



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.

Of 3619 initial citations identi

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 ^{54,55} : A69osequ pla-3323rhage

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 medications¹⁵⁻¹⁷ 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.

be used to drain PFCs, including plastic stents (PSs), fully covered self-expandable metal stents (SEMSs), and

the ASGE guideline on the role of endoscopy in the diagnosis and treatment of inflammatory PFCs.⁶³

- D D -CD

EUS-guided direct transmural biliary access (EUS-BD technique) has historically been used as a rescue technique in the setting of failed ERCP⁶⁴ but has more recently become increasingly common as a primary

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}

D

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

D D D

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 ERCP¹⁰⁷ and EUS-directed transenteric ERCP,¹⁰⁸ EUS-guided radiofrequency ablation of pancreatic lesions,¹⁰⁹ and EUS-guided portal pressure gradient mea-

surement.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.

D

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 AE*. 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*. 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

Endoscopy (https://doi.org/10.1055/s-0011-3320071954e25) 6/7

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 anti-thrombotic 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, Ryozaawa S, Fujita A, et al. Complications of endoscopic ultrasound-guided fine needle aspiration: a narrative review. *Diagnosics (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

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.
-

- 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")