off pancreatic necrosis can be safely performed on an outpatient basis: a multicenter study. Endosc Ultrasound 2019;8:36-42.
52. Varadarajulu S, Christein JD, Wilcox CM. Frequency of complications during EUS-guided drainage of pancreatic fluid collections in 148 consecutive patients. J Gastroenterol Hepatol 2011;26:1504-8.
53. Brimhall B, Han S, Tatman PD, et al. Increased incidence of pseudoaneurysm bleeding with lumen-apposing metal stents compared to double-pigtail plastic stents in patients with peripancreatic fluid collections. Clin Gastroenterol Hepatol 2018;16:1521-8.
54. Bang JY, Hasan M, Navaneethan U, et al. Lumen-apposing metal stents (LAMS) for pancreatic fluid collection (PFC) drainage: may not be business as usual. Gut 2017;66:2054-6.
55. Park CH, Park SW, Nam E, et al. Comparative efficacy of stents in endoscopic ultrasonography-guided peripancreatic fluid collection drainage: a systematic review and network meta-analysis. J Gastroenterol Hepatol 2020;35:941-52.
56. Yang D, Perbtani YB, Mramba LK, et al. Safety and rate of delayed adverse events with lumen-apposing metal stents (LAMS) for pancreatic fluid collections: a multicenter study. Endosc Int Open 2018;6:E1267-75.
57. Guo J, Feng L, Sun S, et al. Risk factors for infection after endoscopic ultrasonography-guided drainage of specific types of pancreatic and peripancreatic fluid collections (with video). Surg Endosc 2016;30:3114-20.
58. Saunders R, Ramesh J, Cicconi S, et al. A systematic review and meta-analysis of metal versus plastic stents for drainage of pancreatic fluid collections: metal stents are advantageous. Surg Endosc 2019;33:1412-25.
59. Puga M, Consiglieri CF, Busquets J, et al. Safety of lumen-apposing stent with or without coaxial plastic stent for endoscopic ultrasound-guided drainage of pancreatic fluid collections: a retrospective study. Endoscopy 2018;50:1022-6.
60. Chandran S, Efthymiou M, Kaffes A, et al. Management of pancreatic collections with a novel endoscopically placed fully covered self-expandable metal stent: a national experience (with videos). Gastrointest Endosc 2015;81:127-35.
61. Siddiqui A, Naveed M, Basha J, et al. International, multicenter retrospective trial comparing the efficacy and safety of bi-flanged versus lumen-apposing metal stents for endoscopic drainage of walled-off pancreatic necrosis. Ann Gastroenterol 2021;34:273-81.
62. Lakhtakia S, Basha J, Talukdar R, et al. Endoscopic “step-up approach” using a dedicated biflanged metal stent reduces the need for direct necrosectomy in walled-off necrosis (with videos). Gastrointest Endosc 2017;85:1243-52.
63. Muthusamy VR, Chandrasekhara V, Acosta RD, et al. The role of endoscopy in the diagnosis and treatment of inflammatory pancreatic fluid collections. Gastrointest Endosc 2016;83:481-8.
64. Giovannini M, Moutardier V, Pesenti C, et al. Endoscopic ultrasound-guided bilioduodenal anastomosis: a new technique for biliary drainage. Endoscopy 2001;33:898-900.
65. Bishay K, Boyne D, Yaghoobi M, et al. Endoscopic ultrasound-guided transmural approach versus ERCP-guided transpapillary approach for primary decompression of malignant biliary obstruction: a meta-analysis. Endoscopy 2019;51:950-60.
66. Khashab MA, Levy MJ, Itoi T, et al. EUS-guided biliary drainage. Gastrointest Endosc 2015;82:993-1001.
67. Baars JE, Kaffes AJ, Saxena P. EUS-guided biliary drainage: a comprehensive review of the literature. Endosc Ultrasound 2018;7:4-9.
68. Paik WH, Lee TH, Park DH, et al. EUS-guided biliary drainage versus ERCP for the primary palliation of malignant biliary obstruction: a multicenter randomized clinical trial. [Erratum appears in Am J Gastroenterol 2018 Aug 23;PMID: 30140030.]. Am J Gastroenterol 2018;113:1566.
69. Park JK, Woo YS, Noh DH, et al. Efficacy of EUS-guided and ERCP-guided biliary drainage for malignant biliary obstruction: prospective randomized controlled study. Gastrointest Endosc 2018;88:277-82.
70. Bang JY, Navaneethan U, Hasan M, et al. Stent placement by EUS or ERCP for primary biliary decompression in pancreatic cancer: a randomized trial (with videos). Gastrointest Endosc 2018;88:9-17.
71. Oh D, Song TJ, Cho DH, et al. EUS-guided cholecystostomy versus endoscopic transpapillary cholecystostomy for acute cholecystitis in high-risk surgical patients. Gastrointest Endosc 2019;89:289-98.
72. Ogura T, Nishioka N, Ueno S, et al. Antiplatelet and/or anticoagulant treatment does not increase hemorrhagic adverse events during EUS-guided biliary drainage. Gastrointest Endosc 2020;92:659-66.
73. Tyberg A, Jha K, Shah S, et al. EUS-guided gallbladder drainage: a learning curve modified by technical progress. Endosc Int Open 2020;8:E92-6.
74. Teoh AYB, Kongkam P, Bapaye A, et al. The use of a novel lumen apposing metallic stent for drainage of the bile duct and gallbladder: long term outcomes of a prospective international trial. Dig Endosc 2020 Online ahead of print (doi: 10.1111/den.13911).
75. Dollhopf M, Larghi A, Will U, et al. EUS-guided gallbladder drainage in patients with acute cholecystitis and high surgical risk using an electrocautery-enhanced lumen-apposing metal stent device. Gastrointest Endosc 2017;86:636-43.
76. Arcidiacono PG, Calori G, Carrara S, et al. Celiac plexus block for pancreatic cancer pain in adults. Cochrane Database Syst Rev 2011;2011:Cd007519.
77. Hastings RH, McKay WR. Treatment of benign chronic abdominal pain with neurolytic celiac plexus block. Anesthesiology 1991;75:156-8.
78. Yasuda I, Wang HP. Endoscopic ultrasound-guided celiac plexus block and neurolysis. Dig Endosc 2017;29:455-62.
79. Alvarez-Sánchez MV, Jenssen C, Faiss S, et al. Interventional endoscopic ultrasonography: an overview of safety and complications. Surg Endosc 2014;28:712-34.
80. Kanno Y, Koshita S, Masu K, et al. Efficacy of EUS-guided celiac plexus neurolysis compared with medication alone for unresectable pancreatic cancer in the oxycodone/fentanyl era: a prospective randomized control study. Gastrointest Endosc 2020;92:120-30.
81. LeBlanc JK, Al-Haddad M, McHenry L, et al. A prospective, randomized study of EUS-guided celiac plexus neurolysis for pancreatic cancer: one injection or two? Gastrointest Endosc 2011;74:1300-7.
82. Wyse JM, Carone M, Paquin SC, et al. Randomized, double-blind, controlled trial of early endoscopic ultrasound-guided celiac plexus neurolysis to prevent pain progression in patients with newly diagnosed, painful, inoperable pancreatic cancer. J Clin Oncol 2011;29:3541-6.
83. Doi S, Yasuda I, Kawakami H, et al. Endoscopic ultrasound-guided celiac ganglia neurolysis vs. celiac plexus neurolysis: a randomized multicenter trial. Endoscopy 2013;45:362-9.
84. Gress F, Schmitt C, Sherman S, et al. Endoscopic ultrasound-guided celiac plexus block for managing abdominal pain associated with chronic pancreatitis: a prospective single center experience. Am J Gastroenterol 2001;96:409-16.
85. O'Toole TM, Schmulewitz N. Complication rates of EUS-guided celiac plexus blockade and neurolysis: results of a large case series. Endoscopy 2009;41:593-7.
86. Muscatiello N, Panella C, Pietrini L, et al. Complication of endoscopic ultrasound-guided celiac plexus neurolysis. Endoscopy 2006;38:858.
87. Loeve US, Mortensen MB. Lethal necrosis and perforation of the stomach and the aorta after multiple EUS-guided celiac plexus neurolysis procedures in a patient with chronic pancreatitis. Gastrointest Endosc 2013;77:151-2.
88. Gimeno-García AZ, Elwassief A, Paquin SC, et al. Fatal complication after endoscopic ultrasound-guided celiac plexus neurolysis. Endoscopy 2012;44(Suppl 2 UCTN):E267.

89. Mittal MK, Rabinstein AA, Wijdicks EF. Pearls & oysters: acute spinal cord infarction following endoscopic ultrasound-guided celiac plexus neurolysis. Neurology 2012;78:e57-9.
90. Fujii L, Clain JE, Morris JM, et al. Anterior spinal cord infarction with permanent paralysis following endoscopic ultrasound celiac plexus neurolysis. Endoscopy 2012;44(Suppl 2 UCTN):E265-6.
91. Wong GY, Brown DL. Transient paraplegia following alcohol celiac plexus block. Reg Anesth 1995;20:352-5.
92. Oguz G, Senel G, Kocak N. Transient paraplegia after neurolytic splanchnic block in a patient with metastatic colon carcinoma. Korean J Pain 2018;31:50-3.
93. McCarty TR, Bazarbashi AN, Hathorn KE, et al. Combination therapy versus monotherapy for EUS-guided management of gastric varices: a systematic review and meta-analysis. Endosc Ultrasound 2020;9:6-15.
94. Lee YT, Chan FK, Ng EK, et al. EUS-guided injection of cyanoacrylate for bleeding gastric varices. Gastrointest Endosc 2000;52:168-74.
95. Mohan BP, Chandan S, Khan SR, et al. Efficacy and safety of endoscopic ultrasound-guided therapy versus direct endoscopic glue injection therapy for gastric varices: systematic review and meta-analysis. Endoscopy 2020;52:259-67.
96. Bhat YM, Weilert F, Fredrick RT, et al. EUS-guided treatment of gastric fundal varices with combined injection of coils and cyanoacrylate glue: a large U.S. experience over 6 years (with video). Gastrointest Endosc 2016;83:1164-72.
97. Bick BL, Al-Haddad M, Liangpunsakul S, et al. EUS-guided fine needle injection is superior to direct endoscopic injection of 2-octyl cyanoacrylate for the treatment of gastric variceal bleeding. Surg Endosc 2019;33:1837-45.
98. Lôbo MRA, Chaves DM, De Moura DTH, et al. Safety and efficacy of EUS-guided coil plus cyanoacrylate versus conventional cyanoacrylate technique in the treatment of gastric varices: a randomized controlled trial. Arq Gastroenterol 2019;56:99-105.
99. Robles-Medranda C, Valero M, Nebel JA, et al. Endoscopic-ultrasound-guided coil and cyanoacrylate embolization for gastric varices and the roles of endoscopic Doppler and endosonographic varicealography in vascular targeting. Dig Endosc 2019;31:283-90.
100. Gubler C, Bauerfeind P. Safe and successful endoscopic initial treatment and long-term eradication of gastric varices by endoscopic ultrasound-guided histoacryl (N-butyl-2-cyanoacrylate) injection. Scand J Gastroenterol 2014;49:1136-42.
101. Chandan S, Khan SR, Mohan BP, et al. EUS-guided gastroenterostomy versus enteral stenting for gastric outlet obstruction: systematic review and meta-analysis. Endosc Int Open 2021;9:E496-504.
102. Iqbal U, Khara HS, Hu Y, et al. EUS-guided gastroenterostomy for the management of gastric outlet obstruction: a systematic review and meta-analysis. Endosc Ultrasound 2020;9:16-23.
103. Chen YI, Kunda R, Storm AC, et al. EUS-guided gastroenterostomy: a multicenter study comparing the direct and balloon-assisted techniques. Gastrointest Endosc 2018;87:1215-21.
104. Ge PS, Young JY, Dong W, et al. EUS-guided gastroenterostomy versus enteral stent placement for palliation of malignant gastric outlet obstruction. Surg Endosc 2019;33:3404-11.
105. Tyberg A, Perez-Miranda M, Sanchez-Ocaña R, et al. Endoscopic ultrasound-guided gastrojejunostomy with a lumen-apposing metal stent: a multicenter, international experience. Endosc Int Open 2016;4:E276-81.
106. Khashab MA, Bukhari M, Baron TH, et al. International multicenter comparative trial of endoscopic ultrasonography-guided gastroenterostomy versus surgical gastrojejunostomy for the treatment of malignant gastric outlet obstruction. Endosc Int Open 2017;5:E275-81.
107. Prakash S, Elmunzer BJ, Forster EM, et al. EUS-directed transgastric ERCP: systematic review to describe outcomes, adverse events and knowledge gaps. Endoscopy 2021 online ahead of print (doi: 10.1055/a-1376-2394).
108. Ichkhanian Y, Yang J, James TW, et al. EUS-directed transenteric ERCP in non-Roux-en-Y gastric bypass surgical anatomy patients (with video). Gastrointest Endosc 2020;91:1188-94.
109. Barthet M, Giovannini M, Lesavre N, et al. Endoscopic ultrasound-guided radiofrequency ablation for pancreatic neuroendocrine tumors and pancreatic cystic neoplasms: a prospective multicenter study. Endoscopy 2019;51:836-42.
110. Xu H, Ding H. EUS-guided portal pressure gradient measurement: a promising tool in noncirrhotic portal hypertension. Gastrointest Endosc 2021;93:287.
111. Facciorusso A, Mohan BP, Tacelli M, et al. Use of antibiotic prophylaxis is not needed for endoscopic ultrasound-guided fine-needle aspiration of pancreatic cysts: a meta-analysis. Expert Rev Gastroenterol Hepatol 2020;14:999-1005.
112. Siddiqui AA, Adler DG, Nieto J, et al. EUS-guided drainage of peripancreatic fluid collections and necrosis by using a novel lumen-apposing stent: a large retrospective, multicenter U.S. experience (with videos). Gastrointest Endosc 2016;83:699-707.

Abbreviations: AE, adverse event; ASGE, American Society for Gastrointestinal Endoscopy; CI, confidence interval; CPB, celiac plexus blockade; CPN, celiac plexus neurolysis; FNB, fine-needle biopsy sampling; EUS-BD, EUS-guided biliary drainage; EUS-GD, EUS-guided gallbladder drainage; EUS-GE, EUS-guided gastroenterostomy; LAMS, lumen-apposing metal stent; PFC, pancreatic fluid collection; PS, plastic stent; RCT, randomized controlled trial; SEMS, self-expanding metal stent; WON, walled-off necrosis

0016-5107/$36.00
https://doi.org/10.1016/j.gie.2021.09.009

Received September 3, 2021. Accepted September 9, 2021.

Current affiliations: Department of Medicine (1), Department of Community Health Sciences (2), Cumming School of Medicine, University of Calgary, Calgary, AB, Canada; Department of Gastroenterology, Mayo Clinic, Rochester, MN, USA (3), Division of Gastroenterology, Indiana School of Medicine, Indianapolis, IN, USA (4), Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI, USA (5), Division of Gastroenterology, Department of Medicine, University of Minnesota, Minneapolis, MN, USA (6), Division of Gastrointestinal and Liver Diseases, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA (7), Section of Gastroenterology and Hepatology, Department of Medicine, Geisel School of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA (8), Department of Internal Medicine, Texas Tech University, Paul L Foster School of Medicine, El Paso, TX, USA (9), Gastroenterology Service, University of Hawaii, Honolulu, HI, USA (10), Division of Gastroenterology and Hepatology, Kansas City VA Medical Center, Kansas City, MO, USA (11), Department of Medicine, Section on Gastroenterology, Wake Forest School of Medicine, Winston-Salem, NC, USA (12), Center for Interventional Gastroenterology (iGUT), McGovern Medical School, UTHealth, Houston, TX, USA (13), Department of Gastroenterology, University of Florida, Gainesville, FL, USA (14).

Reprint requests: Bashar J. Qumseya, MD, MPH, FASGE, Department of Gastroenterology, Hepatology and Nutrition, University of Florida, PO Box 100214, 1329 SW 16th St, Ste 5251. Gainesville, Florida 32610-0214.

APPENDIX 1. FULL ELECTRONIC SEARCH STRATEGY

1. EUS.ab,ti.
2. "endoscopic ultrasound".ab,ti.
3. "endosonograph*".ab,ti.
4. exp Endosonography/
5. "endoscop*".ab,ti.
6. exp Endoscopy/ or exp Endoscopy, Gastrointestinal/ or exp Endoscopy, Digestive System/
7. "ultrasonograph*".ab,ti.
8. exp Ultrasonography/
9. exp Sigmoidoscopy/
10. "sigmoidoscop*".ab,ti.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10

Search 1 (EUS and FNA/FNB)

12. exp Endoscopic Ultrasound-Guided Fine Needle Aspiration/
13. exp Biopsy, Needle/
14. "needle biopsy".ab,ti.
15. FNA.ab,ti.
16. FNB.ab,ti.
17. "fine-needle aspiration".ab,ti.
18. "fine-needle biopsy".ab,ti.
19. exp Biopsy, Fine-Needle/
20. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19

Search 2 (EUS and celiac plexus)

21. "celiac plexus".ab,ti.
22. exp Celiac Plexus/
23. exp Nerve Block/
24. "nerve block".ab,ti.
25. neurolysis.ab,ti.
26. "celiac neurolysis".ab,ti.
27. 21 or 22 or 23 or 24 or 25 or 26

Search 3: (EUS and PFC)

28. "pancreatic fluid collection* ".ab,ti.
29. PFC.ab,ti.
30. "pancreatic pseudocyst".ab,ti.
31. exp Pancreatic Pseudocyst/
32. exp Necrosis/
33. necrosis.ab,ti.
34. WON.ab,ti.
35. "walled-off necrosis".ab,ti.
36. 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35

Search 4: (EUS and BD)

37. biliary.ab,ti.
38. "biliary tract obstruction".ab,ti.
39. "biliary drainage".ab,ti.
40. "percutaneous transhepatic biliary drainage".ab,ti.
41. obstruction.ab,ti.
42. drainage.ab,ti.
43. exp Drainage/
44. exp Decompression/
45. decompression.ab,ti.
46. 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45
47. gallbladder.ab,ti.
48. exp Gallbladder/
49. "gallbladder drainage".ab,ti.
50. exp Gallbladder Emptying/
51. exp Cholecystostomy/
52. cholecystostomy.ab,ti.
53. "radiofrequency ablation".ab,ti.
54. RFA.ab,ti.
55. exp Radiofrequency Ablation/
56. exp Gastric Outlet Obstruction/
57. "gastric outlet obstruction".ab,ti.
58. GOO.ab,ti.
59. gastroenterostomy.ab,ti.
60. exp Gastroenterostomy/
61. 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60

Search 5: (EUS and other)

62. "adverse event* ".ab,ti.
63. "adverse effect* ".ab,ti.
64. pancreatitis.ab,ti.
65. exp Pancreatitis/
66. exp Hemorrhage/
67. hemorrhage.ab,ti.
68. haemorrhage.ab,ti.
69. bleeding.ab,ti.
70. "infection*".ab,ti.
71. exp Infections/
72. perforation.ab,ti.
73. cardiopulmonary.ab,ti.
74. sepsis.ab,ti.
75. exp Sepsis/
76. "complication*".ab,ti.
77. sedation.ab,ti.
78. "risk factor* ".ab,ti.
79. exp Risk Factors/
80. exp Inflammation/
81. inflammation.ab,ti.
82. rupture.ab,ti.
83. exp Rupture/
84. exp Cysts/
85. "cyst*".ab,ti.
86. "gastrointestinal hemorrhage".ab,ti.
87. exp Gastrointestinal Hemorrhage/
88. "gastrointestinal haemorrhage".ab,ti.
89. hypotension.ab,ti.
90. exp Hypotension/
91. 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90
92. 11 and 20 and 91

93. 11 and 27 and 91
94. 11 and 36 and 91
95. 11 and 46 and 91
96. 11 and 61 and 91
97. limit 92 to (english language and yr="2000 -Current")
98. limit 93 to (english language and yr="2000 -Current")
99. limit 94 to (english language and yr="2000 -Current")
100. limit 95 to (english language and yr="2000 -Current")
101. limit 96 to (english language and yr="2000 -Current")
102. limit 97 to (guideline or "review")
103. limit 98 to (guideline or "review")
104. limit 99 to (guideline or "review")
105. limit 100 to (guideline or "review")
106. limit 101 to (guideline or "review")