Communication from the ASGE Technology Committee

STATUS EVALUATION REPORT

Interventional EUS (with videos)

Prepared by: ASGE TECHNOLOGY COMMITTEE

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

The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methodology is used, performing a MEDLINE literature search to identify pertinent clinical studies on the topic and a MAUDE (U.S. Food and Drug Administration [FDA] Center for Devices and Radiological Health) database search to identify the reported adverse events of a given technology. Both are supplemented by accessing the "related articles" feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases data from randomized controlled trials (RCTs) are lacking. In such cases large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors. Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the Committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. For this review, the MEDLINE database was searched through February 2016 for relevant articles by using key words such as "endoscopic ultrasound," "endoscopic ultrasonography," and "EUS," combined with other relevant terms such as "therapeutic," "interventional," and "adverse events," among others. Articles reporting on specific procedures such as pseudocyst drainage, biliary/pancreatic drainage, celiac plexus neurolysis, and gastric variceal therapy, among others, were also searched for individually with appropriate relevant terms. Technology Status Evaluation Reports are scientific reviews provided solely for educational and informational purposes. Technology Status Evaluation Reports are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment or payment for such treatment.

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2016.11.021

BACKGROUND

In the mid-1990s seminal descriptions of EUS-guided cyst gastrostomy[1] and EUS-guided celiac plexus neurolysis[2] shifted perceptions of EUS from a purely diagnostic examination to a modality capable of guiding therapeutic interventions. The early 2000s saw the development of echoendoscopes with larger instrument-channel diameters capable of allowing advancement of 10F instruments and stents.[3] Numerous advances have been made subsequently in diverse areas, including EUS-directed biliary and pancreatic drainage, treatment of neoplasia, anastomosis creation, and the treatment of bleeding. Although some tools and techniques are still in development and others simply represent useful alternatives to established interventions, certain EUS-directed interventions are potentially disruptive technologies and techniques that may shift therapeutic approaches in the near future. This document reviews the technologies and techniques that comprise interventional EUS.

TECHNOLOGY UNDER REVIEW

Echoendoscopes

The most commonly used echoendoscopes for interventional EUS procedures are electronic curved linear array (CLA) instruments with a 5- to 12-MHz acoustic frequency, oblique-viewing camera optics, and a 3.7- or 3.8-mm

working channel diameter. These CLA echoendoscopes scan longitudinally over a 180-degree field of view in the same 2-dimensional plane as devices exiting the instrument channel, allowing their sonographic visualization. Devices such as needles exit CLA echoendoscopes at an oblique angle, and the echoendoscope elevator can facilitate manipulation of the device trajectory. All modern CLA echoendoscopes allow various forms of duplex endosonography to permit identification of vascular flow. Echoendoscopes meeting these parameters are available from all 3 major manufacturers (eg, GF-UCT 180; Olympus America, Center Valley, Pa; EG-3870UTK; Pentax Medical, Montvale, NJ; and EG-530UT2; Fujifilm Medical Systems, Wayne, NJ). CLA echoendoscopes with smaller instrument channel diameters may also be used for interventional procedures; however, 10F devices and stents cannot be accommodated, necessitating use of smaller-caliber device platforms or intraprocedural wire-assisted exchange to an endoscope with a larger working channel, such as a duodenoscope.

A CLA echoendoscope with forward-viewing camera optics and a 3.7-mm instrument channel is also available and used for therapeutic procedures (TGF-UC180J; Olympus America). This instrument scans over a 90-degree field of view that is forward-viewing (directed away from the tip of the scope). Potential advantages of this instrument over oblique-viewing CLA echoendoscopes include improved endoscopic visualization, improved maneuverability because of a shorter nonbending portion at the tip of the insertion tube, and device egress parallel to the insertion tube axis, possibly resulting in improved transfer of mechanical force during attempted needle/device puncture. Potential disadvantages include a more limited scanning sector (90 degrees compared with 180 degrees), and the absence of an elevator to assist in device trajectory manipulation and the securing of guidewires during device exchanges.

Fluoroscopy

Given that EUS provides an excellent imaging platform, adjunctive imaging with fluoroscopy is not always necessary for therapeutic procedures. Typically, fluoroscopy has been used to facilitate guidewire manipulation and device or stent positioning during interventions that create nonanatomic fistulae, such as pancreatic or biliary drainage procedures or luminal anastomosis creation (eg, gastrojejunostomy). Conversely, fluoroscopy is not necessary for celiac plexus neurolysis or interventions on pancreatic neoplasia (eg, fine-needle injection [FNI], fiducial placement, or radiofrequency ablation). Two case series have reported safe and effective EUS-directed drainage of peripancreatic collections including walled-off necrosis without the use of fluoroscopy.[4,5] The performance of therapeutic maneuvers such as sphincterotomy and biliary stent placement using a CLA echoendoscope without fluoroscopy has been reported in a small case series.[6]

Devices for interventional EUS procedures

Needles. Most interventional EUS procedures can be completed using standard 19G or 22G EUS-FNA needles, available from many manufacturers. Specialty needles are available that may offer potential advantages for some interventional procedures (Fig. 1). The Echotip Ultra HD ultrasound access needle (Cook Medical, Inc, Bloomington, Ind; Fig. 1A) is characterized by a sharply beveled stylet housed within a blunt, nonbeveled 19G needle sheath. The sharp stylet facilitates puncture, whereas the blunt needle tip may reduce the incidence of guidewire shearing or fracture during to-and-fro manipulations of the wire. A 19G nitinol needle (Expect 19G Flex Needle; Boston Scientific, Natick, Mass; Fig. 1B) may facilitate use in angulated scope positions (eg, postpyloric) as compared with steel needles. The Echotip Ultra Celiac Plexus Neurolysis needle (Cook Medical, Inc; Fig. 1C) is a 20G needle that features a sharp conical tip, no indwelling stylet, and several side holes in the distal aspect of the needle that may potentially increase the diffusion area of the injectate. A needle platform is available that features a delivery sheath capable of housing multiple different FNA needle calibers (Beacon FNA Exchange System; Medtronic, Minneapolis, Minn; Fig. 1D). This system may facilitate procedures when use of more than 1 needle caliber is desired (eg, FNA followed by fiducial placement). As future device technologies evolve, this type of multipurpose sheath could potentially serve as a useful conduit to deliver various unique devices. The Echotip Fiducial Needle (Cook Medical, Inc; Fig. 1E) is a 22G needle preloaded with four 5-mm-long, .43-mm diameter gold fiducials. The stylet has been augmented with a thumb ring to facilitate stylet manipulation during fiducial deployment. Similarly, the Beacon FNF Needle (Medtronic) is preloaded with 2 gold fiducials and is available in 22G and 19G calibers.

Cystotomes and other access devices. Use of devices other than FNA needles for initial transluminal puncture during EUS-guided cyst gastrostomy or biliary drainage procedures has been reported. The Cystotome cyst enterostomy knife (Cook Medical, Inc) comprises a 5F, 190-cm inner catheter with a removable .038-inch needle-knife electrode advanced to its tip, housed within a 10F, 165-cm outer catheter that has a diathermic ring electrode at its distal end. Typically, initial transluminal puncture is achieved using the needle-knife electrode, which is then retracted out of the 5F catheter to allow guidewire passage. The 10F diathermic ring may then be advanced to further enlarge the tract using cautery. Needle-knife sphincterotomes marketed for use in ERCP have also been used similarly for initial transluminal puncture.

Guidewires. Existing single-use guidewires marketed for use in ERCP are commonly used during interventional EUS procedures. Longer (≥450 cm) wires are necessary to facilitate secure wire position during device exchanges.

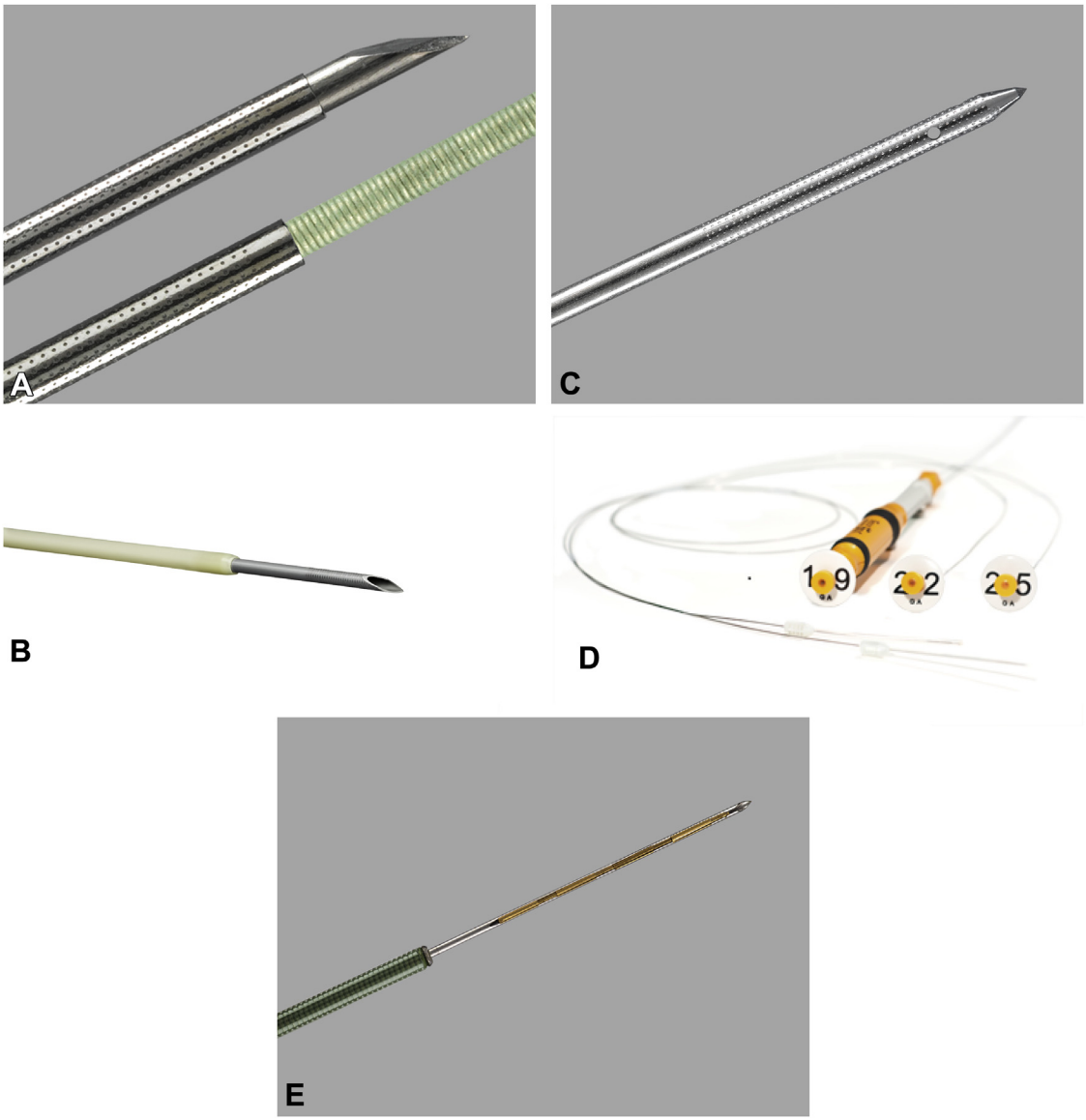

Figure 1. A, Echotip Ultra HD ultrasound access needle (Cook Medical). **B,** Expect 19G Flex Needle (Boston Scientific). **C,** Echotip Ultra Celiac Plexus Neurolysis needle (Cook Medical). **D,** BNX System (Beacon Endoscopic, Sunnyvale, Calif). **E,** Echotip Fiducial Needle (Cook Medical). Cook Medical images: Permission for use granted by Cook Medical. Boston Scientific images: Images provided courtesy of Boston Scientific Corporation. Beacon Endoscopic image: All rights reserved. Used with the permission of Medtronic.

Nineteen-gauge EUS needles accommodate guidewires up to .035 inches in caliber, whereas 22G needles accommodate guidewires up to .021 inches in caliber. In most interventional EUS procedures, wire platforms smaller than .025 inches are only used when puncture into the lumen of interest cannot be achieved with a 19G needle (eg, into a nondilated pancreatic duct). Although there is some risk for shearing off the polymer jacket when coated wires are retracted into a beveled needle, coated wires are still generally favored over monofilament stainless steel wires because of superior maneuverability. Coated wires also effectively insulate against short circuits and induced currents when used with electrosurgical devices (eg, cystotome, needle-knife sphincterotome). It has been anecdotally suggested that use of .025-inch guidewires in 19G needles may result in less shearing than with .035-inch wires.

Devices for tract dilation and drainage. An array of existing ERCP and endoluminal devices have been used for tract dilation and drainage during procedures such as cyst gastrostomy or various biliary drainage procedures. After initial guidewire placement, tract dilation can be achieved with noncautery devices such as biliary dilation catheters, biliary dilation balloons, or tapered tip ERCP cannulas or with cautery devices such as cystotomes or needle-knife sphincterotomes. Biliary dilation balloons are often used for tract dilation up to 10 mm, whereas wire-guided 12- to 20-mm esophageal-type dilating balloons are frequently used when a larger tract diameter is desired.

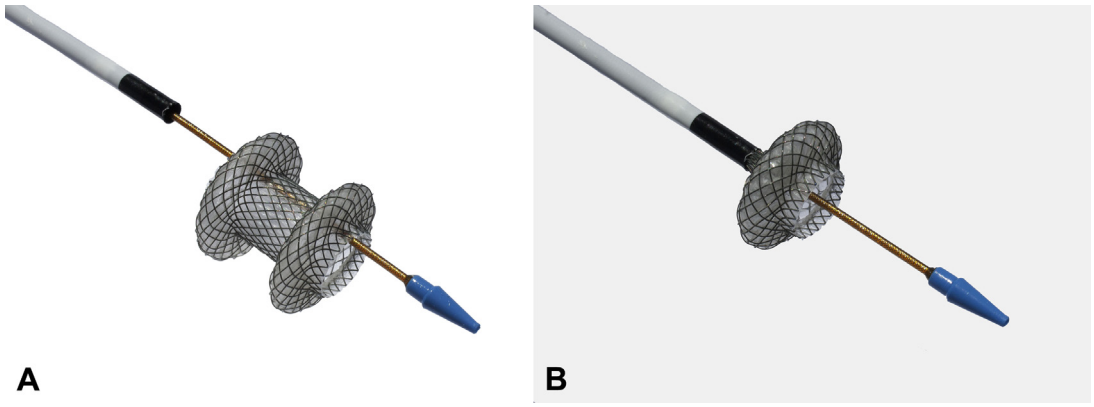

Figure 2. AXIOS Stent and Delivery System (Boston Scientific). Images provided courtesy of Boston Scientific Corporation.

Drainage has been described with a variety of plastic polymer biliary stents and self-expanding metal stents (SEMSs), either biliary or esophageal.

A stent system has been developed specifically for interventional EUS drainage procedures and is approved by the U.S. FDA for the transgastric or transduodenal drainage of pancreatic pseudocysts (AXIOS Stent and Delivery System; Boston Scientific; Fig. 2). The AXIOS delivery system comprises a control handle and a 146-cm-long wire-guided 10.8F catheter with a constrained stent at its distal end. The control handle attaches to the Luer-lock style hub on the echoendoscope instrument channel similar to FNA needle handles. The handle permits advancement and retraction of the delivery sheath in a series of 4 discrete steps that allow deployment of the AXIOS stent under sonographic and endoscopic guidance. The AXIOS stent is a fully covered SEMS with a spool-like configuration, featuring a tubular central saddle that is 10 mm in length and 10 to 15 mm in diameter, flanked by larger 21- to 24-mm diameter disks at each end of the stent that are intended to facilitate lumen apposition. Other similarly styled lumen-apposing stents have been developed (eg, NAGI stent; Taewoong Medical, Goyang, South Korea) but are not FDA-approved and are thus unavailable in the United States.

A modification of the AXIOS stent delivery system has been developed that may simplify interventional EUS drainage procedures. The AXIOS Electrocautery Enhanced Delivery System (Boston Scientific; Fig. 3) features a 9F or 10.8F stent delivery catheter with 2 thin wire electrodes positioned 180 degrees apart on the conical tip of the catheter. As such, the delivery catheter also functions as a cystotome and can accomplish the functions of transluminal access and stent deployment with a single device. Video 1 (available online at www.giejournal.org) demonstrates EUS-guided endoscopic cyst gastrostomy using an electrocautery-enhanced lumen-apposing SEMS system. The Electrocautery Enhanced AXIOS system also offers smaller AXIOS stents with 6- and 8-mm saddle diameters that are marketed for bile duct and gallbladder drainage procedures.

Fiducials and coils. Fiducials are inert radiographic markers implanted into a malignant tumor to allow more precise targeting of image-guided radiation therapy. Fiducials are typically made of gold and are available in many different configurations, including "seeds" that can be deployed via a 19G EUS needle and also smaller diameter coil designs that can be deployed with a 22G needle. Video 2 (available online at www.giejournal.org) demonstrates EUS-guided fiducial placement into a pancreatic head cancer.

Endovascular coils have been used historically for the treatment of bleeding and aneurysms. In interventional EUS, coils have been used to treat a variety of bleeding lesions, most commonly gastric varices. Coils are variable lengths of wire tightly wound into a spring shape and are usually constructed from platinum or other soft metal alloys. Many coils are enlaced with synthetic fibers (so-called wooly coils) to enhance thrombogenesis. There are no dedicated coil deployment systems for use during EUS, but existing .018-inch and .035-inch coil platforms correspond to deliverability through 22G and 19G EUS needles, respectively. The needle stylet or a guidewire can be used to mechanically deliver a coil; alternatively, hydraulic pressure from saline injected into the needle hub may also be used for coil deployment. Video 3 (available online at www.giejournal.org) demonstrates EUS-guided coil placement and glue injection into large gastric fundal varices. Both fiducials and coils come in an array of sizes and configurations and are available from multiple manufacturers.

Techniques

General principles. Interventional EUS procedures are generally more complex than routine EUS or ERCP cases; as such, proper preparation is vital to minimize the risk of adverse events and maximize the likelihood of technical success. Diligence with appropriate patient selection includes consultation with other colleagues (eg, surgery, interventional radiology) in most instances. Detailed informed consent is critical to ensure that patients and

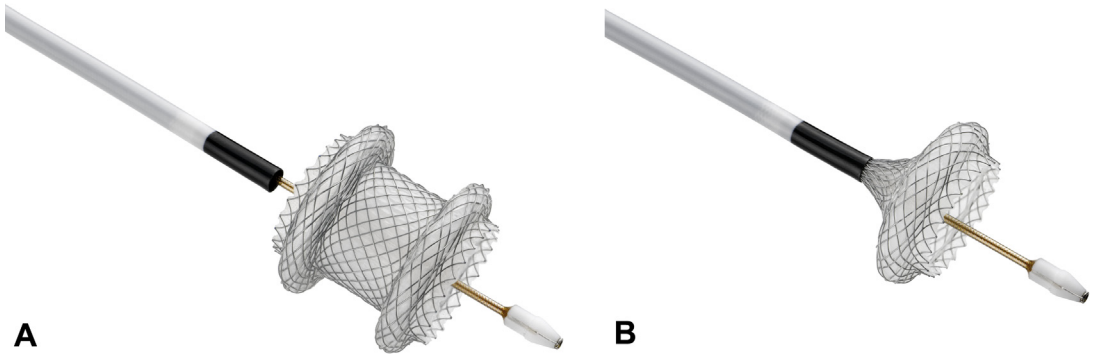

Figure 3. AXIOS Electrocautery Enhanced Delivery System (Boston Scientific). Images provided courtesy of Boston Scientific Corporation.

their families fully understand all the risks and benefits of the proposed procedure as well as the risks and benefits of competing options. For interventional EUS procedures that are still evolving (eg, EUS-guided treatment of pancreatic neoplasia) with limited data supporting their use, careful consideration should be given to conducting these procedures under the auspices of an institutional review board–approved research protocol.

Safe and effective interventional EUS procedures have been reported with a variety of sedation approaches, including moderate sedation, deep sedation, and general anesthesia. Several factors inform this decision, including anticipated procedure duration, patient comorbidities and body habitus, and perceived need for airway protection (eg, during drainage of a large pseudocyst). Cross-sectional imaging studies (ie, CT, magnetic resonance imaging) should be meticulously reviewed, or if existing imaging is inadequate for planning purposes, appropriate studies should be obtained before undertaking the interventional EUS procedure. Consideration should be given as to whether or not fluoroscopy will be helpful during the procedure. Similarly, the endoscopist should review the anticipated procedural equipment and device needs with the endoscopy team in advance to ensure that these items will be readily available during the case.

Carbon dioxide insufflation is preferable to air insufflation in most interventional EUS procedures, particularly those involving transenteric fistula creation, to minimize the risk for significant pneumoperitoneum. The need for intraprocedural antibiotics should be considered; this aspect is not well standardized for many interventional EUS procedures and thus should be an individualized decision based on procedure- and patient-specific risks. Finally, appropriate aftercare (eg, hospital admission vs same-day discharge, appropriate follow-up imaging) is essential to the safety and success of these complex interventions and should be thoughtfully addressed.

Cyst drainage. The CLA echoendoscope is used to inspect the cyst for its size, content, and proximity to the digestive tract. Cysts that are not well apposed to the gut lumen may pose a higher risk for peritonitis because of cyst or digestive tract content leaking extraluminally.[7] Although EUS-guided endoscopic cyst gastrostomy is the prototypical example of this procedure type, drainage of a variety of cysts and abscesses has been described with access points throughout the entire GI tract, from esophagus to rectum.[8] Transrectal or transcolonic drainage should be preceded by oral colonoscopy preparation or enemas to cleanse the segment to be traversed.

A duplex Doppler mode should be used to evaluate for any intervening mural vessels, including varices. The endoscopist should attempt to keep a relatively straight scope position. When cyst puncture is performed with the scope in a looped or tightly angulated position, subsequent device manipulations including stent placement will be predictably difficult. A 19G needle or cystotome is typically used to puncture the cyst under sonographic guidance. Fluid may be aspirated from the cyst to confirm needle location and also for microbial culture, particularly when infection is clinically suspected. Endoscopists who use fluoroscopy during EUS-guided cyst drainage may choose to inject contrast into the cyst to optimize fluoroscopic visualization. A $\geq$450-cm, .35-inch soft-tip guidewire is then advanced through the puncture device and coiled within the cyst under sonographic and/or fluoroscopic guidance. At this point, typically the puncture device is removed over the guidewire, and a device is selected to dilate the cyst-enterostomy tract before stent placement.

If placement of a SEMS is planned, the initial dilation may be modest (4 or 6 mm) because this is sufficient to facilitate passage of a 10F to 11F SEMS delivery catheter. Consideration should be given to postdeployment dilation of the SEMS to its full luminal diameter; this is essential when draining walled-off pancreatic necrosis (WOPN) if endoscopic necrosectomy is planned in the index case. If placement of biliary double-pigtail type stents is planned, prestent tract dilation should be more robust and may approximate 8 to 12 mm for a cyst containing only fluid or even greater (12-20 mm) for WOPN. If placement of more than 1 double-pigtail stent is planned, use of a long

10F catheter to facilitate coaxial placement of 2 guidewires into a pseudocyst will avoid the need to recannulate the cyst gastrostomy for placement of the second double-pigtail stent.[9] Video 1 demonstrates EUS-guided endoscopic cyst gastrostomy using an electrocautery-enhanced lumen-apposing SEMS system.

WOPN is a more challenging clinical entity, and many ancillary techniques have been described to aid in resolution of the cavity beyond access and drainage alone, including placement of an irrigation catheter,[10] direct endoscopic necrosectomy,[11] combined percutaneous and transenteric drainage,[12] creation of more than 1 cyst enterostomy,[13] and lavage with hydrogen peroxide,[14] among others. Stents are commonly removed endoscopically after cyst resolution on follow-up imaging, although some physicians do not routinely remove stents from drained pancreatic collections, particularly if disconnected pancreatic duct syndrome is suspected.[15]

Biliary and pancreatic access and drainage. EUS-directed pancreaticobiliary access and drainage procedures primarily represent potential alternatives to percutaneous or surgical interventions after failed ERCP but soon may directly compete with ERCP as a primary approach in selected settings. EUS-guided pancreaticobiliary interventions broadly fall into the following categories: (1) wire rendezvous procedures to facilitate retrograde pancreatic or biliary access, (2) antegrade introduction of a balloon or stent through a pancreaticobiliary-enteric fistula with subsequent dilation or antegrade stent deployment across a native or surgically created pancreatic or biliary orifice, and (3) creation and stenting of a transluminal pancreaticobiliary- or cholecystoenteric fistula.

Guidewire rendezvous (EUS-guided rendezvous [EUS-RV]). For biliary procedures, typically the common bile duct is visualized from the proximal duodenum or antrum, and a 19G FNA needle is used to puncture into the duct. Bile aspiration and needle cholangiography are then frequently used to confirm position and facilitate fluoroscopic guidance of the procedure, respectively. Subsequently, a long (≥450 cm) soft-tip guidewire is passed through the needle and manipulated across the biliary orifice and coiled in the duodenum. To accomplish this the CLA echoendoscope should ideally be in the "short" scope position while visualizing the common bile duct, such that the tip of the scope is directed caudally to allow wire advancement distally rather than proximally toward the intrahepatic biliary tree. The echoendoscope is then exchanged over the guidewire as it is withdrawn from the patient. A duodenoscope can then be advanced alongside the guidewire to the papilla, through which the transbiliary guidewire exits. The simplest approach is to then perform retrograde biliary cannulation alongside this guidewire. A more cumbersome approach is grasping the transbiliary wire with a snare or forceps and pulling it through the length of the instrument channel, allowing subsequent back-loading of a cannula or other device onto the wire.

A variant of this procedure involves puncture into the left intrahepatic biliary tree from the gastric body or cardia; this approach may be particularly useful for more proximal biliary obstructions. Fluoroscopy is used to ensure a rightward needle direction toward the hepatic hilum rather than the peripheral left intrahepatic ducts. With this approach, passage of a 4F to 5F cannula across the hepaticogastric fistula may aid in efforts to manipulate the wire within the extrahepatic bile duct and across the biliary orifice.[16]

EUS-RV for pancreatic duct access is typically considered after failed conventional retrograde cannulation and a compelling indication, such as a pancreatic duct or pancreaticojejunal anastomotic stricture. Puncture and guidewire delivery into the pancreatic duct is more technically challenging than biliary access. When possible, a 19G needle is preferable to allow the use of more stable .025-inch and .035-inch guidewires, but in some cases a fibrotic pancreas or a minimally dilated pancreatic duct may necessitate use of a 22G needle. The CLA echoendoscope is positioned in the gastric body while imaging the pancreatic duct in the area of the pancreatic body/genu, and fluoroscopy is used to ensure that the scope tip is directed toward the patient's anatomic right to ensure proper downstream orientation (toward the papilla) of the guidewire exiting the needle tip. A needle pancreatogram is then obtained to confirm intraductal position and direct wire manipulation efforts. Fully hydrophilic or hydrophilic-tip .025-inch to .035-inch angled guidewires are commonly used for their visibility, pushability, and ready alpha-loop formation. If wire manipulation is encumbered by friction at the needle tip, consideration can be given to removing the needle over the wire and advancing a tapered 4F to 5F cannula across the pancreaticogastrostomy tract into the pancreatic duct to better facilitate wire manipulation.[17] Once the wire has been advanced across the pancreatic orifice or pancreaticojejunal anastomosis, a length of wire is coiled in the small bowel. The echoendoscope is exchanged off the wire and a duodenoscope or (for patient status post-pancreaticodudenectomy) a colonoscope/enteroscope is advanced to rendezvous with the transpancreatic wire.

Antegrade dilation and stent delivery. After attaining transbiliary or transhepatic antegrade guidewire passage across the biliary orifice, an alternative to rendezvous is undertaking further interventions over the wire in an antegrade direction. This approach may be particularly useful in patients in whom endoscopic access to the biliary orifice is difficult or impossible because of tumor obstruction or surgically altered anatomy. The choledochoduodenal or hepaticogastric tract must be dilated sufficiently to allow passage of the intended therapeutic device (eg, stent delivery system). The most common antegrade intervention is deployment

of a plastic stent or SEMS across the biliary orifice solely under fluoroscopic guidance. However, other interventions such as antegrade balloon dilation to manage a biliary-enteric anastomotic stricture or balloon sphincteroplasty to facilitate biliary stone removal have also been reported.[18,19]

Antegrade interventions in the pancreatic duct are performed almost exclusively for the management of ductal or anastomotic strictures, with the intent of stent placement to improve drainage. Before antegrade stent placement, the pancreaticogastric tract first must be dilated. This is preferentially performed using noncautery dilation, with use of cautery dilation reserved for cases of difficult entry. When possible, guidewire manipulation across the pancreatic orifice or pancreaticojejunal anastomosis is preferable, with subsequent antegrade stent delivery such that the distal aspect of the stent traverses the pancreatic orifice/anastomosis and the proximal end of the stent lies in the main pancreatic duct or the stomach.

Transluminal drainage. The immediate proximity of the mid-portion of the extrahepatic bile duct to the posterior wall of the duodenal bulb is the basis for the creation of an EUS-guided choledochoduodenostomy (EUS-CDD; Video 4 available online at www.giejournal.org). The most common indication for EUS-CDD is malignant distal biliary obstruction and failed biliary access at ERCP. Unlike in EUS-RV or antegrade stenting procedures, a stable "long" scope position is favored for EUS-CDD. With the CLA echoendoscope tip in the duodenal bulb, a 19G FNA needle or cautery device is used to puncture into the common bile duct, typically in a cephalad direction. After confirmation of position with bile aspiration and/or needle cholangiography, a long .025-inch to .035-inch soft-tip guidewire is advanced into the intrahepatic biliary tree. The CDD tract is then dilated sufficiently to accommodate the intended stent delivery system. Many different stents have been described for drainage in this setting, most commonly 7F to 10F plastic double-pigtail biliary stents, partially or fully covered biliary SEMSs, and lumen-apposing SEMSs. Straight plastic biliary stents may pose a higher risk for migration, and uncovered SEMSs pose a higher risk for bile leakage.

An alternative to EUS-CDD for EUS-guided biliary drainage (EUS-BD) is the creation and stenting of a hepaticogastrostomy. This technique may be preferable to EUS-CDD in the setting of more proximal obstructions or when the duodenal bulb is obstructed or inaccessible. The left intrahepatic biliary tree is accessed with a 19G needle via the gastric cardia or body; avoidance of very peripheral ducts may reduce the risk for bile leakage. After needle cholangiography, a guidewire is then advanced either into the contralateral (right) intrahepatic biliary tree or distally into, or through, the extrahepatic bile duct. After appropriate dilation of the hepaticogastrostomy tract, stent placement is performed, typically using either long plastic biliary stents or a partially covered SEMS.

EUS-guided gallbladder drainage (EUS-GBD) has been reported using both transantral and transduodenal approaches, with drainage attained using nasobiliary drains, double-pigtail plastic stents, covered SEMSs, and lumen-apposing SEMSs. The indication for the vast majority of EUS-GBD procedures is acute cholecystitis in patients unsuitable for surgery. A variety of management approaches has been described, including using EUS-GBD as a bridge to surgery, leaving stents in indefinitely, and routine removal of stents after clinical resolution of cholecystitis and fistula maturation.[20]

In cases where the guidewire cannot traverse a pancreatic ductal stricture or obstruction, a pancreaticogastrostomy stent may be placed such that the distal aspect of the stent lies in the main pancreatic duct and the proximal end of the stent is in the stomach. A stent without side holes (eg, a biliary stent) may be preferable for this indication to avoid leakage of pancreatic or gastric secretions into the lesser peritoneal sac. The utility of a stent system in which the stent is secured to the pushing catheter with a string has been reported (Advanix; Boston Scientific) because transluminal stenting can be difficult despite prior tract dilation.[17] Pancreaticobulbostomy has also been described.[21]

Angiotherapy. Bleeding gastric varices are the most commonly reported indication for EUS-guided angiotherapy.[22,23] Patients undergoing EUS-guided variceal interventions require appropriate antibiotic prophylaxis. Both oblique-viewing and forward-viewing CLA echoendoscopes have been used in this setting, and approaches to cardia/fundus varices from the gastric lumen or in a transesophageal/transcrural manner have been reported. Varices are visualized sonographically, and blood flow before, during, and after treatments is monitored with a duplex Doppler mode. Instillation of water into the gastric fundus may facilitate sonographic imaging. Reports most commonly describe use of 19G or 22G FNA needles for delivery of therapeutic agent(s) into the variceal lumen, although deliberate identification and targeting of the afferent feeding vein into a varix has also been described. One or more embolization coils, cyanoacrylate glue, or both coil(s) and glue, are injected to induce variceal thrombosis. Fluoroscopy is typically used for adjunctive imaging, particularly if coils are used. Some endoscopists have added lipiodol to cyanoacrylate to aid in fluoroscopic visualization and to monitor for pulmonary glue embolism. EUS-guided treatment of gastric varices using coil and glue injection is demonstrated in Video 3.

EUS-guided angiotherapy has also been used for esophageal varices and a variety of ectopic varices including rectal, duodenal, choledochal, and parastomal.[24,25] Use of alternate therapeutic agents including traditional sclerosants and thrombin has been reported. EUS-guided angiotherapy has also been used in the treatment of nonvariceal GI bleeding from arterial pseudo-aneurysms,

bleeding tumors, Dieulafoy lesions, and refractory bleeding ulcers.[25]

Treatment of malignant and premalignant lesions. *Pancreatic cystic lesions.* EUS-guided ethanol ablation of potentially premalignant pancreatic cystic lesions was first reported in 2005.[26] A CLA echoendoscope is used to image the pancreatic cyst in a transgastric or transduodenal manner. It has been suggested that unilocular or oligolocular (≤3 locules) cysts 2 to 4 cm in diameter are best suited for this technique.[27] After puncture into the cyst with a 22G needle, aspiration of some or all indwelling cyst fluid is performed. The cyst is then injected with 80% to 100% ethanol in a volume equal to that of the aspirated cyst fluid, and the cyclical process of aspiration and lavage is then repeated for 3 to 5 minutes, after which the ethanol is fully evacuated from the cyst. Several reports have excluded patients in whom the cyst is clearly in communication with the main pancreatic duct, because this might increase the risk for pancreatitis. Some investigations have concluded the ethanol lavage with instillation of a 3-mg/mL paclitaxel solution into the cyst cavity.[28] In many series patients have undergone more than 1 ethanol lavage procedure. EUS-guided radiofrequency ablation of pancreatic cystic lesions has been reported in a small case series.[29]

Solid intra-abdominal malignancies. EUS-FNI of an antitumor agent (allogeneic mixed lymphocyte culture) into pancreatic adenocarcinoma was first described in 2000.[30] EUS-FNI of other agents, including immature dendritic cells, oncolytic viruses, vectors facilitating tumor necrosis factor-α gene transfer, and a DNA plasmid developed to target the expression of diphtheria-toxin gene, have been reported in small phase I studies, often adjunctively with chemotherapy or radiation therapy.[31] EUS-guided ethanol injection of pancreatic endocrine tumors has been described.[32]

EUS-guided ablation of solid pancreatic malignancies has been described using radiofrequency ablation probes,[33] cryothermal probes (capable of both radiofrequency ablation and cryogenic cooling),[34] and photodynamic therapy.[35] Brachytherapy to treat advanced pancreatic adenocarcinoma using iodine-125 (^{125}I) seeds delivered using EUS has been reported in small trials, with and without adjuvant chemotherapy.[36,37] EUS-guided interventions on nonpancreatic malignancies, including esophageal and hepatocellular carcinoma and metastatic lymph nodes, have also been reported.[38,39] All EUS-guided treatment of neoplasia remains investigational, and best indications and techniques have not been established.

Fiducial placement. EUS-guided fiducial placement to facilitate image-guided radiotherapy has been used, most commonly for pancreatic cancer. A 19G or 22G FNA needle is preloaded with 1 or more appropriate-caliber fiducial(s) by retracting the needle stylet several centimeters and back-loading the fiducial(s) into the needle tip. The needle tip may be sealed with sterile bone wax to prevent fiducial loss during needle advancement through the echoendoscope; wax may also be used to separate multiple fiducials in the needle.[40] Dedicated, preloaded fiducial needles for use in EUS are also commercially available. The CLA echoendoscope is used to visualize the tumor, and the needle is used to puncture into the mass. Deployment of the fiducial may be achieved by simultaneous retraction of the needle and advancement of the stylet. Hydraulic deployment with sterile water injection at the needle hub has also been reported. Placement of 2 to 6 fiducials into a tumor is typical, with efforts to maintain adequate spacing between fiducials. Video 2 demonstrates EUS-guided fiducial placement into a pancreatic head cancer.

Celiac plexus neurolysis and block. EUS-guided celiac plexus neurolysis (CPN) has generally been used for the management of pain associated with pancreatic cancer, whereas chronic pancreatitis pain has been addressed more commonly using celiac plexus block (CPB). In both techniques, a CLA echoendoscope is positioned in the proximal stomach and the celiac artery is visualized as it arises from the aorta. A primed 22G FNA needle is most commonly used for transgastric puncture and injectate delivery; less commonly, 19G or 25G FNA needles or a commercially available dedicated 20G CPN needle is used. Needle aspiration before injection aids in confirmation of a proper, nonvascular needle-tip position. Ethanol at concentrations of >50% (typically ≥98% "absolute" ethanol) and 6% to 7% phenol have been used as neurolytic agents, with injection volumes of 10 to 20 mL most commonly reported.[41,42] Preinjection with 1 to 20 mL of .25% to .75% bupivacaine or 1% lidocaine is frequently used to reduce immediate postprocedure pain after ethanol neurolysis. Injection protocols have used a single "central" injection at the base of the celiac artery, bilateral injections on either side of the celiac artery, direct injection into visualized celiac ganglia, and bilateral injections on either side of the superior mesenteric artery.[43-45] The same techniques are used for CPB, with the injectates usually comprising 10 to 20 mL of bupivacaine and 80 mg triamcinolone or methylprednisolone in a volume of 2 to 6 mL. Periprocedural intravenous antibiotics are frequently used for CPB. Brachytherapy of the celiac ganglia to treat pancreatic cancer pain using EUS-delivered ^{125}I seeds has also been reported.[46]

Anastomosis creation and other emerging interventions. EUS-guided creation of gastroenterostomies has been reported for the management of gastric outlet obstruction and afferent loop syndrome.[47-49] Small series describe advancing a balloon device over a previously placed orojejunal guidewire to a point beyond the obstruction. A CLA echoendoscope is then advanced through the mouth coaxially alongside the balloon catheter and is positioned in the gastric body. The balloon is inflated in the

distal duodenum or proximal jejunum and is used to assist in EUS targeting for transenteric needle puncture. After small bowel puncture with a 19G needle or cystotome, a long .035-inch wire is coiled in the bowel lumen, and tract dilation is performed to accommodate placement of a lumen-apposing SEMS. Both the original AXIOS and HOT AXIOS stent systems have been used for this indication. Direct jejunal puncture without guidance from a coaxial balloon catheter has also been reported,[49] as has the use of a novel dual-balloon catheter system that allows water filling of the bowel segment between the inflated balloons; this technology is not FDA-approved and is thus unavailable in the United States.[50]

EUS-guided puncture into the excluded stomach of patients who have undergone Roux-en-Y gastric bypass has been reported to facilitate subsequent ERCP. Instillation of contrast media and carbon dioxide via the FNA needle has been used to distend the excluded stomach to allow direct (ie, Russell introducer technique) PEG placement. Subsequent transgastric ERCP has been described in a delayed manner after gastrostomy tract maturation[51] as well as during the index case after the placement of a T-tag gastropexy[52] or fully covered esophageal stent[53] across the gastrostomy tract. Placement of a lumen-apposing SEMS across an EUS-created gastrogastric or jejunogastric fistula to facilitate transfistula ERCP in Roux-en-Y gastric bypass patients has also been reported.[54]

OUTCOMES DATA AND COMPARATIVE EFFECTIVENESS

Cyst drainage

Pancreatic pseudocysts. A systematic review of 2115 patients in 57 studies reported pooled mean technical and clinical success rates of 97% and 90%, respectively, for EUS-guided drainage of pancreatic pseudocysts, with a mean adverse event rate of 17% and a mean recurrence rate of 8%.[31] In a randomized controlled trial (RCT) of 40 patients with pancreatic pseudocysts, 20 patients each were assigned to open surgical cyst gastrostomy or to EUS-guided cyst gastrostomy and ERCP with pancreatic duct stenting if a fistula was observed.[55] The index intervention was successful in 100% of patients in the surgical arm and 95% of the patients in the endoscopy arm, and cyst recurrence was observed in 1 patient in the surgical arm and no patients in the endoscopy arm during a 24-month follow-up period. Endoscopic intervention was associated with a shorter median hospital stay (2 days vs 6 days, $P < .001$) and lower mean cost ($7011 vs $15,052, $P = .003$).

In 2 RCTs evaluating EUS-guided cyst gastrostomy versus conventional endoscopic cyst gastrostomy, EUS-guided drainage was associated with higher rates of technical success (94%-100%) than conventional endoscopic drainage (33%-72%), with failures in conventional endoscopic drainage occurring almost exclusively in patients with nonbulging pseudocysts.[56,57] No significant difference in rates of adverse events was reported in these small trials, although 2 serious bleeding events, including 1 death, were seen in the conventional drainage group in 1 study.[57] Similar rates of technical success, clinical success, and adverse events have been reported for EUS-guided drainage and conventional endoscopic drainage of pancreatic pseudocysts when conventional drainage is applied to patients with bulging collections and no evidence of portal hypertension.[58]

Prospective comparative data are lacking regarding the effectiveness of stent type and number for EUS-guided pancreatic pseudocyst drainage; available retrospective data do not demonstrate a difference in clinical success rates for 7F plastic stents versus 10F plastic stents, 1 plastic stent versus more than 1 plastic stent, or for plastic stents versus SEMSs.[59-61] In a Korean RCT of 50 patients with pancreatic fluid collections undergoing EUS-guided drainage, no differences in technical or clinical success or adverse events were observed in patients randomized to fully covered SEMSs versus plastic stents, but median procedure time was significantly shorter in the SEMS arm (15.0 minutes vs 29.5 minutes, $P < .01$).[62] In a multicenter RCT of 58 patients with pancreatic fluid collections undergoing EUS-guided drainage, no differences in any clinical outcomes were observed in those procedures performed with a forward-viewing CLA echoendoscope versus an oblique-viewing CLA echoendoscope.[63]

In a small single-center RCT of 28 patients status post-successful EUS-guided drainage of pancreatic pseudocysts, the rate of pseudocyst recurrence was significantly higher in those patients randomized to removal of the transmural stents (5/13, 38%) compared with patients whose stents were not removed (0/15, $P = .013$).[15] However, in a prospective series of patients who underwent EUS-guided pseudocyst drainage with fully covered SEMSs, the SEMSs were removed in 42 patients at 3 weeks, and the pancreatic duct was evaluated with an MRCP.[64] No pseudocyst recurrences were observed in 37 patients without pancreatic duct pathology or in 3 patients who had a pancreatic stent placed for an observed pancreatic duct leak, whereas 2 of 2 patients with disconnected pancreatic duct syndrome developed recurrent pseudocysts.

Walled-off pancreatic necrosis. The management of WOPN is controversial with multiple treatment options including conservative management, percutaneous drainage, endoscopic drainage, and various surgical approaches. Several factors, including presence of infection, size and location of the collection, the proportional amount of intracavitary necrosis, patient comorbidities, and local expertise, influence treatment outcomes. An understanding of reported outcomes with available options will inform the endoscopist's decision regarding the role of EUS-guided drainage. The PANTER trial was an RCT of 88

patients with documented or suspected infection in WOPN in which 45 patients were assigned to laparotomy and necrosectomy and 43 patients were randomized to a step-up approach that most commonly featured retroperitoneal percutaneous catheter drainage followed by video-assisted retroperitoneal debridement.[65] Fewer patients in the step-up arm (17/43, 40%) experienced a composite primary endpoint of major adverse events or death as compared to the open necrosectomy arm (31/45, 69%, $P = .006$). The PENGUIN trial was an RCT of 22 patients with documented or suspected infection in WOPN, most of whom had failed initial percutaneous drainage.[66] Ten patients underwent EUS-guided drainage with plastic stents and a nasocystic flushing catheter and subsequent direct endoscopic necrosectomies, whereas 10 patients underwent video-assisted retroperitoneal debridement or laparotomy and necrosectomy. Fewer patients in the endoscopic arm experienced a composite clinical endpoint of major adverse events or death (2/10) than in the surgical arm (8/10, $P = .03$), and endoscopic treatment was not associated with new-onset multiple-organ failure (0/10), unlike surgery (5/10, $P = .03$).

A systematic review of 10 studies comprising 260 patients undergoing endoscopic necrosectomy (with EUS-guided entry in most studies) reported complete resolution in 76% and a mean adverse event rate of 27%.[67] In a single-center retrospective analysis of 45 patients with WOPN, successful resolution was attained in 45% of patients (9/20) managed with endoscopic transmural cyst drainage using plastic stents and nasocystic flushing catheters, compared with 88% of patients (22/25) managed with the same interventions plus direct endoscopic necrosectomy ($P < .01$).[68] In a Japanese single-center retrospective analysis of 70 patients with WOPN treated with EUS-guided drainage, plastic stents and nasocystic flushing catheters were placed in 27 patients, and lumen-apposing SEMSs (usually without a nasocystic flushing catheter) were placed in 43 patients.[69] Direct endoscopic necrosectomy was used in both groups as needed but was not performed at the index drainage procedure. Although there were no differences in technical or clinical success rates or total costs, shorter procedure times were noted in the SEMS group for both the index procedure (29 minutes vs 43 minutes, $P < .001$) and for reinterventions (35 minutes vs 42 minutes, $P < .001$). At this time the role for adjunctive treatment measures (eg, direct necrosectomy, flushing catheters, multiple-cyst enterostomies, hydrogen peroxide lavage) in the EUS-guided drainage of WOPN is unknown when a large-caliber (>10 mm) lumen-apposing SEMS is used.

Nonpancreatic abdominal and pelvic collections. Data for EUS-guided drainage of various nonpancreatic collections and abscesses in the abdomen and pelvis remain at the case report and small case series level. A systematic review of 120 patients in 20 studies reported pooled mean technical and clinical success rates of 99% and 92%, respectively, for EUS-guided drainage of these collections.[31]

Biliary and pancreatic access and drainage

Biliary access and drainage. A single-center, retrospective cohort study of failed biliary cannulation at ERCP compared 144 patients who underwent precut sphincterotomy with 58 patients who underwent transduodenal EUS-RV. The technical success of precut sphincterotomy was 90% compared with 98% for EUS-RV ($P = .03$).[70] However, the pooled technical success rate for biliary EUS-RV in a review of 7 series comprising 247 patients was 74% (83% for transduodenal and 62% for transhepatic) with an overall adverse event rate of 11% (8% for transduodenal and 17% for transhepatic).[71]

Most outcomes data for EUS-BD are series in which multiple techniques are used, often in a sequential manner (eg, transluminal stenting following failed EUS-RV). For all EUS-BD procedures, technical success rates of 86% to 96% and clinical success rates of 87% to 92% have been reported.[16,72-77] Adverse event rates have ranged from 9% to 34%, most commonly bile leak, bleeding, cholangitis, or pneumoperitoneum. In 1 retrospective series of 68 patients treated with a mix of EUS-BD techniques, hepatic access was associated with a higher rate of adverse events compared with duodenal access (30.5% vs 9.3%, $P = .03$).[73] An RCT of 49 patients with unresectable malignant distal common bile duct obstruction and failed ERCP assigned 24 patients to EUS-CDD and 25 patients to EUS-hepaticogastrostomy, using partially covered SEMSs for both.[78] In this trial, overall rates of technical success (94%), clinical success (85%, per protocol), and adverse events (16%) were reported, without significant differences between the 2 approaches.

Small prospective trials have compared EUS-BD with conventional drainage approaches. Twenty-five patients with malignant distal common bile duct obstruction and failed ERCP were randomized to biliary drainage with a percutaneous transhepatic biliary drain (n = 12) or EUS-CDD (n = 13) using a 10 mm × 60 mm partially covered SEMS.[79] All procedures were technically and clinically successful in both groups, and no differences were reported in adverse events or total cost. The same author reported an RCT of 32 patients with unresectable malignant distal biliary obstruction that assigned 16 patients to surgical biliary bypass (hepaticojejunostomy) and 16 patients to EUS-CDD.[80] No significant differences in technical success, clinical success, quality of life, or survival were reported.

Gallbladder access and drainage. A systematic review of 157 patients in 20 studies reported pooled mean technical success rates of 97.5% and clinical success rates of 99.3% for EUS-GBD drainage, with a mean adverse event rate of 8% (eg, pneumoperitoneum, bile leakage, stent migration).[81] An RCT of 59 patients with acute cholecystitis who were not responding to conservative

therapy and who were unsuitable for cholecystectomy assigned 29 patients to percutaneous transhepatic gallbladder drainage and 30 patients to EUS-guided placement of a 5F nasobiliary tube into the gallbladder via either transduodenal or transgastric puncture. EUS-GBD and percutaneous drainage showed similar technical (97% vs 97%) and clinical (100% vs 96%, per protocol) success rates and similar rates of adverse events (7% vs 3%).[82] However, median pain scores at 24 hours postprocedure were significantly lower in the EUS-GBD group (1 vs 5, $P <$ .001). Currently, no data are available to guide the best access point or drain/stent type for EUS-GBD.

Pancreatic access and drainage. Data for EUS-guided pancreatic access and drainage are limited to case series with fewer than 50 patients. Technical success rates are not as high as those reported for EUS-BD. The technical success specifically for EUS-RV in 2 larger series was 48% to 56%,[77,83] whereas the overall technical success for EUS-guided pancreatic drainage (any transpapillary/transanastomotic or transluminal stent) typically approximates 70% to 75%.[17,77,84] EUS-RV has been associated with mild adverse events, including mild pancreatitis and mild pancreatic fluid leakage.[17] In contrast, serious adverse events have been reported with transluminal stenting, including severe pancreatitis, peripancreatic abscess, and hematoma formation; the rate of severe events has approximated 6% to 7%.[17,21,77,84] Nonspecific postprocedural pain is a common event.[84]

Angiotherapy

The management of bleeding gastric varices is complex, and a thorough discussion of all considerations is beyond the scope of this document. Transjugular portosystemic intrahepatic shunts, balloon-occluded retrograde transvenous obliteration, and surgical shunts represent common non-endoscopic therapeutic options. Endoscopic injection of cyanoacrylate has demonstrated higher hemostasis rates and lower rebleeding rates than sclerotherapy or band ligation, although with a finite rate of adverse events including glue embolization.[85] EUS-guided variceal interventions represent another option in the treatment armamentarium for gastric varices, but at present no data directly compare EUS-guided treatments with conventional endoscopic or nonendoscopic treatment approaches.

A multicenter retrospective study evaluated 30 patients with gastric varices who were poor candidates for, refused, or had failed transjugular portosystemic intrahepatic shunts and who had cardiofundal varices fed by a single large vessel.[22] In 11 patients in whom the feeding vein could be identified by sonographic and fluoroscopic imaging, 1 or more .035-inch coils were deployed into the feeding vein until thrombosis was documented by contrast injection. In the remaining 19 patients, 1 mL of a 1:1 mixture of N-butyl-2-cyanoacrylate and lipiodol was injected into the varix. All patients had a second EUS 1 week later with repeat delivery of the same agent initially used if incomplete variceal obliteration was observed. Complete variceal obliteration was achieved in 94.7% and 90.9% ($P =$ not significant [NS]) of the patients treated with cyanoacrylate and coils, respectively, in a mean of 1.4 treatments. Symptomatic adverse events were infrequent and not different between the 2 groups, but asymptomatic pulmonary glue emboli were detected in 9 of 19 patients (47%) on postprocedure chest CTs that were performed routinely in this treatment protocol.

A single-center retrospective series described 112 patients with recently bleeding cardiofundal gastric varices and an additional 40 patients with high-risk gastric varices that had never bled, all of whom underwent EUS-guided coil and glue injection. Procedures were performed using either forward-viewing or oblique-viewing CLA echoendoscopes, and the route of puncture was preferably in a transesophageal, transcrural manner and less often in a transgastric manner.[86] One .035-inch coil was deployed followed by injection of 1 mL 2-octyl-cyanoacrylate and Doppler reassessment of variceal flow, with delivery of additional coils or glue if obliteration was incomplete. The procedure was technically successful in 151 of 152 patients; the mean number of coils deployed was 1.4 and the mean volume of glue was 2 mL per patient. Of 125 patients who had at least 30 days of follow-up, 20 (16%) had recurrent upper GI bleeding. Ten of these 20 recurrent bleeding events were because of gastric varices, with the remainder caused by other sources. Procedure-related adverse events were reported in 9 patients (7%), including 1 pulmonary embolism.

An RCT of 50 cirrhotic patients with medium or large esophageal varices assigned 25 patients to conventional sclerotherapy with ethanolamine oleate and 25 patients to EUS-guided sclerotherapy in which the needle was deliberately positioned in a feeder vessel rather than the varix itself.[24] The mean number of sessions until eradication was 4.3 for the conventional group and 4.1 for the EUS group ($P =$NS). Adverse events were mild and similar, and over a follow-up period of approximately 2 years, variceal recurrence was seen in 4 patients in the conventional group and in 2 patients in the EUS group ($P =$NS). Outcomes data for EUS-guided treatment of ectopic varices and for the treatment of nonportal hypertensive bleeding lesions are limited to case reports and small case series.

Treatment of malignant and premalignant lesions

In a double-blinded RCT (n = 42) comparing pancreatic cyst lavage with ethanol versus saline solution, complete cyst resolution after lavage with ethanol was observed in 33% of patients.[87] Other prospective series have reported complete cyst resolution in 9% to 38% of patients after ethanol lavage.[88,89] Complete cyst resolution has been numerically higher in series describing ethanol lavage and paclitaxel instillation, ranging from 50% to 79%.[90]

Pancreatic carcinoma has been observed developing in a cystic neoplasm that had partially responded to ethanol lavage.[88] Outcomes data for various EUS-guided interventions (eg, EUS-FNI, radiofrequency ablation, photodynamic therapy, etc) on solid malignancies are limited to small phase I trials and case reports.

Fiducial placement. In a systematic review of 13 studies comprising 278 patients (most with pancreatic tumors), technical success with fiducial placement ranged from 85% to 100%.[31] In a retrospective single-center series that compared EUS-guided placement of .8-mm diameter, 5-mm long fiducials versus .35-mm diameter, 10-mm long fiducials, the .8-mm fiducials were associated with improved visibility on CT, but no differences were noted in technical difficulty of placement or fiducial migration rate between the 2 types.[91] Available data suggest that fiducials improve the accuracy of daily target delineation of pancreatic tumors in patients undergoing imaging-guided radiotherapy as compared with localization using adjacent bony anatomy or biliary stents.[92]

CPB and CPN. In a meta-analysis and systematic review of observational series of EUS-CPN for the management of pancreatic cancer pain, EUS-CPN was associated with pain relief in 80.1% of patients.[93] Similarly, an RCT of 96 patients with inoperable pancreatic adenocarcinoma randomized 48 patients each to EUS-CPN and to conventional pain management.[94] Pain relief was significantly better in the EUS-CPN group at 3 months, and there was a trend toward reduced opiate utilization at 3 months. Although nonrandomized data regarding the relative efficacy of 1 (central) versus 2 (bilateral) injections at EUS-CPN have been conflicting,[43,95] the only RCT to address this issue of technique found no difference in the proportion of patients that experienced pain relief, in the rapidity of onset, or in the duration of pain relief between patients receiving 1 or 2 injections.[96] In a retrospective series of EUS-CPN that compared bilateral injection on either side of the celiac artery versus the superior mesenteric artery, the injectate contained contrast media and patients underwent postinjection CT scanning.[44] Pain relief was strongly correlated with the extent of diffusion of the injectate; injections around the superior mesenteric artery were associated with a broader diffusion of the injectate on CT imaging and better pain reduction at 7 and 30 days compared with injections around the celiac artery. Both an RCT (n = 34) and a larger, nonrandomized series (n = 64) have indicated superior pain relief with direct injection of the celiac ganglia compared with the traditional EUS-CPN technique,[45,97] and in a multivariate model of predictors of response, visualization of the ganglia was the best predictor of pain relief.[45] Descriptions of EUS-CPN for chronic pancreatitis pain are limited.[43]

A systematic review of 6 studies comprising 221 patients undergoing EUS-CPB reported a pooled estimate of 51.5% (95% confidence interval, 32%-100%) for pain relief.[98] Two RCTs have reported improved pain outcomes for chronic pancreatitis patients assigned to EUS-CPB as compared with percutaneous CPB.[99,100] An RCT (n = 50) that evaluated patients undergoing EUS-CPB for chronic pancreatitis pain found no difference in the proportion of patients that experienced pain relief or the onset or duration of pain relief between the groups of patients that received 1 versus 2 injections.[96] An RCT (n = 40) assigned 21 patients to EUS-CPB with bupivicaine + triamcinolone and 19 patients to EUS-CPB with bupivicaine alone and reassessed pain scores at 1 month using a validated pain disability index (0-70 scoring possible).[101] The proportion of patients that experienced a 10-point decrease in the pain disability index at 1 month (the primary endpoint) was low, approximating 15% in both treatment arms (P =NS).

Anastomosis creation and other emerging interventions

Outcomes data for EUS-guided gastrojejunostomy creation and for EUS-guided access to the excluded stomach in Roux-en-Y gastric bypass patients requiring ERCP are limited to case reports and small case series.

SAFETY

A large systematic review of EUS-guided drainage of pancreatic fluid collections reported a pooled adverse event rate of 17%, with bleeding, infection, and stent migration representing the most common adverse events.[31] Perforation requiring surgery was reported in 1.3% of patients, and death occurred in .2% of patients in this review. The rate of adverse events has been reported to be higher (up to 37%) in the drainage of WOPN as compared with pseudocysts.[102]

Pooled adverse event rates for EUS-guided biliary drainage of 14% to 18% have been reported, most commonly bile leak, bleeding, cholangitis, or pneumoperitoneum.[103] A lower pooled adverse event rate has been reported for EUS-RV biliary drainage (11%) as compared with transmural techniques such as EUS-CDD (19%) and EUS-hepaticogastrostomy (24%).[103] Reported adverse event rates associated with EUS-guided pancreatic drainage have approximated 20% (range, 7%-55%), including pancreatitis, pancreatic leakage, peripancreatic abscess, and hematoma formation.[31,104] EUS-RV may be associated with fewer adverse events than transenteric stenting of the pancreatic duct.[17] Guidewire shearing or fracture is an uncommon but important adverse event of EUS-guided pancreaticobiliary drainage; use of specialty access needles and/or .025-inch wires potentially may limit the incidence of this adverse event.

Clinically significant pulmonary glue emboli complicate about 1% (0%-4.3%) of endoscopic procedures to treat gastric varices with cyanoacrylate.[105] Although these data are from non–EUS-guided injections, there is no

indication that the incidence with EUS-guided injection would differ, and the rate of asymptomatic pulmonary glue emboli was 47% in a series using EUS.[22] In a large series of 152 patients with gastric varices undergoing EUS-guided coil and glue injection, the reported clinically evident embolization rate was .6%.[86] Infectious adverse events are common in patients with cirrhosis with variceal bleeding, and antibiotic prophylaxis is recommended irrespective of the variceal treatment approach.[106]

EUS-guided treatment of neoplasia remains investigational, and the safety profile of various reported techniques is not well defined. Fiducial placement has been associated with a very low incidence of adverse events. Minor, manageable adverse events including hypotension, diarrhea, and a transient increase in pain have been reported in 21% of patients undergoing EUS-CPN and 7% of patients undergoing EUS-CPB.[103] More serious adverse events, including paraplegia because of anterior spinal artery thrombosis or multiorgan ischemia (in some cases, fatal) because of celiac artery thrombosis, have been described in case reports.[107] EUS-CPB has rarely been associated with infectious adverse events.

EASE OF USE

Need for specialized training

Interventional EUS procedures are typically more challenging than either routine ERCP or diagnostic EUS procedures and frequently are associated with a significant risk for adverse events. Endoscopists undertaking interventional EUS procedures should be highly skilled in ERCP techniques such as wire manipulation and fluoroscopic interpretation in addition to being proficient in EUS-FNA. Although prior ASGE documents have suggested minimum procedure thresholds for assessing competency in ERCP and EUS,[108,109] there are no defined competency criteria for interventional EUS procedures. Further, within interventional EUS procedures there is a spectrum of difficulty and risk, and individual endoscopists may choose to pursue proficiency at only selected procedures. Even under the auspices of fourth-year advanced endoscopy training programs at high-volume centers, trainees may not attain proficiency in many interventional EUS procedures, with these skills ultimately acquired in clinical practice, ideally with guidance from a mentor.

In a summary from a 2011 consortium meeting of experts regarding EUS-BD, recommendations made regarding necessary competencies for EUS-BD included high volume (>200-300 EUS and ERCP per year), experienced (>4-5 years of experience), and skilled (95%-98% success rate for standard ERCP with normal anatomy) endoscopists practicing in a center with interventional radiology (IR) and/or pancreaticobiliary surgery backup.[110] Other experts recommend completion of >10 (and preferably >20-25) EUS-guided pseudocyst drainage procedures before attempting EUS-guided pancreaticobiliary drainage and recommend beginning with easier EUS-BD techniques such as EUS-RV before attempting more complex biliary techniques such as EUS-hepaticogastrostomy or any pancreatic intervention.[111]

Various training models have been used to teach interventional EUS procedures, including realistic but expensive live porcine models.[112] An ex vivo model for training in EUS-BD procedures that includes a 3-dimensional printer–constructed polycarbonate model of the biliary tree surrounded by porcine liver tissue has been used in interventional EUS courses.[113] Similarly, an ex vivo porcine model that replicates pancreatic fluid collections using gelatin-filled segments of sigmoid colon that are capable of withstanding multiple punctures has also been used in interventional EUS courses.[114] A virtual endoscopic simulator with an EUS module (GI Mentor; Simbionix, Cleveland, Ohio) and a physical model with parenchymal organs and key blood vessels (Olympus America) have been used for training in diagnostic EUS. The role of simulators in interventional EUS training is not yet known.

Logistical issues

Most interventional EUS procedures are more resource-intensive than routine endoscopic procedures. Factors such as anticipated duration, the need for concomitant EUS and fluoroscopic imaging, the potential need for anesthesia assistance, and the potential need for specialized devices should all be considered as these procedures are planned. Also, because some procedures may not be successful, a contingency plan should be in place, such as proceeding to EUS-CDD or referral to interventional radiology for percutaneous drainage if a biliary EUS-RV is unsuccessful.

FINANCIAL CONSIDERATIONS

Reimbursement

As a field in evolution, the coding and reimbursement for interventional EUS procedures has undergone recent changes but remains inconsistent, with dedicated codes for some interventions but not others. The Current Procedural Terminology codes for EUS and EUS-FNA when imaging is conducted from the esophagus, stomach, and duodenum are 43259 and 43242, respectively. If imaging is conducted at only 1 or 2 of these sites, code 43237 is used for EUS and 43238 for EUS-FNA. If imaging is conducted from esophagus alone, codes 43231 and 43232, respectively, are used.

Code 43240 is used for endoscopic transmural pseudocyst drainage and includes needle aspiration and the use of EUS. There is no existing Current Procedural Terminology code for endoscopic debridement of WOPN; the use of code 48999 (unlisted procedure, pancreas) is most

appropriate, either as a single code or together with the base service(s) to which it is added. When reporting unlisted or "miscellaneous" codes, supporting documentation should be included with each claim. The information should detail the nature, extent, and need for the procedure and the time, effort, and equipment necessary to provide the procedure. Additional items to include are the complexity of symptoms, final diagnosis, pertinent patient findings, diagnostic and therapeutic procedures, concurrent problems, and follow-up care. It is helpful in such a cover letter to compare the work Relative Value Unit (RVU) or total RVU for the procedure to an existing code of similar intraservice time and intensity. For example, the supporting letter in this context might state, "for comparison to an existing service, the intra-service time (scope in to scope out) and intensity for this procedure was approximately twice that of 43240." Although code 48105 describes pancreatic necrosectomy, this is an open surgical code with a 90-day global service. Although this code could potentially be reported with a 52 (reduced service) modifier to describe endoscopic necrosectomy, any related services within 90 days would not be separately reportable, and experience and outcomes with this approach to coding are lacking. EUS-guided transrectal drainage of an abscess should be reported using codes 45342 (flexible sigmoidoscopy with EUS-FNA) and 49407 (image-guided fluid collection drainage by catheter, transrectal or transvaginal), which are zero-day global services.

For EUS-guided pancreaticobiliary drainage procedures, code 43253 describes EUS-guided transmural injection. However, for the steps beyond ductography, dedicated codes are lacking. The codes for unlisted procedures in the biliary tract (47999) and pancreas (48999) may be used, along with codes for endoscopic catheterization and radiologic supervision and interpretation of the biliary ductal system (74328) and pancreatic ductal system (74329), where appropriate. Open or laparoscopic biliary-enteric anastomosis codes (eg, 47760) are not applicable to endoscopic procedures.

The code most relevant to EUS-guided angiotherapy is 43253 (EUS-guided transmural injection). Many cancer-related EUS interventions such as fiducial placement, ethanol ablation, or FNI can also be described with the 43253 code. The codes 64530 and 64680, which describe CPB and CPN, are not separately reportable because these are components of 43253.

AREAS FOR FUTURE RESEARCH

For newer therapeutic EUS procedures that compete with existing interventions, such as EUS-BD, comparative outcomes data, ideally in the form of RCTs, will help define the role of these EUS interventions within the traditional armamentarium. EUS-GBD is an exciting and potentially disruptive technique but requires both refinement of technique and prospective evaluation in larger and more diverse study populations to define its clinical role. Outcomes data to date for EUS-guided ablation of pancreatic cystic neoplasia have been mixed; further trials are necessary before adoption in clinical practice. For interventional EUS procedures that are well established, such as drainage of pseudocysts and WOPN, cost-effectiveness studies are needed as new and effective, but expensive, dedicated devices are evaluated. Many interventional EUS procedures remain in an investigational phase, such as EUS-guided treatment of solid neoplasia, EUS-guided treatment of gastric varices, or EUS-guided gastrojejunal anastomosis creation. Use of these techniques should be limited to institutional review board–approved protocols at this time.

SUMMARY

The field of interventional EUS encompasses a broad range of procedures and continues to evolve rapidly. Many interventional EUS procedures harbor potential to augment or replace traditional interventions that are more invasive or cumbersome. However, interventional EUS procedures are frequently technically challenging, and a strong background in both EUS and ERCP is needed. This skill barrier, along with currently inadequate reimbursement, may limit interventional EUS to tertiary centers for the near future. However, as further research better defines the techniques and clinical applications for these procedures and as dedicated devices evolve, adoption appears likely to increase.

DISCLOSURE

All authors disclosed no financial relationships relevant to this publication.

Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; CLA, curved linear array; CPB, celiac plexus block; EUS-BD, EUS-guided biliary drainage; EUS-CDD, EUS-guided choledochoduodenostomy; EUS-CPN, EUS-guided celiac plexus neurolysis; EUS-GBD, EUS-guided gallbladder drainage; EUS-RV, EUS-guided rendezvous; FDA, U.S. Food and Drug Administration; FNI, fine-needle injection; RCT, randomized controlled trials; SEMS, self-expanding metal stent; WOPN, walled-off pancreatic necrosis.

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