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REVIEW

Endoscopic ultrasound-guided interventions in special situations

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Abstract

Endoscopic ultrasound (EUS) was introduced in 1982 and has since become a popular advanced procedure for diagnosis and therapeutic intervention. Initially, EUS was most commonly used for the diagnosis of pancreatobiliary diseases and tissue acquisition. EUS was first used for guided cholangiography in 1996, followed by EUS-guided biliary drainage in 2001. Advancements in equipment and endoscopic accessories have led to an expansion of EUS-guided procedures, which now include EUS-guided drainage of intra-abdominal abscesses or collections, intravascular treatment of refractory variceal and nonvariceal bleeding, transmural pancreatic drainage, common bile duct stone clearance, enteral feeding tube placement and entero-enteric anastomosis. Patients with surgically altered upper gastrointestinal anatomies have greatly benefited from EUS also. This systematic review describes and discusses EUS procedures performed in uncommon diseases and conditions, as well as applications on more vulnerable patients such as young children and pregnant women. In these cases, routine approaches do not always apply, and thus may require the use of innovative and unconventional techniques. Increased knowledge of such special applications will help increase the success rates of these procedures and provide a foundation for additional advances and utilizations of the technique.

Key words: Children; Endoscopic ultrasonography; Intra-abdominal abscesses; Pregnancy; Special situation; Surgically altered anatomy; Therapeutic; Uncommon

Core tip: This article reviews the clinical applications of endoscopic ultrasound-guided interventions reported to date, including drainage of intra-abdominal collections, gallbladder and pancreas. Procedures used in pregnant women and children are also described. The aim of this review was to promote knowledge of special clinical applications in which endoscopic ultrasound is applicable.

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INTRODUCTION

Human endoscopic ultrasound (EUS), first described in 1982 by Dimagno *et al*[1], has become a popular procedure for diagnosis and therapeutic intervention. Since the first report on EUS-guided cholangiography, advances in equipment and the development of endoscopic accessories have led to a substantial growth in the number and types of EUS-guided therapies[2]. These techniques allow for real-time visualization of structures beyond the endoscopic view, thus increasing the success rate and minimizing complications associated with the procedures. As a result, EUS has also been applied to uncommon or special clinical scenarios recently, such as intra-abdominal abscesses or collections, refractory variceal and non-variceal bleeding, and transmural pancreatic drainage. Furthermore, pregnant women and children have greatly benefited from EUS applications. The aim of this review was to identify and highlight these additional uses for EUS. The PubMed database was searched for human studies written in the English language and published between 1990 and March 2015. The following keywords were used either alone or in combination with EUS: Children, pregnancy, pancreatic drainage, surgically altered anatomy, refractory bleeding and angio-therapeutic interventions, tumor ablation, tumor injection, anti-tumoral therapy, and common bile duct (CBD) stone. The references in the identified articles were also searched for potentially relevant studies. The initial search identified 196 articles, of which 89 full-text articles were considered to be related to this topic and were chosen for review and analysis.

COMMON EUS-GUIDED INTERVENTIONS

Currently, the most common EUS applications are for diagnosing pancreatobiliary disease and tissue acquisition. EUS provides a precise evaluation of the pancreas, peripancreatic organs, CBD and gallbladder. Soon after its original use for pancreatic pseudocyst drainage, EUS was utilized for biliary drainage in cases were endoscopic retrograde cholangiopancreatography (ERCP) had failed. In fact, EUS produced superior outcomes in patients with post-surgical altered anatomy, according to both technical and clinical success rates compared to enteroscopic-based ERCP-related procedures (89%-100% *vs* 50%-95%, respectively)[3-11]. The complication rates in the EUS-guided procedure, such as procedures with a transpapillary approach, using transgastric or transduodenal routes for EUS-guided rendezvous, or a transmural approach in EUS-guided hepaticogastrostomy or choledochoduodenostomy, were in an acceptable range (25%-35%)[5-11]. However, despite their relative success and routine performance, the feasibility and possibility of complications should always be considered when performing these advanced procedures[12,13]. EUS-guided pancreatic pseudocyst drainage is commonly accepted in the treatment of fluid collection due to acute pancreatitis; however, this particular application will not be reviewed in the present article.

SPECIAL EUS-GUIDED INTERVENTIONS

EUS-guided interventions have also been utilized when dealing with uncommon diseases or conditions. More susceptible patients, such as young children and critically ill or pregnant patients, have greatly benefited from EUS-guided procedures. Since these groups of patients usually require alternative approaches, each application will be reviewed and described in detail.

EUS-guided pancreatic drainage

EUS-guided pancreatic duct drainage is one of the most difficult and advanced endosonography-based interventions. This procedure is associated with relatively high complication rates, up to 43%[14-20], and thus should be carried out only by dedicated and highly skilled endoscopists with extensive experience in therapeutic ERCP and EUS procedures. Although similar to EUS-guided biliary drainage, EUS-guided pancreatic drainage is limited to patients in whom ERCP has failed, such as those with symptomatic chronic pancreatitis and pancreatic duct obstruction (due to stone or stricture).

EUS-guided pancreatic duct drainage can be performed in two ways: EUS-guided rendezvous of the pancreatic duct and EUS-guided pancreaticogastrostomy. For EUS-guided rendezvous of the main pancreatic duct, the approach involves puncture from a gastric site and guidewire manipulation until it is passed down to the ampulla, followed by guidewire grasping and scope exchange. For EUS-guided pancreaticogastrostomy, the main pancreatic duct is punctured using a transgastric approach, which is followed by neo-tract creation-dilation and stent insertion from the pancreatic duct through the gastric cavity. The success of both of these procedures is due in part to improvements in the techniques and use of the proper instruments (dilating catheters, dilating balloons, or cauterizing devices for pancreatogastric tract creation). The case series and case reports[21-26] involving EUS-guided pancreatic duct drainage are shown in Table 1.

EUS-guided biliary interventions due to surgically altered anatomy

ERCP with overtube-assisted enteroscopy has a success rate average of 75% with 3%-5% complication rates, while percutaneous biliary drainage, with similar success rate, has 0.5%-15% complication rates, including 0%-4.9% mortality[27,28]. Currently, EUS-guided biliary drainage is a preferred alternative treatment option when the patient with surgically altered anatomy prefers internal drainage. Approximately one-third of the patients

Table 1 Clinical details of case series on endoscopic ultrasound-guided pancreatic duct drainage

Ref.	Technical success	Clinical success	Complications
Shah *et al*[21] (*n* = 25)	Pancreatography, 100% Pancreatic rendezvous, 50% Pancreatic duct intervention, 71%	N/A	10.5% (pneumoperitoneum, severe pancreatitis)
Ergun *et al*[22] (*n* = 20)	Pancreaticogastrostomy, 79% Rendezvous, 100%	Long-term, 72% Mean FU time = 7 mo FU range: 3 mo to 120 mo	10% (bleeding, peripancreatic collection) Long-term: Stent dysfunction 50% (plastic stents in all cases)
Will *et al*[23] (*n* = 12)	Pancreaticogastrotomy and rendezvous, 69%	73.2% FU range: 1 mo to 72 mo	42.9% (bleeding, perforation, pain)
Tessier *et al*[24] (*n* = 36)	Pancreaticogastrostomy and pancreaticobulbostomy, 92%	69.4% Mean FU time = 14.5 mo FU range: 4 mo to 55 mo	13.2% (fluid collection, hematoma)
Fujii *et al*[25] (*n* = 43)	Pancreaticogastrostomy, (antegrade: 18, retrograde: 14) overall: 74%	83% Mean FU time = 23 mo	Major: 6% (bleeding, perforation), overall: 24%
Barkay *et al*[26] (*n* = 21)	Pancreatography, 86% Pancreatic duct drainage, 48%	70% Mean FU time = 1 yr	2% (peri-pancreatic abscess, guidewire shearing)

N/A: Data not available; FU: Follow-up.

who undergo EUS-guided pancreatic duct drainage and one-fifth who undergo EUS-guided biliary drainage have surgically altered anatomies. This is typically due to a preceding Whipple's operation (pancreaticoduodenectomy-choledochojejunostomy and pancreatojejunostomy), post-gastrectomy, or other internal bypass surgeries. Prior to the advent of EUS procedures, the only treatment options for these patients were percutaneous drainage or repeat surgical operations. Advancements in EUS techniques provided alternatives, including EUS-guided rendezvous followed by ERCP or enteroscopy-assisted ERCP, EUS-guided transmural drainage procedures (hepaticogastrostomy, choledochoduodenostomy, or pancreaticogastrostomy), and EUS-guided antegrade stent insertion. The techniques for these EUS-guided interventions are the same as the ones used for conventional (non-altered anatomy) cases, with technical and clinical success rates of 85%-100% and acceptable complications[28]. The EUS-guided biliary drainage is performed as follows: the punctured site is first localized (intra or extra-hepatic bile duct), followed by a neo-tract creation (either by cauterization or non-cauterization methods), neo-tract dilation (either by graded dilation or balloon dilatation techniques) and finally a stent placement (either plastic or metallic stents)[5,6,28,29]. Details of the case series and case reports involving EUS-guided interventions in patients with surgically altered upper gastrointestinal anatomy are shown in Table 2.

EUS-guided CBD stone clearance

The conventional CBD stone removal fails in 5%-10% of cases[30,31], half of which require other treatments such as intraductal therapy (laser lithotripsy or electrohydraulic lithotripsy)[32,33]. Patients with a surgically altered anatomy are at an increased risk for clearance failure. Itoi *et al*[29] reported a case series of 5 patients with surgically altered upper gastrointestinal anatomy who underwent EUS-guided transhepatic antegrade CBD stone removal. The success rate of complete CBD stone clearance in one session was 60%. The group used transgastric (3 cases) or transjejunum (2 cases) puncture of the CBD with a 19- or 22-gauge needle and a contrast study to evaluate the CBD stones. Next, a guidewire was introduced, traversing the ampulla down to the duodenum, and the papilla was dilated in an antegrade fashion *via* inflation of a balloon catheter to push the stones down until they passed the ampulla. In cases of incomplete CBD stone clearance, a stent was inserted.

A randomized controlled trial showed an equivalent success rate of EUS-guided CBD stone removal compared to standard ERCP for the treatment of small (< 10 mm) CBD stones[34]. The success rate was calculated based on the CBD clearance rate, procedure time, and complications. In the trial, CBD cannulation was performed only under EUS guidance to demonstrate the feasibility of EUS-only CBD stone removal. Hence, the need for fluoroscopy was eliminated, providing a feasible alternative for treatment of pregnant patients or in bedside procedures performed in the intensive care unit.

EUS-guided enteral feeding tube placement and enteric anastomosis

EUS guidance can be utilized for placement of enteral feeding tubes, such as in the case of gastrostomy or internal anastomosis. Khashab *et al*[35] described a case report involving EUS-guided gastroenterostomy. For this technique, the desired duodenal or seminal loop closest to the EUS curvilinear echoscope was identified, and the lumen was punctured to allow passage of a 0.035-inch guidewire. The sphincterotome was inserted over the guidewire for infusion of water (< 500 mL to avoid metabolic derangement), and the gastroenteric tract was dilated in preparation for placement of the anastomotic stent. There is a risk of leakage with this technique due to the mobility of the small bowel, particularly the jejunum. A recent report by Ikeuchi *et al*[36] described an endoscopic treatment in a patient with afferent loop syndrome who underwent surgical bypass. The neo-gastrojejunal

Table 2 Clinical details of case series on endoscopic ultrasound-guided biliary drainage due to surgically altered anatomy

Ref.	Etiology	Procedure (technical success rate, %)	Complications
Iwashita *et al*[28] (*n* = 7)	Stone (*n* = 5) Stricture (*n* = 1) Malignant (*n* = 1)	Stone removal, 100% Dilation, 100% Stent placement, 100% (SEMS)	Minor: 28%
Itoi *et al*[29] (*n* = 14)	Stone (*n* = 14)	Single session clearance, 60% Overall clearance, 71.4%	None

SEMS: Self-expandable metallic stent.

tract was created using a curvilinear echoscope, and a 19-gauge needle passed from the stomach into the bowel lumen. After guidewire insertion, the two lumens were stabilized, and a lumen-apposing metal stent was inserted and deployed. This neo-type of lumen secures the tract and prevents leakage, the most common problem encountered with this type of procedure. Recently, Itoi *et al*[37] reported a case series of EUS-guided gastrojejunostomy using a special gastrojejunal tube with balloon fixation technique. This specific instrument was developed to stabilize the jejunal lumen allowing for easier creation of a neo-gastrojejunal tract while minimizing the occurrence of complications, especially of leakage or perforation. Firstly, the gastroscope with overtube was inserted into the strictured region, followed by placement of a guidewire *via* the strictured region to the jejunum. After the scope was removed, a special gastrojejunal tube with balloon fixation was inserted over the guidewire down to the jejunum (in the same fashion as a naso-jejunal tube placement). Secondly, the two balloons were inflated separately using contrast media followed by water infusion through the catheter (the opening of the water channel was located between these two balloons) to form a fixed jejunal segment-like tubular structure that was easy to find with an echoscope. Therefore, this particular jejunal segment was fully dilated and very close to the gastric wall. Then, EUS was performed to locate the puncture site, which appeared on the endosonographer as a sausage-like hypoechoic structure very close to the gastric wall. A 19-gauge needle was used to puncture into that segment and a guidewire was inserted and looped. Finally, a single-step lumen-apposing stent with cautery enable-access catheter unit (Hot AXIOS stent; Xlumena Inc., Mountain View, CA, United States) was inserted over the guidewire and deployed. EUS-guided gastrojejunostomy performed by Itoi *et al*[37] appears to be safer than two other techniques mentioned previously. The new incoming type of lumen-apposing stent is currently being developed, aiming at the possibility of greater ease of deployment compared to the previous model[38].

EUS-guided intra-abdominal abscess and collection drainage

EUS-guided drainage of an intra-abdominal abscess was first reported by Giovannini *et al*[39] in 2001. EUS-guided procedures have also been reported in the drainage of pelvic and hepatic abscesses (tuberculous, pyogenic/ruptured, and concealed), as well as for prostatic, mediastinum, sub-phrenic and retroperitoneal abscesses[40-50]. These procedures use the curvilinear echoscope to locate the abscess and verify that it is well formed. After ensuring that there are no intervening blood vessels, the abscess is punctured and contents aspirated with a 19-gauge needle. Next, a guidewire is inserted into the abscess and a contrast agent is injected to allow for visualization. Then, a small-caliber sphincterotome or catheter is inserted to flush the abscess cavity with saline (50 mL). The tract is then gradually dilated using either a graded dilation technique or a balloon dilation to allow for insertion of a 7 Fr, 8.5 Fr or 10 Fr straight stent, or a single/double pigtail stent with or without nasal-abscess drainage catheter for routine flushing of saline to enhance the drainage. Follow-up studies are still needed to verify resolution of the abscesses. The size of abscesses involved varied from 4 cm to 12 cm in diameter, and the time for resolution of these abscess ranged from 3 mo to 10 mo. Details on the case series involving EUS-guided intra-abdominal abscess drainage are shown in Table 3.

EUS-guided arteriovenous interventions

In 2000, Lee *et al*[51] was first to report EUS-guided injection of cyanoacrylate for stoppage of gastric variceal bleeding. In 2008, Levy *et al*[52] combined the glue injection with microcoil embolization to treat refractory gastric variceal bleeding. Since then, there have been additional reports demonstrating success of this procedure, with variceal and non-variceal re-bleeding rates of < 10% in most cases[53-58]. A similar clinical outcome was reported by Kinzel *et al*[59] for a 31-year-old man with duodenal variceal bleeding.

Kuramochi *et al*[60] used EUS to demonstrate the increased risk of recurrence of esophageal varices in high-risk patients who exhibited anterior branch dominance and flow velocity of 12 cm/s. EUS was found to be a very sensitive tool for early detection of heightened portal pressure, observed as dilation of the collateral circulation and small gastroesophageal varices, which are often missed *via* endoscopic evaluation[61]. EUS has been shown to improve the detection and diagnosis of gastroesophageal varices and collateral veins. Furthermore, EUS can be used as an endoscopic therapy of gastroesophageal varices, such as EUS-guided sclerotherapy of esophageal collateral vessels and EUS-

Table 3 Case series on endoscopic ultrasound-guided abscess drainage

Ref.	Location of abscesses/size	Route of drainage	Complete resolution/complications
Mandai *et al*[40] (*n* = 4)	Post-operative abscess/4.5 cm to 7.0 cm	TG	100%/none
Hadithi *et al*[41] (*n* = 8)	Perirectal (*n* = 6), Perisigmoid (*n* = 2)/4.0 cm to 9.0 cm	TR	100%/none
Puri *et al*[42] (*n* = 30)	Periprostatic (*n* = 4) Perirectal (*n* = 19) Perisigmoid (*n* = 7)/2.5 cm to 5.4 cm	TR/TS	93.4%/none Re-intervention 16.5%
Varadarajulu *et al*[43] (*n* = 25)	Perirectal (*n* = 19), Perisigmoid (*n* = 6)/5.0 cm to 6.9 cm	TR/TS	96%/none Re-intervention 3%
Wehrmann *et al*[44] (*n* = 20)	Para-esophageal (*n* = 15)/> 2 cm	TE	95%/mortality 7%

N/A: Data not available; TG: Transgastric route; TR: Transrectal route; TS: Transigmoid route; TE: Transesophageal route.

Table 4 Case series on endoscopic ultrasound-guided interventions in gastrointestinal oncology

Ref.	Diseases	Therapeutic interventions	Clinical response rate	Complications
Pai *et al*[70] (*n* = 8)	Pancreatic cyst (*n* = 6) Pancreatic NET (*n* = 2)	RFA	100% Complete, 20%	20% (pain)
Park do *et al*[71] (*n* = 11)	Pancreatic NET (*n* = 11)	Alcohol injection volume: 0.5 mL to 7.0 mL Mass size: 9 mm to 19 mm	61.50% Single session, 53.3%	36.30% (pancreatitis, pain)
DeWitt *et al*[72] (*n* = 22)	Pancreatic cyst (*n* = 22)	Alcohol + Paclitaxel Cyst size: 15 mm to 43 mm	Complete, 50% No response, 25%	13% (pancreatitis, peritonitis)
Oh *et al*[73] (*n* = 14)	Pancreatic cyst (*n* = 14)	Alcohol + Paclitaxel Mass size: 17 mm to 52 mm	Complete, 78%, No response, 7%	7% (pancreatitis)
Wang *et al*[74] (*n* = 23)	Pancreatic cancer (*n* = 23)	I^{125} seed	Partial pain control at 12 wk, 77.8%	12.50% (constipation, nausea/vomiting)

RFA: Radio frequency ablation; NET: Neuroendocrine tumor.

guided cyanoacrylate (glue) injection of gastric varices. EUS can also provide knowledge on the efficacy of pharmacotherapy of portal hypertension. Furthermore, EUS can provide assessment and prediction of variceal recurrence after endoscopic therapy and assessment of portal hemodynamics, such as the E-Flow Doppler ultrasound study of the azygous and portal veins. Additionally, Giday *et al*[62,63] demonstrated the feasibility of portal vein puncture for measuring pressure and injection of contrast agents without inducing liver injury in an animal model. This was followed by a case report by Buscaglia *et al*[64] describing EUS-guided insertion of an intrahepatic portosystemic shunt. Matthes *et al*[65] demonstrated the feasibility of EUS-guided portal vein embolization using Enteryx, a swine model. However, there is no report in the literature of these invasive portal vein interventions being applied in a clinical setting as of yet.

EUS-guided interventions in gastrointestinal oncology

Patients with pancreatobiliary malignancy who were not surgical candidates benefited from EUS-guided interventions for local control and treatment of tumors. Many treatment applications have been used in these cases, including ablative therapy (by absolute alcohol injection), thermal ablative therapy using radio frequency ablation, or cold therapy by the cryo-based probe, or a combination of the techniques. In all these techniques, the catheter was introduced through the echoscope channel, localizing the treatment location under EUS guidance[66,67]. Intra-tumoral injections of cell products such as tumoral dendritic cells, TNFerade or brachytherapy using I^{125} have also been reported[68,69]. However, the clinical outcomes of these therapeutic platforms were not impressive. Although newer treatment modalities, such as new cell types and new chemical situations, are being developed, there is yet too little information available for a reasonable discussion in this review. The large case series on local tumor treatments are shown in Table 4[70-74].

EUS in pregnancy

The incidence of pancreatobiliary disease, including choledocholithiasis, in pregnant women, is estimated to be 2%-6%[75]. However, ERCP, the conventional method for CBD clearance, is not appropriate for these patients due to risks associated with fluoroscopy. Thus, EUS-guided CBD stone removal with or without intraductal visualization *via* spyglass or cholangioscopy represents a suitable alternative. With this method, CBD diagnosis can be confirmed *via* radial EUS, followed by intraductal evaluation or CBD cannulation *via* duodenoscopy[76-78]. The position of the CBD stone can be confirmed through detection of aspirated bile content allowing for a complete stone removal and/or a stent placement to avoid recurrence.

EUS in children

EUS-guided interventions are equally feasible in pediatric patients. However, compared to adults, the child's organs and ducts are smaller, requiring extra care by the endoscopists who perform the procedures. The first EUS-guided intervention in a pediatric patient was reported in 1993, and it used a fine-needle aspiration (FNA)[79]. Since then, additional advanced procedures have been performed in pediatric patients[80,81]. In 2009, Attila *et al*[82] reported a case series of EUS procedures performed in 38 children. Of these, 30% of the cases used EUS with FNA, which established the correct diagnosis in 75% of the patients who underwent FNA without any complication. Recently, Scheers *et al*[83] also reported a case series of EUS procedures in 48 children. In this case series, 13 therapeutic EUS procedures, including 9 combined EUS-ERCP procedures, were performed without adverse events. The authors also proposed that the adult endoscopes and accessories can be used safely in children > 3 years of age (or > 15 kg body weight) and that a single endoscopic treatment session is feasible in children.

CONCLUSION

EUS-guided interventions can be used to treat various conditions, with favorable outcomes in most cases. In addition to pancreatic and biliary draining procedures, EUS guidance has been utilized in CBD stone clearance, enteral feeding tube placement, enteric anastomosis, and intra-abdominal abscess drainage. Such techniques are particularly well suited for patients with altered anatomy, pregnant women, or children. Increased knowledge of such special applications will help increase the success rates of these procedures and provide a foundation for additional advances and utilizations of EUS.

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