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REVIEW

Uncommon complications of therapeutic endoscopic ultrasonography: What, why, and how to prevent

Tanyaporn Chantarojanasiri, Pitulak Aswakul, Varayu Prachayakul

Tanyaporn Chantarojanasiri, Division of Gastroenterology, Department of Internal Medicine, Police General Hospital, Bangkok 10330, Thailand

Pitulak Aswakul, Liver and Digestive Institute, Samitivej Sukhumvit Hospital, Bangkok 10120, Thailand

Varayu Prachayakul, Siriraj GI Endoscopy Center, Division of Gastroenterology, Department of Internal Medicine, Siriraj Hospital, Faculty of Medicine, Mahidol University, Bangkok 10700, Thailand

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Correspondence to: Varayu Prachayakul, Associate Professor, Siriraj GI Endoscopy Center, Division of Gastroenterology, Department of Internal Medicine, Siriraj Hospital, Faculty of Medicine, Mahidol University, Bangkok 10700, Thailand. kaiyjr@gmail.com
Telephone: +66-841-8654646
Fax: +66-2-4115013

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Abstract

There is an increasing role for endoscopic ultrasound (EUS)-guided interventions in the treatment of many conditions. Although it has been shown that these types of interventions are effective and safe, they continue to be considered only as alternative treatments in some situations. This is in part due to the occurrence of complications with these techniques, which can occur even when performed by experienced endosonographers. Although common complications have been described for many procedures, it is also crucial to be aware of uncommon complications. This review describes rare complications that have been reported with several EUS-guided interventions. EUS-guided biliary drainage is accepted as an alternative treatment for malignant biliary obstruction. Most of the uncommon complications related to this procedure involve stent malfunction, such as the migration or malposition of stents. Rare complications of EUS-guided pancreatic pseudocyst drainage can result from air embolism and infection. Finally, a range of uncommon complications has been reported for EUS-guided celiac plexus neurolysis, involving neural and vascular injuries that can be fatal. The goal of this review is to identify possible complications and promote an understanding of how they occur in order to increase general awareness of these adverse events with the hope that they can be avoided in the future.

Key words: Complications; Endoscopic ultrasonography; Rare; Therapeutic; Uncommon

Core tip: This article reviews the rare complications that occur with endoscopic ultrasound-guided interventions, including those for biliary and pancreatic pseudocyst drainage and celiac plexus neurolysis. Knowledge

of the types of rare complications will promote an understanding of their causes, and help to reduce their occurrence.

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INTRODUCTION

Endoscopic ultrasound (EUS)-guided interventions have recently been accepted as an alternative to percutaneous or radiologic-guided treatments, as well as for more invasive treatments such as surgery, for many conditions. Accumulating evidence continues to demonstrate the feasibility, efficacy, and safety of these novel procedures. Although such methods are less invasive, there are reports of adverse events with EUS-guided transluminal therapies. It is important for endosonographers to have adequate knowledge of the indications, techniques, and potential risks before performing any given procedure. Indeed, many reviews have been published describing common complications related to EUS-guided procedures. However, only a limited number of studies report on rare complications. Thus, the purpose of this review was to identify the uncommon complications related to these interventions, evaluate how they occurred, and ascertain how to prevent them. To achieve this, a search was made of English-language human studies listed in the PubMed database that were published between1991 and December 2014. The following keywords were used alone or in combination with EUS: therapeutic complication, drainage, guidewire, celiac plexus neurolysis, tumor ablation, ethanol ablation, pancreatic fluid collection, pancreatic drainage, fiducial, cystogastrostomy, abscess drainage, antibiotics, endoscopy, vascular, glue injection, oncolytic virus, and cryotherapy. References of identified articles were also searched for potentially relevant studies.

EUS-GUIDED BILIARY DRAINAGE

EUS-guided procedures have recently gained popularity for performing biliary drainage in patients for whom endoscopic retrograde cholangiopancreatography (ERCP) has failed. The initial report of EUS-guided cholangiography in 1996 was followed by a description of EUS-guided choledochoduodenostomy in 2001[1]. Since then, additional techniques for EUS-guided transluminal biliary drainage have been described, including creating a bilo-enteric fistula, using an EUS-antegrade approach, and a rendezvous technique to assist transpapillary cannulation[2]. Fistula tracts can be created either between the intrahepatic bile duct and stomach, as in EUS-guided hepaticogastrostomy, or between the extrahepatic bile duct and duodenum, as in EUS-guided choledochoduodenostomy[3]. These procedures have become a rescue therapy[4]. Although small case series of no more than five patients describe successful procedures with no complications[5-7], larger series report complication rates ranging from 9.5% to 40%[3,8-14]. The most common complications were bile leakage, stent misplacement, bleeding, and pneumoperitoneum, which accounted for 5.2%, 3.1%, 2.1%, and 1.0% of cases, respectively[3,15].Other rare complications such as biloma, cholangitis and perforation were also reported, all of which were related to the use of needle knife cautery in the multivariate analysis[15].

Most complications can be treated conservatively[15,16]. For example, biloma as a result of stent migration can be treated with a variety of methods[8,11], including percutaneous[3] or EUS-guided[17] drainage. Only one fatality was reported, which involved severe peritonitis[18]. A case of retrogastric fluid collection was successfully treated with antibiotics and percutaneous drainage[19]. Several series reported cholangitis as an early or late complication resulting from reflux of gastrointestinal (GI) contents or stent migration[11,14,15,20]. In other cases, shortening of the metallic stent after deployment caused misplacement into to the abdominal cavity or gastroduodenal perforation, which required surgical intervention[3,19,21]. Cases of bleeding from the puncture site[3,9,19] or from a hepatic artery aneurysm, which was treated by angiographic embolization[22], were also reported. One technical concern involving guidewire shearing by the EUS-needle bevel was reported, which was treated by radiologic intervention[23].

Preventative measures

When inserting stents into the bilo-enteric tract, the membrane from fully/partially covered or specially designed metal stents prevents leakage of bile from the newly created tract. As stent shortening was related to cases of biloma, perforation, and peritonitis, an appropriate-length stent should be carefully selected and placed in the optimal position. Stent dislocation can be prevented by placing clips at the endoluminal stent margins[9], or, as we have observed, by placing a double-pigtail plastic stent inside the fully covered self-expanding metal stent. In addition, the maneuver applied during stent deployment is critical, and it is recommended that the endoscopist perform the initial stent deployment under fluoroscopic monitoring, before switching to endoscopic monitoring.

Infectious complications were reported[3], including a case of cholecystitis due to previous ERCP contamination of the obstructed biliary system[20]. Although the role of antibiotic prophylaxis in such procedures has not been established[24], it has been used by several authors who found that 4-5 d (nil per mouth) of antibiotic treatment was essential for preventing minor leakage and perito-

neum contamination[4,10,20].

Although guidewire shearing during the procedure is not common during EUS-guided biliary drainage, the risk could be eliminated by avoiding acute angles during needle retraction and by retracting slowly with a lot of caution for any resistance. If any resistance is felt, the needle and the wire should be retracted concurrently[25]. Other authors recommend changing the EUS needle after puncture to a 4 Fr cannula for guidewire manipulation[26], or using a blunt-ended needle with a sharp needle-tip stylet (Access needle®; Wilson Cook Inc., Winston-Salem, NC, United States) for biliary access[23,27]. In one case, guidewire knotting occurred in an EUS-guided rendezvous procedure as a result of guidewire loop formation during endoscopic–catheter exchange[28]. In this report, the guidewire was untangled with rat-toothed forceps using a gastroscope, and the author suggested that, to prevent looping, constant tension on the wire should be maintained during exchanges. A summary of uncommon complications from EUS-guided biliary drainage is presented in Table 1.

EUS-GUIDED PANCREATIC DRAINAGE

EUS-guided pancreatic drainage can be performed to remove accumulated fluid due to acute pancreatitis or pancreatic duct obstruction. This procedure is typically performed *via* transpapillary, transluminal, or transanastomotic approaches with neotract formation or by the rendezvous technique in patients for whom ERCP has failed or who have surgically altered anatomy[25,29,30]. EUS-guided pancreatic drainage is effective with a lower morbidity compared to the other platforms[31]. The success rate depends on the type of fluid collection, and ranges from 50.0%-63.2% up to 100%[32,33]. The common complications of pancreatic duct drainage are pancreatitis, bleeding, perforation, and stent migration, with overall complication rates ranging from 0% to 52%[25,30,34]. In some case series, the complication rate was significantly higher in patients with necrosis compared to those with pseudocysts[34].

Less common complications that have been reported with EUS-guided pancreatic drainage include peri-pancreatic abscesses, fluid collection, and shearing of the guidewire during diagnostic pancreatography and therapeutic drainage[29,35-37]. In these reports, peri-pancreatic collection was the result of pancreatic fluid or pseudocyst leakage. To prevent bacterial peritonitis, some endoscopists recommend antibiotic prophylaxis[37]. Guidewire shearing occurred more frequently than was reported for EUS-guided biliary drainage, likely due to the greater angle between the EUS needle and the desired direction of the pancreatic duct[29,36], with similar remedies for prevention. A splenic artery aneurysm within the pancreatic pseudocyst was the cause of bleeding in one case, which was treated by selective angiographic embolization[38]. A summary of uncommon complications from EUS-guided pancreatic drainage is presented in Table 2.

The rare but fatal complication of air embolism was also reported, occurring in one patient who had previously undergone ERCP, and in one case of EUS with fine-needle aspiration of an accessory spleen[39]. A fatal case occurred in a patient who underwent EUS-guided pancreatic pseudocyst drainage[40]. Hikichi *et al*[41] reported a case of gallbladder puncture and drainage following misdiagnosis of a pancreatic pseudocyst, which was treated with nasocystic-tube drainage and antibiotic administration. The authors strongly recommended that every endosonographer should verify the location of the puncture site *via* EUS-scanning before initiating any drainage intervention.

EUS-GUIDED CELIAC PLEXUS NEUROLYSIS AND CELIAC PLEXUS BLOCK

Celiac plexus neurolysis (CPN) and celiac plexus block (CPB) have been performed for more than five decades in patients with upper abdominal pain of pancreatic origin and from stomach, intestinal, and intra-abdominal metastases. CPB has been performed under guidance of radiography, fluoroscopy, CT, and ultrasonography. Common complications with this procedure include local pain, diarrhea, and hypotension, whereas lower extremity weakness, paresthesia, lumbar puncture, pneumothorax, pleuritic pain, hiccups, and hematuria occur in only 1% of patients[42]. EUS-guided CPB has gained in popularity since the 1990s as it enables the endoscopist to easily and accurately determine the location for injection[43]. For EUS-guided CPN, the complications are similar, with hypotension, pain, and diarrhea occurring in 3.4%-20.0%, 6.8%-9.0%, and 10.3%-17.0% of cases, respectively[44-46].

Uncommon complications, which occurred less than 1%, from EUS-guided CPN have primarily been described within case reports. Despite the improved injection-site localization, there were reports of anterior spinal cord infarction due to alcohol-induced injury to the lumbar artery and prolonged hypotension[44-48]. Nevertheless, the occurrence is much more infrequent than is observed with other approaches[49-54]. It is possible that spinal arterial spasm or thrombosis due to the chemical agent or the direct injection into the cerebrospinal fluid in cases of percutaneous injection caused the infarctions[49,55]. Other reports describe celiac artery thrombosis resulting in gastric ulceration with hepatosplenic infarction[42,56,57] or fatal multiple organ ischemia[58]. In two of these cases[56,58], color Doppler was performed either before or after the procedure to ensure celiac artery patency. Aspiration tests were also conducted after needle puncture in two cases[56,57]. The cause of arterial thrombosis was attributed to a vasospasm of affected vessels from alcohol irritation, as the amount of alcohol was similar among the cases. There was one case of peri-pancreatic collection after absolute alcohol injection that was treated by EUS-

Table 1 Uncommon complications of endoscopic ultrasound-guided biliary drainage

Ref.	Procedure	Stent	Complications (*n*/total successful cases)	Postulated causes	Treatment	Prevention recommendation
Püspök *et al*[20]	EUS-CDS, EUS-HGS, rendezvous	Plastic stent, FCSEMS, UCSEMS	Cholangitis (1/6), cholecystitis from previous ERCP (1/6)	Cholangitis may result from previous ERCP attempt	Antibiotics, PTBD, surgery	Consider antibiotic prophylaxis
Bories *et al*[11]	EUS-HGS, rendezvous	FCSEMS	Biloma (1/11), cholangitis (1/11)	Stent shortening	Percutaneous drainage (biloma), second stent insertion (cholangitis)	Select a stent of appropriate length Observe stent position during deployment (both endoscopic and fluoroscopic views)
Attasaranya *et al*[19]	EUS-CDS, EUS-HGS, cholecystoduodenostomy, transduodenal FCSEMS insertion	Plastic stent, FCSEMS	Duodenal perforation (1/31), retrogastric collection (1/31), cholangitis (1/31)	Stent shortening	Surgery (duodenal perforation), percutaneous drainage (retrogastric collection)	Keep at least 2 cm length of stent at the mural site
Martin *et al*[18]	EUS-HGS	PCSEMS	Stent migration and biloma	Stent migration	(Dead)	
Siddiqui *et al*[21]	EUS-CDS	FCSEMS	Duodenal perforation (1/8)	Stent shortening	Surgery	
Khashab *et al*[23]	EUS-HGS	Not mentioned	Wire shearing (1/1)	Injury from EUS needle	Percutaneous intervention	Avoid acute angulation of guidewire and retract it gently Change needle to a small-size cannula during guidewire manipulation
Prachayakul *et al*[8]	EUS-CDS, EUS-HGS	FCSEMS	Biloma (1/21)	Malpositioned stent	Percutaneous drainage[17]	Observe stent position during deployment (both endoscopic and fluoroscopic views)
Prachayakul *et al*[22]	EUS-HGS	FCSEMS	Bleeding from hepatic artery aneurysm (1/1)	Iatrogenic trauma during EUS-HGS	Angiographic embolization	Puncture site should be away from major vascular structure
Kawakubo *et al*[3]	EUS-CDS, EUS-HGS	Plastic stents, FCSEMS	Cholangitis (1/61), biloma (1/61), perforation (1/61)	Stent misplacement	Percutaneous drainage (biloma), surgery (perforation)	Observe stent position during deployment (both endoscopic and fluoroscopic views)
Saxena *et al*[28]	Rendezvous	FCSEMS	Guidewire knot	Guidewire formed a knot during exchanges	Untangled using forceps	Maintain constant pressure on the guidewire during exchanges

ERCP: Endoscopic retrograde cholangiopancreatography; EUS-CDS: Endoscopic ultrasound-guided choledochoduodenostomy; EUS-HGS: Endoscopic ultrasound-guided hepaticogastrostomy; FCSEMS: Fully covered self-expandable metallic stent; PCSEMS: Partially covered self-expandable metallic stent; PTBD: Percutaneous transhepatic biliary drainage; UCSEMS: Uncovered self-expandable metallic stent.

guided drainage and intravenous antibiotics[59]. Another case involved a mixed fungal and bacterial brain abscess as a result of hematogenous spread[60]. As with the other EUS-guided procedures, the use of antibiotic prophylaxis has not been established for these rare infectious complications[24]. A summary of uncommon complications from EUS-guided CPN is presented in Table 3.

EUS-GUIDED INTRA-ABDOMINAL INTERVENTIONS

Intra-abdominal abscess drainage

Only a limited number of cases using EUS-guided intra-abdominal drainage for liver abscesses have been reported, which were performed without complications[61-65]. In addition, several reports involving 4-25 cases each of pelvic abscess drainage using a transrectal approach with or without an irrigation tube to prevent stent occlusion by fecal material have been described, also without complications[66-70]. One case series describes abscess drainage in nine patients through the esophagus, stomach, and colon[64]. Mediastinitis and pneumothorax developed in one patient who underwent transesophageal drainage of a pancreatic pseudocyst, and was treated conservatively. Stent migration occurred in another patient undergoing transcolonic drainage, which was treated endoscopically.

Vascular therapy

EUS-guided interventions have been used for creating portosystemic shunts to treat GI bleeding (both variceal and non-variceal bleeding)[71]. In addition, EUS-guided injection of cyanoacrylate or coil embolization has

Table 2 Uncommon complications of endoscopic ultrasound-guided pancreatic drainage

Ref.	Procedure	Stent	Complication (*n*/total successful cases)	Postulated causes	Treatment	Prevention recommendation
Hikishi *et al*[41]	EUS-cystogastrostomy drainage	Plastic stent, nasobiliary drainage	Gallbladder puncture and drainage	Marked distension of gallbladder with debris, overlapping location between pseudocyst and gallbladder in fluoroscopy	Conservative with antibiotics	EUS scanning prior to initiating drainage intervention
Barkay *et al*[29]	EUS-PD rendezvous, dye injection	Plastic stent	Peripancreatic abscess (1/10), wire shearing (1/10)	Failed to inject PD (peripancreatic abscess), repeated to-and-fro movements of wire	Percutaneous drainage (abscess), transluminal removal (wire)	Carefully manipulate the guidewire, avoid acute angles
Jow *et al*[40]	EUS-cystogastrostomy drainage	Not mentioned	Air emboli	Prolonged high pressure air sufflation, inflammation, mechanical injury	(Dead)	Use CO_2 inflation instead of air
Fujii *et al*[36]	EUS-PD stent (antegrade and retrograde)	Plastic stents	Peripancreatic abscess (1/32), wire shearing (1/32)	Balloon dilation? Multiple devices (peripancreatic abscess), injury from EUS needle (wire shearing)	EUS-guided transmural drainage (abscess)	Carefully manipulate the guidewire
Kurihara *et al*[38]	EUS-PD rendezvous, and PD stenting	Plastic stents, UCSEMS	Pancreatic pseudocyst with splenic artery aneurysm	Pancreatic juice leakage	Angiographic embolization	Avoid major vascular structures

EUS-PD: Endoscopic ultrasound-guided pancreatic duct drainage; PD: Pancreatic duct; UCSEMS: Uncovered self-expandable metallic stent.

Table 3 Uncommon complications of endoscopic ultrasound-guided celiac plexus neurolysis

Ref.	Composition of injection solution	Complication	Treatment and outcome	Prevention recommendation
Fujii *et al*[47]	0.25% bupivacaine in 99% alcohol (ganglia: 1 mL; plexus: 23 mL)	Paraplegia	Remained paraplegic until death	Use color Doppler to avoid intravascular injection
Mittal *et al*[48]	0.25% bupivacaine and epinephrine with alcohol (1:5) (ganglia: 5 mL; around the celiac artery: 19 mL)	Paraplegia	Lumbar drainage but no improvement	Minimize the volume of absolute alcohol
Jang *et al*[56]	0.25% bupivacaine (5 mL), 98% ethanol (10 mL), triamcinolone (1 mL)	Hepatosplenic, stomach, and small bowel infarctions, gastroduodenal ulcers	Supportive treatment, died 27 d later	
Ahmed *et al*[57]	0.25% bupivacaine (20 mL), 98% ethanol (20 mL)	Pancreaticosplenic infarction, gastric ischemia and stenosis	Subtotal gastrectomy with Roux-en-Y gastrojejunostomy	
Gimeno-García *et al*[58]	0.5% bupivacaine (5 mL), absolute alcohol (10 mL) on each side of the celiac takeoff	Thrombosis of celiac artery, pneumatosis of the stomach andsmall and large intestines, and liver, kidney, and spleen infarctions	Conservative treatment, died 8 d later	
Muscatiello *et al*[59]	Not mentioned	Peripancreatic abscess	EUS-guided aspiration of abscess and ceftazidime injection	Consider antibiotic prophylaxis
Lalueza *et al*[60]	Not mentioned	Brain abscess by *Cladosporium macrocarpum* and *Streptococcus constellatus*	Surgery, antibiotics, and antifungal	

EUS: Endoscopic ultrasound.

emerged for treatment of refractory variceal bleeding. Numerous studies have reported on the feasibility, efficacy, and safety of such methods with the aid of EUS Doppler for treatment of esophagogastric[72-75] and ectopic varices[76-78]. EUS-guidance allows for optimization of the obliteration rate as well as reduction of cyanoacrylate to lower the risk of embolization, which, though not completely eliminated, is not fatal[73]. Sclerotherapy and cyanoacrylate injections have also been used for non-variceal bleeding from duodenal

ulcers, aneurysms, and Dieulafoy's lesion[79,80]. EUS-guided injection of cyanoacrylate and polidocanol for treatment of upper GI bleeding had a success rate of 87.5%, with only one of these eight cases experiencing asymptomatic cyanoacrylate diffusion into the hepatic artery[79].

Tumor-ablative therapy

EUS-guided procedures have also shown promise for the treatment of intra-abdominal tumors and cystic lesions, such as pancreatic cystic neoplasms. Currently, there are only a few reports of ethanol ablation with or without paclitaxel lavage for pancreatic cystic lesions[81-86]. Common complications with these procedures included acute pancreatitis, abdominal pain, and hyperamylasemia. One case experienced asymptomatic splenic vein obliteration with collateral formations after 27 mo[86]. Ethanol ablation has also been described for solid tumors in the abdomen, including pancreatic neuroendocrine tumors[87-90], a GI stromal tumor[91], metastatic lymph nodes[92], and metastatic tumors in the liver[93,94] and adrenal glands[95]. The majority of these cases were treated successfully without complications, except for low-grade fever and hematomas following liver tumor ablation[94].

There are a few reports describing EUS-guided injection of biologic agents[96] and oncolytic virus therapy[97], and insertion of radioactive seed, cryotherapy, and fiducial placement for stereotactic body radiotherapy[98-103] to treat pancreatic adenocarcinoma, a deadly cancer for which only 15%-20% of patients are candidates for curative resection[96]. Adverse events were rare for these procedures, consisting of duodenal perforations due to the EUS tip, effects from the injected agents[97], mild pancreatitis, cholangitis, bleeding and fever[99-101]. Antibiotic prophylaxis was utilized in one study[100], in order to prevent cholangitis.

CONCLUSION

Therapeutic EUS is becoming more prominent in the treatment of many diseases due to the increased accuracy afforded by real-time high-resolution imaging. As a result, information regarding possible complications is greatly needed. The review presented here describes some of the less common complications that have been reported in various EUS-guided applications. By acknowledging the adverse events that occur, we can gain a better understanding of their causes and preventative actions to increase the safety of these techniques. EUS-guided interventions have been utilized for procedures of biliary and pancreatic drainage and CPN, as well as for various intra-abdominal conditions. Potential complications and preventive strategies will become clearer in the future as the number of patients treated and procedures reported increase. The authors recommended that endosonographers apply this knowledge in routine endoscopic practice for monitoring and early detection (including treatment) of these uncommon adverse events for the best clinical outcomes.

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