REVIEW
Print ISSN 2234-2400 / On-line ISSN 2234-2443
Clin Endosc 2014;47:432-439
http://dx.doi.org/10.5946/ce.2014.47.5.432

Open Access

Endoscopic Ultrasound-Guided Treatment beyond Drainage: Hemostasis, Anastomosis, and Others

Jessica L. Widmer and Michel Kahaleh
Division of Gastroenterology and Hepatology, Weill Cornell Medical College, New York, NY, USA

Since the introduction of endoscopic ultrasound (EUS) in the 1990s, it has evolved from a primarily diagnostic modality into an instrument that can be used in various therapeutic interventions. EUS-guided fine-needle injection was initially described for celiac plexus neurolysis. By using the fundamentals of this method, drainage techniques emerged for the biliary and pancreatic ducts, fluid collections, and abscesses. More recently, EUS has been used for ablative techniques and injection therapies for patients with for gastrointestinal malignancies. As the search for minimally invasive techniques continued, EUS-guided hemostasis methods have also been described. The technical advances in EUS-guided therapies may appear to be limitless; however, in many instances, these procedures have been described only in small case series. More data are required to determine the efficacy and safety of these techniques, and new accessories will be needed to facilitate their implementation into practice.

Key Words: Endosonography; Therapeutic endoscopy; Endoscopic ultrasound-guided drainage; Endoscopic ultrasound-guided intervention

INTRODUCTION

Endoscopic ultrasound (EUS) was initially introduced in the 1990s. The radial echoendoscope was used as a diagnostic tool primarily for cancer staging and evaluating surgical resectability. With the advent of the linear array echoendoscope, EUS rapidly developed into a therapeutic instrument used to perform fine needle aspiration (FNA) for cytologic diagnosis. It is now an accepted therapeutic modality with continually evolving indications, including fine needle injection (FNI), drainage of pancreatic fluid collections (PFCs) and abscesses, EUS-guided biliary and pancreatic drainage after a failed endoscopic retrograde cholangiopancreatography (ERCP), and additional innovative techniques that are currently being investigated. In this article, we review the role of therapeutic EUS for gastrointestinal (GI) diseases.

Received: May 16, 2014 **Accepted:** June 20, 2014

Correspondence: Michel Kahaleh
Division of Gastroenterology and Hepatology, Weill Cornell Medical College, 1305 York Avenue, 4th Floor, New York, NY 10021, USA
Tel: +1-646-962-4000, **Fax:** +1-646-962-0110, **E-mail:** mkahaleh@gmail.com

EUS-FNA

EUS-FNA is a simple, cost-effective technique that has been implemented to obtain tissue for the diagnosis of both the GI tract and other areas outside of the GI luminal tract, including pancreatic cysts and masses, GI subepithelial lesions, and lymph nodes.[1-6] EUS provides a higher sensitivity than both computed tomography (CT) and magnetic resonance imaging, and has proved to be advantageous in reaching a diagnosis after the failure of other diagnostic techniques.[1,3,6,7] It enables tissue acquisition of tiny lesions (<5 to 10 mm) that are often too small to be identified with other imaging modalities, or lesions that are encased by surrounding vasculature.[8] EUS is now accepted as the first-line diagnostic tool for the above-mentioned lesions.

CELIAC PLEXUS BLOCK AND NEUROLYSIS

Celiac plexus neurolysis (CPN) is the injection of absolute alcohol to destroy the sympathetic plexus near the celiac axis to relieve abdominal pain, traditionally in patients with pancreatic cancer or other malignancies. Celiac plexus block (CPB) is the injection of steroids to inhibit the celiac ganglion function mainly in patients with benign conditions such as chronic pancreatitis. A 19-gauge FNA needle is inserted under EUS guidance adjacent to the lateral aspect of the aorta at the level of the celiac trunk. Aspiration should be performed to rule out needle placement within a vessel. This approach allows visualization of intervening vessels and better visualization of the sympathetic ganglia.[9] Absolute alcohol (CPN) or triamcinolone (CPB) is injected into the region of the ganglia under ultrasound guidance. Bupivacaine is also added for initial pain relief.

CPN has a variable reported success rate between 70% and 90%.[10,11] Many patients still require the same dose of analgesic; thus, CPN should be considered an adjunct to pain regimens.[12] Studies suggest that the EUS-guided approach is superior to CT-guided CPN because the celiac plexus can be easily accessed through a transgastric approach, EUS provides continuous real-time visualization of the target area, and color flow Doppler can be used to avoid regional vasculature.[10,11,13] The benefit of repeated CPN was demonstrated in a study of 24 patients; however, the rate of successful pain relief was lower than that for the index CPN procedure (29% vs. 67% at 1 month follow-up).[10] CPB appears to have more of a marginal benefit with a reported success rate of 30% to 60% in chronic pancreatitis patients.[14] The duration of relief may be up to only 3 months; therefore, it should be reserved for periods of severe pain that had not been relieved by conventional methods such as endoscopic treatment of pancreatic duct strictures or stones.[15] The complications of these procedures are fairly rare but include transient hypotension and diarrhea.[9]

EUS-GUIDED DRAINAGE

Pancreatic fluid collections

PFCs can develop as a result of severe pancreatitis. These fluid collections are categorized, on the basis of the Atlanta classification, as acute fluid collections, pseudocysts, or necrosis.[16] Drainage may be indicated if the patient has abdominal pain, rapid enlargement in the size of the collection, biliary or GI tract obstruction, or concern for infection.[17-21] In the past, drainage options included percutaneous or surgical approaches; however, EUS-guided transmural drainage of PCFs is now widely reported in the literature. This minimally invasive technique is now considered to be a feasible option for definitive endoscopic treatment. EUS guidance is preferred over the conventional method of endoscopic drainage as it can localize nonbulging collections and can be performed in patients with venous collaterals, those with coagulopathies, and those with a small anatomic window for drainage.[22]

The linear echoendoscope is advanced into the stomach or the duodenum and is used to locate the PFC. Color flow Doppler is used to localize any regional vasculature. A 19-gauge FNA needle is used to puncture the collection under ultrasound guidance, and fluid is aspirated for culture. A guidewire is coiled within the fluid collection, and dilation of the fistula tract can then be performed. Finally, a stent is placed across the fistula tract for continued drainage. The technical success rate has been reported to be >90%, with a low complication rate of <5%.[23-27]

Variations have been described in an attempt to streamline this technique. Multiple plastic stents may be placed to promote drainage, with or without a nasocystic drain.[25,28] Talreja and colleagues[29] described PFC drainage by using covered self-expandable metal stents in 18 patients, with a 95% overall success rate and complete resolution of the fluid collection in 78%. These stents may be advantageous since they provide a radial force that tamponades vessels and have a wider diameter that facilitates drainage; however, stent migration is a concern.[30,31] Itoi and colleagues[32] described the use of a novel self-expanding, fully covered lumen-apposing metal stent (AXIOS; Xlumena Inc., Mountain View, CA, USA) that appears to be an attractive alternative. The 10-mm-diameter stent has bilateral anchor flanges that are designed to hold tissue in apposition. All cases were reported as successful without complications, although one stent migrated into the stomach without clinical consequence.[32]

Pancreatic necrosis

Approximately 20% of patients with acute pancreatitis develop pancreatic necrosis.[33] Endoscopic pancreatic necrosectomy is now widely described in the literature and increasingly favored over surgical and percutaneous alternatives because of the high rates of morbidity and mortality associated with these options.[34] The Dutch Pancreatitis Study Group demonstrated a decreased inflammatory response, rates of organ failure, and major complications in patients undergoing endoscopic necrosectomy compared with those undergoing surgical necrosectomy.[35] Although the technique for drainage is similar to that of pseudocyst drainage, endoscopic necrosectomy can be more challenging. Necrosis can contain both solid necrotic material and fluid, and this requires a more aggressive approach with repeated endoscopic debridement and/or nasocystic lavage for successful treatment and resolution.[36] Varadarajulu and colleagues[37] described the multiple transluminal gateway technique in which a nasocystic catheter is placed into one region of the necrotic collection, and one or more internal drainage sites with multiple plastic stents are created in other regions to drain the collection into the GI tract lumen. This method has been described to enhance the resolution of necrosis, with less need for additional endoscopic or surgical interventions. Sarkaria and colleagues[34] described the use of larger-caliber fully covered metal esophageal stents to facilitate the resolution of these collections more rapidly. This technique allowed for quicker endoscopic debridement and passive flow of cystic contents after each session. These technical variations are promising options to facilitate minimally invasive drainage of PFCs and necrosis; however, larger, long-term studies are required to validate the safety and efficacy of these novel approaches.

Abscess drainage

Similar drainage techniques have been applied to abscesses, and have been described as safe and effective. Percutaneous drainage of symptomatic postsurgical abdominal collections has been the standardized approach to avoid repeat surgeries; however, because of the difficult and painful locations, EUS has been introduced to overcome these issues.[38,39] This technique has been described for the drainage of gallbladder collections and bilomas,[40,41] perirectal abscesses,[42] hematomas,[43] and postsurgical collections including distal pancreatectomy,[43] splenectomy,[43,44] and lower anterior rectal resections.[43] Singhal and colleagues[45] recently published a review of seven cases of EUS-guided liver abscess drainage. The combined technical and clinical success rate was 100%, without complications. Pelvic abscess drainage through the percutaneous approach has long been a conundrum because of the difficult location and access; moreover, it is painful for patients. EUS provides an excellent platform for the drainage of pelvic abscesses, as these collections are often close to the rectum and left colon wall.[46] On the basis of the published cases series, this procedure is feasible, effective, and safe, and likely is an excellent alternative to surgical or percutaneous options.[42,47,48]

There have been varying reports of ideal stent positions and types depending on the collection. There is a suggestion that multiple plastics stents have a prolonged effect; however, the duration of stent placement is also debatable.[49] Some authors suggest that the stents should be removed after 2 months;[50] however, Ulla-Rocha and colleagues[43] chose to leave the stent indefinitely. It is possible that they are expelled into the GI tract once the collections have resolved.[24] As there are only small reports of abscess drainage, additional studies are needed to determine the appropriate indications and stents used during the procedure.

Biliary drainage

ERCP is the standard treatment for biliary decompression but can fail in 3% to 10% of cases owing to an inability to cannulate the papilla or an inaccessible papilla due to surgically altered anatomy or duodenal obstruction.[51] When ERCP fails, traditional alternatives include percutaneous transhepatic cholangiography (PTC) or surgical interventions; however, these options are associated with increased risks of morbidity and mortality. EUS-guided biliary drainage was first described by Wiersema and colleagues[52] in 1996 and is now well described in the literature. It has become a more mainstream therapeutic option in expert centers, with high success rates and minimal complications.

There are various techniques that can be used to drain the bile duct. Access can be obtained by means of a needle puncture and contrast injection of the intrahepatic or extrahepatic bile duct by using an FNA needle. Drainage can be established in either a transpapillary or transmural fashion. Initially, a guidewire is advanced within the duct. The rendezvous technique (retrograde transpapillary drainage) can be attempted if possible, in which case the guidewire is advanced across the papilla and captured with a snare. Retrograde drainage can then be completed. If the wire cannot be advanced across the papilla, then antegrade transpapillary drainage can be performed through direct stent insertion. If transpapillary drainage is not possible, then dilatation of the puncturing tract is performed by using a cystostome or dilating catheter in anticipation of transmural drainage. A plastic or metallic stent is then introduced across the fistula tract.

Recent reviews of the published case series demonstrate a success rate of approximately 90%, regardless of the approach, with an overall complication rate of 16%.[53,54] The complications included pneumoperitoneum, bile leak/peritonitis, hemobilia, bacteremia, pancreatitis, abdominal pain, and stent migration.[14,53-56] EUS-guided biliary drainage is rapidly evolving and becoming more common in expert centers; however, the indications and techniques have yet to be standardized. A consortium of world experts first met in 2011, and standardization of the nomenclature, definitions, and indications is currently under way.[57]

Pancreatic drainage

The development of interventional EUS has also provided better access to the pancreas. Similar techniques can be used to access a dilated pancreatic duct that cannot be drained by conventional ERCP owing to complete obstruction. The main indications include stenosis of the pancreaticojejunal or pancreaticogastric anastomosis after Whipple resection causing acute recurrent pancreatitis, main pancreatic duct (MPD) stenosis due to chronic pancreatitis, postacute pancreatitis, or postpancreatic trauma after a failed ERCP.[58]

The dilated MPD is localized by using EUS and is punctured with a 19-gauge FNA needle. Initially, a guidewire is advanced in an attempt to cross the anastomosis for a rendezvous. If that is not possible, the needle is exchanged over a guidewire for a diathermic sheath, needle knife, or dilating catheter, which is used to enlarge the transmural fistula. Typically, a

7-Fr pancreaticogastric stent is deployed.

There have been limited numbers of reported cases series, the largest of which was reported by Tessier et al.[59] in 2007 and included 36 patients. Owing to the technical complexity of including puncture of the pancreatic duct and stabilization of the endoscope, variable success rates (range, 25% to 100%) and higher complication rates (range, 15% to 50%) have been reported.[58] Most technical failures are due to the unsuccessful manipulation of the guidewire, whereas most of the complications are related to the management of the transmural fistula.[58] Complications included pancreatitis, abdominal pain, bleeding, perforation, fever, and pancreatic abscess.[60] This approach should be reserved for expert endoscopists, and new techniques and accessories are needed to improve outcomes.

Gallbladder drainage

For patients with acute cholecystitis that are not appropriate candidates for surgical intervention, EUS-guided gallbladder drainage (EUS-GBD) has been described to overcome the limitations of percutaneous drainage. It can be used as a bridge to surgery, for palliation in poor surgical candidates after a failed transpapillary cystic duct drainage, and in patients with covered metal biliary stents for malignant obstructive jaundice.[61] Initially, transpapillary drainage of the gallbladder with cystic duct stents can be attempted, although this is extremely challenging with low reported success rates (approximately 60% to 80%).[40] Alternatively, EUS-guided gallbladder access can be obtained with transmural endoscopic drainage. The resultant drainage may be a temporary measure before cholecystectomy or a long-term palliative option for nonoperative candidates.[62] There are no good long-term data on the patency of plastic stents; however, because of the concern for stenosis, standard self-expanding metal stents have been used.[63]

A recent review of EUS-GBD reported a technical success rate of 97% and a clinical success rate of 100%.[61] Jang and colleagues[64] reported a randomized control trial comparing EUS-GBD and PTC in 59 patients, demonstrating technical and clinical success rates of nearly 100% in both treatment arms. There was no difference in the rate of complications; however, patients drained by using EUS had significantly lower postprocedure pain scores. Pneumoperitoneum, bile peritonitis, and stent migration have been described in the literature.[61,65] To limit these events, a lumen-apposing metal stent Axios (X-Lumena) has successfully been described both in animal models and in the clinical setting.[32,66] It also allows access to the gallbladder lumen with slim gastroscopes to obtain biopsies, and facilitate stone removal or debridement.

EUS-GUIDED ONCOLOGIC INTERVENTIONS

Cyst ablation

EUS-guided ablation of pancreatic cysts with chemotherapeutic agents and/or ethanol has shown promising results. Gan and colleagues[67] first described this technique in 25 patients in 2005. Eight patients had complete resolution of the cysts, and no complications were reported. Various studies have also confirmed a decrease or disappearance of cyst after ablation on follow-up imaging.[67-71]

A recent prospective study on EUS-guided ethanol injection with paclitaxel demonstrated that this method is a safe, feasible, and effective treatment for pancreatic cystic lesions.[71] Seventy-nine percent of patients showed complete resolution without significant complications. Its use has also expanded to include alcohol ablation of GI stromal tumors (GISTs),[72] insulinomas,[73] adrenal glands,[74] and liver metastasis[75] in patients that are poor surgical candidates. This technique remains in debate because it is not clear that patients with these lesions truly require an intervention or whether surveillance would be sufficient. The effect of preventing malignant transformation has not yet been clearly demonstrated.[69]

Ablation therapy for solid tumors

Radiofrequency ablation (RFA) in pancreatic cancer has been described in surgical and percutaneous methods. EUS-guided ablation has some advantages in that it is less invasive and regions for ablation can be more precisely selected; however, its use is still experimental in animal models.[76-79] Complications such as pancreatitis, gastric wall burn, and adhesion of the surrounding tissue have been reported.[78,79] The complications seem to be associated with initial technical problems such as the duration of the ablation or differences between the porcine and human anatomy.[79] Carrara and colleagues[76,80] recently investigated a new flexible ablation device that combines bipolar radiofrequency with cryotechnology into the porcine pancreas, liver, and spleen. These studies demonstrated the feasibility, efficacy, and safety of EUS-guided ablative therapy; however, further studies are required to determine the effectiveness of EUS-guided RFA in pancreatic cancer and decrease the associated risks.

Photodynamic therapy (PDT) provides localized tissue ablation by using a photosensitizer and light exposure. Photosensitizers accumulate more in tumors than in normal tissue, and light can be generated with small optic fibers that can be advanced through an FNA needle. PDT use in the GI tract was first described in patients with Barrett's dysplasia.[81,82] Later, CT-guided percutaneous PDT therapy in patients with unresectable pancreatic cancer was reported.[83] Most recently, EUS-guided PDT has been described by Chan et al.[84] and Yusuf et al.[85] in animal models. Their studies demonstrated localized pancreatic necrosis without significant complications. This, however, needs to be validated.

EUS-guided injection therapy

Advanced pancreatic cancer has a poor prognosis, and no therapy has been shown to increase survival. Localized chemotherapy is gaining favor as it can possibly minimize adverse events related to therapy while increasing therapeutic concentrations within the tumor. Various studies of EUS-guided injection of oncolytic attenuated adenovirus (ONYX-015; Onyx Pharmaceuticals, San Francisco, CA, USA),[86] a replication-deficient adenovirus vector carrying the *TNF-α* gene,[87,88] and activated allogenic lymphocyte culture (Cytoimplant; Meyer, Irvine, CA, USA)[89] have been described. While these techniques are promising, their efficacy has not been clearly demonstrated.

EUS-guided fiducial placement

A fiducial is an object used as a point of reference for external beam radiation therapy and is available to facilitate radiotherapy for locally advanced pancreatic cancer. The fiducials are loaded within a 19-gauge FNA needle and are deployed to the area of interest by using a stylet or sterile water.[90-93] This technique has a high reported success rate, approximately 90% with <5% migration rate and no significant complications.[92,93]

EUS-guided brachytherapy

EUS has also been used to place radioactive material into the pancreas for the local treatment of pancreatic cancer. This technique was first described in 1999 and remains limited to small case series.[94] In a pilot study, iodine-125 radioactive seeds were injected through a 19-gauge FNA needle with a partial response in 26.7% of patients and minimal effect on pain.[94,95] Rare complications such as fever, seed migration, and hyperamylasemia were described. Complications seen in surgical approaches such as GI hemorrhage and pancreatic fistulas were not seen.[95,96] This approach has been employed for treating various tumors, including head and neck cancer,[97] esophageal cancer,[98] and rectal and pancreatic cancer.[94,95] The limited results that have been published in the literature are still preliminary, and more studies are needed to determine the efficacy and safety of this technique.

EUS-GUIDED HEMOSTASIS

Endoscopy is effective in achieving hemostasis in most cases of GI bleeding; however, refractory bleeding may occur in up to 15% to 20% of cases.[8] These lesions may be amenable to vascular interventions such as angiography, coil embolization, glue application, or transjugular intrahepatic portosystemic shunt.[99] Although these procedures have primarily been performed by interventional radiology, more recently, endoscopists have reported their experience of using these treatment modalities with EUS guidance.

With EUS, Doppler flow can be used to identify bleeding vessels and to monitor the success of endoscopic therapy.[99-102] Doppler ultrasound monitored therapy has been successful for recurrent bleeding due to peptic ulcer disease, gastric varices, or Dieulafoy lesions.[100-104] It permits direct targeting of the bleeding vessel, accurate delivery of therapy, and confirming cessation of bleeding. It has been suggested that Doppler ultrasound is more accurate than endoscopic stigmata in predicting the risk of rebleeding;[99] specifically, the absence of a Doppler ultrasound signal after therapy has been associated with a low risk of rebleeding.[105]

EUS-FNI of esophageal or gastric varices has also been described in the literature. A prospective study of 54 patients with gastric varices showed that EUS-guided cyanoacrylate injection can obliterate varices.[106] Another study of 50 patients with GI hemorrhage due to esophageal varices shows that EUS-guided sclerosis of the perforating veins is more effective than conventional sclerosis techniques.[107] Patients with refractory bleeding from hemosuccus pancreaticus, pseudoaneurysms, Dieulafoy lesions, peptic ulcers, or GISTs have been successfully treated with EUS-guided injection of absolute alcohol and/or cyanoacrylate into the bleeding vessel.[108-110] There have also been reports stating that EUS can be used to deliver microcoils to control refractory bleeding episodes due to varices.[99,108,111]

Animal models of EUS-guided transhepatic puncture of the portal vein have been described, and the technique preliminarily appears to be feasible and safe.[112-115] These data led to the description of EUS-guided creation of an intrahepatic portosystemic shunt.[116] EUS-guided vascular therapy is a new and emerging technique that shows promise for cases of refractory GI bleeding; however, case series are still limited and more data are needed to determine their efficacy and safety.

EUS-GUIDED ANASTOMOSES

Patients with surgically altered anatomy pose a unique challenge when ERCP is required. Several techniques, including enteroscopy-assisted ERCP, surgical techniques, and percutaneous techniques, have been employed but are limited because of technical feasibility and complications. A recent abstract has described a technique of using EUS to create a gastrogastric fistula in patients who have undergone Roux-en-Y gastric bypass. Antegrade ERCP can then feasibly be performed.[117]

CONCLUSIONS

EUS continues to evolve to perfect minimally invasive techniques both within and outside the GI tract. As the indications for therapeutic EUS continue to expand, larger case series with better long-term data are needed. To increase the success rates and decrease the complication rates associated with these novel techniques, the development of dedicated accessories are imperative.

Conflicts of Interest

The authors have no financial conflicts of interest.

REFERENCES

1. Erickson RA. EUS-guided FNA. Gastrointest Endosc 2004;60:267-279.
2. Chen VK, Eloubeidi MA. Endoscopic ultrasound-guided fine needle aspiration is superior to lymph node echofeatures: a prospective evaluation of mediastinal and peri-intestinal lymphadenopathy. Am J Gastroenterol 2004;99:628-633.
3. Harewood GC, Wiersema MJ. Endosonography-guided fine needle aspiration biopsy in the evaluation of pancreatic masses. Am J Gastroenterol 2002;97:1386-1391.
4. Moparty B, Logroño R, Nealon WH, et al. The role of endoscopic ultrasound and endoscopic ultrasound-guided fine-needle aspiration in distinguishing pancreatic cystic lesions. Diagn Cytopathol 2007;35:18-25.
5. Al-Haddad M, Raimondo M, Woodward T, et al. Safety and efficacy of cytology brushings versus standard FNA in evaluating cystic lesions of the pancreas: a pilot study. Gastrointest Endosc 2007;65:894-898.
6. Gress F, Gottlieb K, Sherman S, Lehman G. Endoscopic ultrasonography-guided fine-needle aspiration biopsy of suspected pancreatic cancer. Ann Intern Med 2001;134:459-464.
7. Fritscher-Ravens A, Soehendra N, Schirrow L, et al. Role of transesophageal endosonography-guided fine-needle aspiration in the diagnosis of lung cancer. Chest 2000;117:339-345.
8. Vazquez-Sequeiros E, Olcina JR. Endoscopic ultrasound guided vascular access and therapy: a promising indication. World J Gastrointest Endosc 2010;2:198-202.
9. Seicean A. Celiac plexus neurolysis in pancreatic cancer: the endoscopic ultrasound approach. World J Gastroenterol 2014;20:110-117.
10. Puli SR, Reddy JB, Bechtold ML, Antillon MR, Brugge WR. EUS-guided celiac plexus neurolysis for pain due to chronic pancreatitis or pancreatic cancer pain: a meta-analysis and systematic review. Dig Dis Sci 2009;54:2330-2337.
11. Gress F, Schmitt C, Sherman S, Ikenberry S, Lehman G. A prospective randomized comparison of endoscopic ultrasound- and computed tomography-guided celiac plexus block for managing chronic pancreatitis pain. Am J Gastroenterol 1999;94:900-905.
12. Levy MJ, Chari ST, Wiersema MJ. Endoscopic ultrasound-guided celiac neurolysis. Gastrointest Endosc Clin N Am 2012;22:231-247.
13. Tarantino I, Barresi L. Interventional endoscopic ultrasound: therapeutic capability and potential. World J Gastrointest Endosc 2009;1:39-44.
14. Lee KH, Lee JK. Interventional endoscopic ultrasonography: present and future. Clin Endosc 2011;44:6-12.
15. Gress F. Endoscopic ultrasound-guided celiac plexus neurolysis. Gastroenterol Hepatol (NY) 2007;3:279-281.
16. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis 2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102-111.
17. Baron TH, Harewood GC, Morgan DE, Yates MR. Outcome differences after endoscopic drainage of pancreatic necrosis, acute pancreatic pseudocysts, and chronic pancreatic pseudocysts. Gastrointest Endosc 2002;56:7-17.
18. Baron TH, Morgan DE. The diagnosis and management of fluid collections associated with pancreatitis. Am J Med 1997;102:555-563.
19. Yeo CJ, Bastidas JA, Lynch-Nyhan A, Fishman EK, Zinner MJ, Cameron JL. The natural history of pancreatic pseudocysts documented by computed tomography. Surg Gynecol Obstet 1990;170:411-417.
20. Bradley EL, Clements JL Jr, Gonzalez AC. The natural history of pancreatic pseudocysts: a unified concept of management. Am J Surg 1979; 137:135-141.
21. Gouyon B, Lévy P, Ruszniewski P, et al. Predictive factors in the outcome of pseudocysts complicating alcoholic chronic pancreatitis. Gut 1997; 41:821-825.
22. Topazian M. Endoscopic ultrasound-guided drainage of pancreatic fluid collections (with video). Clin Endosc 2012;45:337-340.
23. Varadarajulu S, Wilcox CM, Tamhane A, Eloubeidi MA, Blakely J, Canon CL. Role of EUS in drainage of peripancreatic fluid collections not amenable for endoscopic transmural drainage. Gastrointest Endosc 2007;66:1107-1119.
24. Kruger M, Schneider AS, Manns MP, Meier PN. Endoscopic management of pancreatic pseudocysts or abscesses after an EUS-guided 1-step procedure for initial access. Gastrointest Endosc 2006;63:409-416.
25. Lopes CV, Pesenti C, Bories E, Caillol F, Giovannini M. Endoscopic-ultrasound-guided endoscopic transmural drainage of pancreatic pseudocysts and abscesses. Scand J Gastroenterol 2007;42:524-529.
26. Antillon MR, Shah RJ, Stiegmann G, Chen YK. Single-step EUS-guided transmural drainage of simple and complicated pancreatic pseudocysts. Gastrointest Endosc 2006;63:797-803.
27. Varadarajulu S. EUS followed by endoscopic pancreatic pseudocyst drainage or all-in-one procedure: a review of basic techniques (with video). Gastrointest Endosc 2009;69(2 Suppl):S176-S181.
28. Puri R, Mishra SR, Thandassery RB, Sud R, Eloubeidi MA. Outcome and complications of endoscopic ultrasound guided pancreatic pseudocyst drainage using combined endoprosthesis and naso-cystic drain. J Gastroenterol Hepatol 2012;27:722-727.
29. Talreja JP, Shami VM, Ku J, Morris TD, Ellen K, Kahaleh M. Transenteric drainage of pancreatic-fluid collections with fully covered self-expanding metallic stents (with video). Gastrointest Endosc 2008;68: 1199-1203.
30. Fabbri C, Luigiano C, Cennamo V, et al. Endoscopic ultrasound-guided transmural drainage of infected pancreatic fluid collections with placement of covered self-expanding metal stents: a case series. Endoscopy 2012;44:429-433.
31. Penn DE, Draganov PV, Wagh MS, Forsmark CE, Gupte AR, Chauhan SS. Prospective evaluation of the use of fully covered self-expanding metal stents for EUS-guided transmural drainage of pancreatic pseudocysts. Gastrointest Endosc 2012;76:679-684.
32. Itoi T, Binmoeller KF, Shah J, et al. Clinical evaluation of a novel lumen-apposing metal stent for endosonography-guided pancreatic pseudocyst and gallbladder drainage (with videos). Gastrointest Endosc 2012;75:870-876.
33. Banks PA, Freeman ML; Practice Parameters Committee of the American College of Gastroenterology. Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006;101:2379-2400.
34. Sarkaria S, Sethi A, Rondon C, et al. Pancreatic necrosectomy using covered esophageal stents: a novel approach. J Clin Gastroenterol 2014;48: 145-152.
35. Bakker OJ, van Santvoort HC, van Brunschot S, et al. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancre-

atitis: a randomized trial. JAMA 2012;307:1053-1061.
36. Sadik R, Kalaitzakis E, Thune A, Hansen J, Jonson C. EUS-guided drainage is more successful in pancreatic pseudocysts compared with abscesses. World J Gastroenterol 2011;17:499-505.
37. Varadarajulu S, Phadnis MA, Christein JD, Wilcox CM. Multiple transluminal gateway technique for EUS-guided drainage of symptomatic walled-off pancreatic necrosis. Gastrointest Endosc 2011;74:74-80.
38. Kuligowska E, Keller E, Ferrucci JT. Treatment of pelvic abscesses: value of one-step sonographically guided transrectal needle aspiration and lavage. AJR Am J Roentgenol 1995;164:201-206.
39. Noh SH, Park do H, Kim YR, et al. EUS-guided drainage of hepatic abscesses not accessible to percutaneous drainage (with videos). Gastrointest Endosc 2010;71:1314-1319.
40. Kahaleh M, Wang P, Shami VM, Tokar J, Yeaton P. Drainage of gallbladder fossa fluid collections with endoprosthesis placement under endoscopic ultrasound guidance: a preliminary report of two cases. Endoscopy 2005;37:393-396.
41. Shami VM, Talreja JP, Mahajan A, Phillips MS, Yeaton P, Kahaleh M. EUS-guided drainage of bilomas: a new alternative? Gastrointest Endosc 2008;67:136-140.
42. Giovannini M, Bories E, Moutardier V, et al. Drainage of deep pelvic abscesses using therapeutic echo endoscopy. Endoscopy 2003;35:511-514.
43. Ulla-Rocha JL, Vilar-Cao Z, Sardina-Ferreiro R. EUS-guided drainage and stent placement for postoperative intra-abdominal and pelvic fluid collections in oncological surgery. Therap Adv Gastroenterol 2012;5:95-102.
44. Lee DH, Cash BD, Womeldorph CM, Horwhat JD. Endoscopic therapy of a splenic abscess: definitive treatment via EUS-guided transgastric drainage. Gastrointest Endosc 2006;64:631-634.
45. Singhal S, Changela K, Lane D, Anand S, Duddempudi S. Endoscopic ultrasound-guided hepatic and perihepatic abscess drainage: an evolving technique. Therap Adv Gastroenterol 2014;7:93-98.
46. Fernandez-Urien I, Vila JJ, Jimenez FJ. Endoscopic ultrasound-guided drainage of pelvic collections and abscesses. World J Gastrointest Endosc 2010;2:223-227.
47. Varadarajulu S, Drelichman ER. EUS-guided drainage of pelvic abscess (with video). Gastrointest Endosc 2007;66:372-376.
48. Trevino JM, Drelichman ER, Varadarajulu S. Modified technique for EUS-guided drainage of pelvic abscess (with video). Gastrointest Endosc 2008;68:1215-1219.
49. Varadarajulu S, Drelichman ER. Effectiveness of EUS in drainage of pelvic abscesses in 25 consecutive patients (with video). Gastrointest Endosc 2009;70:1121-1127.
50. Seewald S, Ang TL, Teng KY, et al. Endoscopic ultrasound-guided drainage of abdominal abscesses and infected necrosis. Endoscopy 2009; 41:166-174.
51. Baron TH, Petersen BT, Mergener K, et al. Quality indicators for endoscopic retrograde cholangiopancreatography. Am J Gastroenterol 2006;101:892-897.
52. Wiersema MJ, Sandusky D, Carr R, Wiersema LM, Erdel WC, Frederick PK. Endosonography-guided cholangiopancreatography. Gastrointest Endosc 1996;43(2 Pt 1):102-106.
53. Iqbal S, Friedel DM, Grendell JH, Stavropoulos SN. Outcomes of endoscopic-ultrasound-guided cholangiopancreatography: a literature review. Gastroenterol Res Pract 2013;2013:869214.
54. Kedia P, Gaidhane M, Kahaleh M. Endoscopic guided biliary drainage: how can we achieve efficient biliary drainage? Clin Endosc 2013;46: 543-551.
55. Yamao K, Hara K, Mizuno N, et al. EUS-guided biliary drainage. Gut Liver 2010;4 Suppl 1:S67-S75.
56. Yamao K, Sawaki A, Takahashi K, Imaoka H, Ashida R, Mizuno N. EUS-guided choledochoduodenostomy for palliative biliary drainage in case of papillary obstruction: report of 2 cases. Gastrointest Endosc 2006;64:663-667.
57. Kahaleh M, Artifon EL, Perez-Miranda M, et al. Endoscopic ultrasonography guided biliary drainage: summary of consortium meeting, May 7th, 2011, Chicago. World J Gastroenterol 2013;19:1372-1379.
58. Widmer J, Sharaiha RZ, Kahaleh M. Endoscopic ultrasonography-guided drainage of the pancreatic duct. Gastrointest Endosc Clin N Am 2013;23:847-861.
59. Tessier G, Bories E, Arvanitakis M, et al. EUS-guided pancreatogastrostomy and pancreatobulbostomy for the treatment of pain in patients with pancreatic ductal dilatation inaccessible for transpapillary endoscopic therapy. Gastrointest Endosc 2007;65:233-241.
60. Barkay O, Sherman S, McHenry L, et al. Therapeutic EUS-assisted endoscopic retrograde pancreatography after failed pancreatic duct cannulation at ERCP. Gastrointest Endosc 2010;71:1166-1173.
61. Widmer J, Singhal S, Gaidhane M, Kahaleh M. Endoscopic ultrasound-guided endoluminal drainage of the gallbladder. Dig Endosc 2014;26:525-531.
62. Perez-Miranda M, De la Serna-Higuera C. EUS access to the biliary tree. Curr Gastroenterol Rep 2013;15:349.
63. Widmer J, Alvarez P, Gaidhane M, et al. Endoscopic ultrasonography-guided cholecystogastrostomy in patients with unresectable pancreatic cancer using anti-migratory metal stents: a new approach. Dig Endosc 2014;26:599-602.
64. Jang JW, Lee SS, Park do H, Seo DW, Lee SK, Kim MH. Feasibility and safety of EUS-guided transgastric/transduodenal gallbladder drainage with single-step placement of a modified covered self-expandable metal stent in patients unsuitable for cholecystectomy. Gastrointest Endosc 2011;74:176-181.
65. Adsay NV, Bagci P, Tajiri T, et al. Pathologic staging of pancreatic, ampullary, biliary, and gallbladder cancers: pitfalls and practical limitations of the current AJCC/UICC TNM staging system and opportunities for improvement. Semin Diagn Pathol 2012;29:127-141.
66. de la Serna-Higuera C, Pérez-Miranda M, Gil-Simón P, et al. EUS-guided transenteric gallbladder drainage with a new fistula-forming, lumen-apposing metal stent. Gastrointest Endosc 2013;77:303-308.
67. Gan SI, Thompson CC, Lauwers GY, Bounds BC, Brugge WR. Ethanol lavage of pancreatic cystic lesions: initial pilot study. Gastrointest Endosc 2005;61:746-752.
68. DeWitt J, McGreevy K, Schmidt CM, Brugge WR. EUS-guided ethanol versus saline solution lavage for pancreatic cysts: a randomized, double-blind study. Gastrointest Endosc 2009;70:710-723.
69. DiMaio CJ, DeWitt JM, Brugge WR. Ablation of pancreatic cystic lesions: the use of multiple endoscopic ultrasound-guided ethanol lavage sessions. Pancreas 2011;40:664-668.
70. Oh HC, Seo DW, Song TJ, et al. Endoscopic ultrasonography-guided ethanol lavage with paclitaxel injection treats patients with pancreatic cysts. Gastroenterology 2011;140:172-179.
71. Oh HC, Seo DW, Lee TY, et al. New treatment for cystic tumors of the pancreas: EUS-guided ethanol lavage with paclitaxel injection. Gastrointest Endosc 2008;67:636-642.
72. Gunter E, Lingenfelser T, Eitelbach F, Müller H, Ell C. EUS-guided ethanol injection for treatment of a GI stromal tumor. Gastrointest Endosc 2003;57:113-115.
73. Jurgensen C, Schuppan D, Neser F, Ernstberger J, Junghans U, Stölzel U. EUS-guided alcohol ablation of an insulinoma. Gastrointest Endosc 2006;63:1059-1062.
74. Artifon EL, Lucon AM, Sakai P, et al. EUS-guided alcohol ablation of left adrenal metastasis from non-small-cell lung carcinoma. Gastrointest Endosc 2007;66:1201-1205.
75. Barclay RL, Perez-Miranda M, Giovannini M. EUS-guided treatment of a solid hepatic metastasis. Gastrointest Endosc 2002;55:266-270.
76. Carrara S, Arcidiacono PG, Albarello L, et al. Endoscopic ultrasound-guided application of a new internally gas-cooled radiofrequency ablation probe in the liver and spleen of an animal model: a preliminary study. Endoscopy 2008;40:759-763.

77. Brugge WR. EUS-guided tumor ablation with heat, cold, microwave, or radiofrequency: will there be a winner? Gastrointest Endosc 2009;69(2 Suppl):S212-S216.
78. Goldberg SN, Mallery S, Gazelle GS, Brugge WR. EUS-guided radiofrequency ablation in the pancreas: results in a porcine model. Gastrointest Endosc 1999;50:392-401.
79. Gaidhane M, Smith I, Ellen K, et al. Endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) of the pancreas in a porcine model. Gastroenterol Res Pract 2012;2012:431451.
80. Carrara S, Arcidiacono PG, Albarello L, et al. Endoscopic ultrasound-guided application of a new hybrid cryotherm probe in porcine pancreas: a preliminary study. Endoscopy 2008;40:321-326.
81. Regula J, MacRobert AJ, Gorchein A, et al. Photosensitisation and photodynamic therapy of oesophageal, duodenal, and colorectal tumours using 5 aminolaevulinic acid induced protoporphyrin IX: a pilot study. Gut 1995;36:67-75.
82. Overholt B, Panjehpour M, Tefftellar E, Rose M. Photodynamic therapy for treatment of early adenocarcinoma in Barrett's esophagus. Gastrointest Endosc 1993;39:73-76.
83. Bown SG, Rogowska AZ, Whitelaw DE, et al. Photodynamic therapy for cancer of the pancreas. Gut 2002;50:549-557.
84. Chan HH, Nishioka NS, Mino M, et al. EUS-guided photodynamic therapy of the pancreas: a pilot study. Gastrointest Endosc 2004;59:95-99.
85. Yusuf TE, Matthes K, Brugge WR. EUS-guided photodynamic therapy with verteporfin for ablation of normal pancreatic tissue: a pilot study in a porcine model (with video). Gastrointest Endosc 2008;67:957-961.
86. Hecht JR, Bedford R, Abbruzzese JL, et al. A phase I/II trial of intratumoral endoscopic ultrasound injection of ONYX-015 with intravenous gemcitabine in unresectable pancreatic carcinoma. Clin Cancer Res 2003;9:555-561.
87. Chang KY, Lee YD. Ring-opening polymerization of epsilon-caprolactone initiated by the antitumor agent doxifluridine. Acta Biomater 2009; 5:1075-1081.
88. Chang KJ, Lee JG, Holcombe RF, Kuo J, Muthusamy R, Wu ML. Endoscopic ultrasound delivery of an antitumor agent to treat a case of pancreatic cancer. Nat Clin Pract Gastroenterol Hepatol 2008;5:107-111.
89. Chang KJ, Nguyen PT, Thompson JA, et al. Phase I clinical trial of allogeneic mixed lymphocyte culture (cytoimplant) delivered by endoscopic ultrasound-guided fine-needle injection in patients with advanced pancreatic carcinoma. Cancer 2000;88:1325-1335.
90. Pishvaian AC, Collins B, Gagnon G, Ahlawat S, Haddad NG. EUS-guided fiducial placement for CyberKnife radiotherapy of mediastinal and abdominal malignancies. Gastrointest Endosc 2006;64:412-417.
91. Savides TJ. EUS-guided fine-needle insertion of radiopaque fiducials: X marks the spot. Gastrointest Endosc 2006;64:418-419.
92. Sanders MK, Moser AJ, Khalid A, et al. EUS-guided fiducial placement for stereotactic body radiotherapy in locally advanced and recurrent pancreatic cancer. Gastrointest Endosc 2010;71:1178-1184.
93. 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;71:513-518.
94. Sun S, Xu H, Xin J, Liu J, Guo Q, Li S. Endoscopic ultrasound-guided interstitial brachytherapy of unresectable pancreatic cancer: results of a pilot trial. Endoscopy 2006;38:399-403.
95. Jin Z, Du Y, Li Z, Jiang Y, Chen J, Liu Y. Endoscopic ultrasonography-guided interstitial implantation of iodine 125-seeds combined with chemotherapy in the treatment of unresectable pancreatic carcinoma: a prospective pilot study. Endoscopy 2008;40:314-320.
96. Order SE, Siegel JA, Principato R, et al. Selective tumor irradiation by infusional brachytherapy in nonresectable pancreatic cancer: a phase I study. Int J Radiat Oncol Biol Phys 1996;36:1117-1126.
97. Maier W, Henne K, Krebs A, Schipper J. Endoscopic ultrasound-guided brachytherapy of head and neck tumours. A new procedure for controlled application. J Laryngol Otol 1999;113:41-48.
98. Lah JJ, Kuo JV, Chang KJ, Nguyen PT. EUS-guided brachytherapy. Gastrointest Endosc 2005;62:805-808.
99. Levy MJ, Chak A. EUS 2008 Working Group document: evaluation of EUS-guided vascular therapy. Gastrointest Endosc 2009;69(2 Suppl):S37-S42.
100. Wong RC, Farooq FT, Chak A. Endoscopic Doppler US probe for the diagnosis of gastric varices (with videos). Gastrointest Endosc 2007;65:491-496.
101. Wong RC. Endoscopic Doppler US probe for acute peptic ulcer hemorrhage. Gastrointest Endosc 2004;60:804-812.
102. Kuramochi A, Imazu H, Kakutani H, Uchiyama Y, Hino S, Urashima M. Color Doppler endoscopic ultrasonography in identifying groups at a high-risk of recurrence of esophageal varices after endoscopic treatment. J Gastroenterol 2007;42:219-224.
103. van Leerdam ME, Rauws EA, Geraedts AA, Tijssen JG, Tytgat GN. The role of endoscopic Doppler US in patients with peptic ulcer bleeding. Gastrointest Endosc 2003;58:677-684.
104. Ribeiro A, Vazquez-Sequeiros E, Wiersema MJ. Doppler EUS-guided treatment of gastric Dieulafoy's lesion. Gastrointest Endosc 2001;53:807-809.
105. Kohler B, Riemann JF. Endoscopic injection therapy of Forrest II and III gastroduodenal ulcers guided by endoscopic Doppler ultrasound. Endoscopy 1993;25:219-223.
106. Lee YT, Chan FK, Ng EK, et al. EUS-guided injection of cyanoacrylate for bleeding gastric varices. Gastrointest Endosc 2000;52:168-174.
107. de Paulo GA, Ardengh JC, Nakao FS, Ferrari AP. Treatment of esophageal varices: a randomized controlled trial comparing endoscopic sclerotherapy and EUS-guided sclerotherapy of esophageal collateral veins. Gastrointest Endosc 2006;63:396-402.
108. Levy MJ, Wong Kee Song LM, Farnell MB, Misra S, Sarr MG, Gostout CJ. Endoscopic ultrasound (EUS)-guided angiotherapy of refractory gastrointestinal bleeding. Am J Gastroenterol 2008;103:352-359.
109. Gonzalez JM, Ezzedine S, Vitton V, Grimaud JC, Barthet M. Endoscopic ultrasound treatment of vascular complications in acute pancreatitis. Endoscopy 2009;41:721-724.
110. Roberts KJ, Jones RG, Forde C, Marudanayagam R. Endoscopic ultrasound-guided treatment of visceral artery pseudoaneurysm. HPB (Oxford) 2012;14:489-490.
111. Romero-Castro R, Pellicer-Bautista FJ, Jimenez-Saenz M, et al. EUS-guided injection of cyanoacrylate in perforating feeding veins in gastric varices: results in 5 cases. Gastrointest Endosc 2007;66:402-407.
112. Giday SA, Clarke JO, Buscaglia JM, et al. EUS-guided portal vein catheterization: a promising novel approach for portal angiography and portal vein pressure measurements. Gastrointest Endosc 2008;67:338-342.
113. Giday SA, Ko CW, Clarke JO, et al. EUS-guided portal vein carbon dioxide angiography: a pilot study in a porcine model. Gastrointest Endosc 2007;66:814-819.
114. Brugge WR. EUS is an important new tool for accessing the portal vein. Gastrointest Endosc 2008;67:343-344.
115. Lai L, Poneros J, Santilli J, Brugge W. EUS-guided portal vein catheterization and pressure measurement in an animal model: a pilot study of feasibility. Gastrointest Endosc 2004;59:280-283.
116. Buscaglia JM, Dray X, Shin EJ, et al. A new alternative for a transjugular intrahepatic portosystemic shunt: EUS-guided creation of an intrahepatic portosystemic shunt (with video). Gastrointest Endosc 2009;69:941-947.
117. Kedia P, Kumta NA, Sharaiha R, Kahaleh M. Bypassing the bypass: EUS-directed transgastric ERCP for Roux-en-Y anatomy. Gastrointest Endosc. Epub 2014 May 15. DOI: http://dx.doi.org/10.1016/j.gie.2014.04.007.