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Author(s)	Kawakubo, Kazumichi; Kawakami, Hiroshi; Kuwatani, Masaki et al.
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TOPIC HIGHLIGHT

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Recent advances in endoscopic ultrasonography-guided biliary interventions

Kazumichi Kawakubo, Hiroshi Kawakami, Masaki Kuwatani, Shin Haba, Shuhei Kawahata, Yoko Abe, Yoshimasa Kubota, Kimitoshi Kubo, Hiroyuki Isayama, Naoya Sakamoto

Kazumichi Kawakubo, Hiroshi Kawakami, Masaki Kuwatani, Shin Haba, Shuhei Kawahata, Yoko Abe, Yoshimasa Kubota, Kimitoshi Kubo, Naoya Sakamoto, Department of Gastroenterology and Hepatology, Hokkaido University Graduate School of Medicine, Sapporo 0608638, Japan

Hiroyuki Isayama, Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo 113-8655, Japan

Author contributions: Kawakubo K wrote the manuscript, reviewed the literature and revised the manuscript; Kawakami H and Kuwatani M revised the manuscript; Haba S, Kawahata S, Abe Y, Kubota Y and Kubo K collected the data; Isayama H and Sakaoto N supervised the manuscript; all authors approved the final manuscript for publication.

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Correspondence to: Kazumichi Kawakubo, MD, PhD, Department of Gastroenterology and Hepatology, Hokkaido University Graduate School of Medicine, Kita 15, Nishi 7, Kita-ku, Sapporo 0608638, Japan. kkawakubo-gi@umin.ac.jp
Telephone: +81-11-7161161
Fax: +81-11-7167867

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Abstract

Interventional endoscopic ultrasonography (EUS) based on EUS-guided fine-needle aspiration has rapidly spread as a minimally invasive procedure. Especially in patients with failed endoscopic retrograde cholangiopancreatography, EUS-guided biliary intervention is reported to be useful as salvage therapy. EUS-guided biliary interventions are carried out using three techniques: EUS-guided bilioenteric anastomosis, EUS-guided rendezvous procedure, and EUS-guided antegrade treatment. Although interventional EUS is not yet a standardized procedure, there have been recent advances in this field that address various biliary diseases. Here, we summarize the indications, techniques, clinical results of previous studies, and future perspectives.

Key words: Endosonography-guided biliary intervention; Choledochoduodenostomy; Hepaticogastrostomy; Rendezvous procedure; Antegrade treatment

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Core tip: Endoscopic-ultrasonography-guided biliary drainage (EUS-BD) is widely accepted as salvage therapy for transpapillary treatment. However, there are few data comparing the clinical efficacy of EUS-BD and endoscopic retrograde cholangiopancreatography (ERCP) with regard to which is the treatment of choice. As EUS-BD is performed under direct visualization, it has the potential to replace ERCP. However, a prospective randomized study is necessary to confirm it.

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INTRODUCTION

The endoscopic transpapillary approach based on the endoscopic retrograde cholangiopancreatography (ERCP) technique has been a standard treatment for various biliary diseases, such as choledocholithiasis and biliary obstruction[1,2]. ERCP sometimes fails, however, for various reasons[3]. Recently, interventional endoscopic ultrasonography (EUS) based on EUS-guided fine-needle aspiration (EUS-FNA) has been developed as a salvage therapy for transpapillary treatment. In patients with failed ERCP, percutaneous or surgical interventions are mandatory but are associated with considerable morbidity and mortality[4-6]. Interventional EUS could manage these patients with minimal invasion. Although interventional EUS is not yet a standardized procedure, there have been recent advances in this field that address various biliary diseases.

EUS-GUIDED BILIARY INTERVENTION TECHNIQUES

EUS-guided biliary interventions are carried out using three techniques: EUS-guided bilioenteric anastomosis (EUS-BEA), EUS-guided rendezvous procedure (EUS-RV), and EUS-guided antegrade treatment (EUS-AT). EUS-guided biliary drainage is performed with the armamentarium available for EUS-FNA and ERCP-related procedures such as an EUS-FNA needle, a guidewire, and a biliary stent.

EUS-BEA

EUS-BEA is performed to create an artificial fistula between the intestine and the bile duct by placing a stent. One indication for this procedure is the palliation of obstructive jaundice in patients with malignant diseases who have failed biliary drainage by ERCP. The procedure is mainly divided into three methods according to the anatomical site of the fistula: EUS-guided choledochoduodenostomy (EUS-CDS), EUS-guided hepaticogastrostomy (EUS-HGS), and EUS-guided gallbladder drainage (EUS-GBD). In these cases, the echoendoscope is advanced into the upper gastrointestinal tract (stomach, duodenum and jejunum), after which, the biliary system (bile duct or gallbladder) is punctured by a needle. The guidewire is then advanced into the biliary system followed by dilation of the fistula. Finally, the stent is deployed between the biliary system and the gastrointestinal tract.

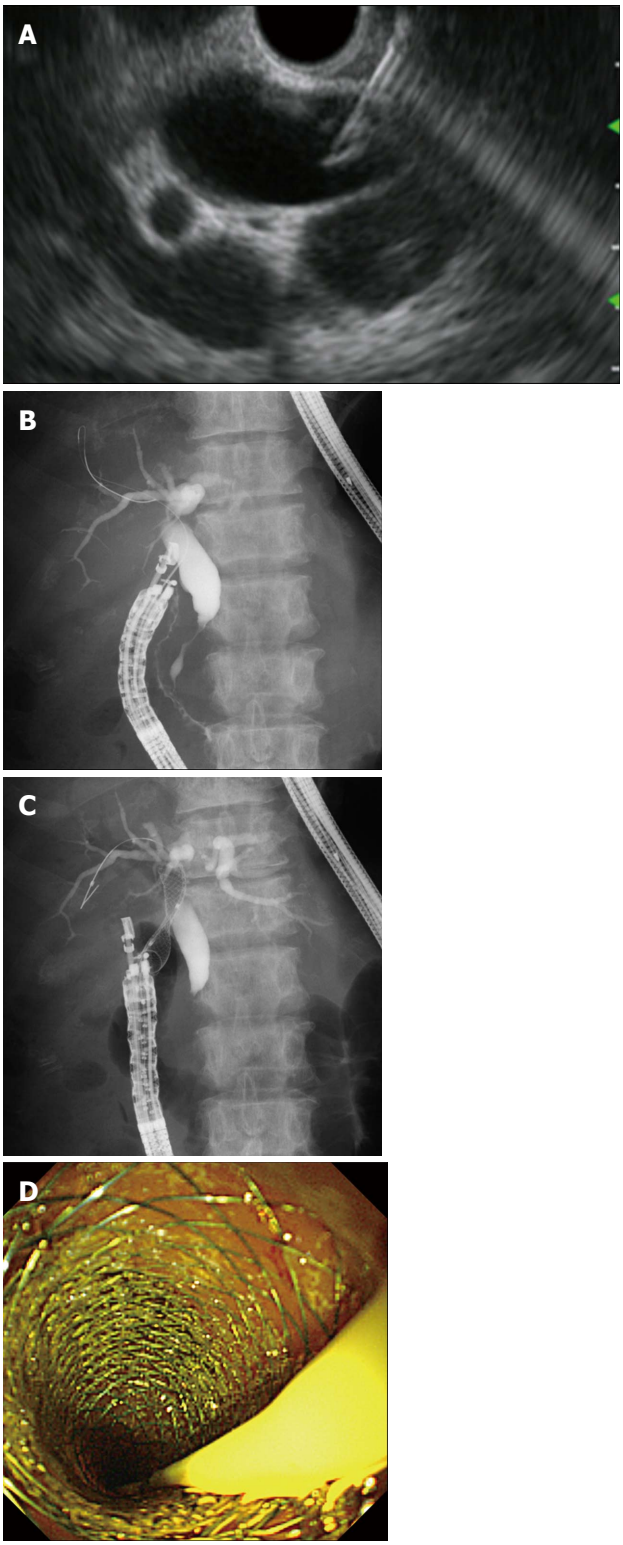

Figure 1 Endoscopic ultrasonography-guided choledochoduodenostomy. A: Endoscopic ultrasonography showing that extrahepatic bile duct was punctured by the needle; B: Guidewire was advanced through the needle into the right liver lobe; C: A self-expandable metallic stent (SEMS) was placed between the bile duct and the duodenum; D: Endoscopic view showing that the distal end of a SEMS was located at the duodenum.

EUS-CDS is undertaken to create a fistula between the extrahepatic bile duct and the duodenal bulb (Figure 1). Since the first report in 2001 by Giovannini

Table 1 Published data of endoscopic ultrasonography-guided choledochoduodenostomy (EUS-CDS or HGS) (n > 20)

Ref.	No. of patients	Study design	CDS or HGS	Stent	Technical success	Complication rate	Patency	Complication
Park *et al*[9]	55	P	CDS, HGS	PS, MS	92, 100	21, 19	152, 132	Peritonitis, pneumoperitoneum, Bleeding
Hara *et al*[11]	18	P	CDS	PS	94	17	272	Peritonitis, hemobilia
Khashab *et al*[25]	20	R	CDS, HGS	PS, MS	100	10	-	NA
Kawakubo *et al*[8]	64	R	CDS, HGS	PS, MS	95, 95	14, 30	-	Bile leak, stent misplacement, bleeding
Hara *et al*[12]	18	P	CDS	MS	94	11	NR	peritonitis
Vila *et al*[10]	65	R	CDS, HGS	NA	86, 65	15, 29	-	Biloma, bleeding, perforation, pancreatitis, cholangitis, hematoma, abscess, pseudocyst
Dhir *et al*[13]	30	R	CDS, HGS	MS	92.3	20	-	Cholangitis, perforation, bile leak, pneumoperitoneum, death

P: Prospective; R: Retrospective; CDS: Choledochoduodenostomy; HGS: Hepaticogastrostomy; PS: Plastic stent; MS: Metallic stent; NA: Not available; NR: Not reached.

et al[7], EUS-CDS has been widely accepted as an effective alternative therapy for palliation of distal malignant biliary obstruction after failed ERCP (Table 1)[8-13], although it is impossible to perform EUS-CDS in patients with altered upper gastrointestinal tract anatomy. Because of the anatomical proximity of the viscera, EUS-CDS is not technically challenging. The technical success rate is reported to be 86%-100%. Artifon *et al*[14] reported that the clinical success and complication rates were similar for EUS-CDS and percutaneous transhepatic biliary drainage (PTBD) for patients in whom ERCP failed. Plastic stents were mainly placed in the early cases of EUS-CDS, whereas more recently self-expandable metallic stents (SEMSs) have played a major role. EUS-CDS is mainly indicated for patients with distal malignant biliary obstruction in whom ERCP has failed. However, the feasibility of EUS-CDS as the first-line treatment for distal malignant biliary obstruction was recently reported[12]. The complication rate was reported at 9%-23%. Biliary peritonitis and pneumoperitoneum were the most frequent complications. Others were stent migration, bleeding, and cholangitis. There are no standardized techniques for managing these complications, so it is important to be ready to handle any situation[15-19]. Recently, the feasibility of performing EUS-CDS with specialized stents has been reported[20-22]. Widespread use of sophisticated SEMSs for EUS-CDS could reduce the incidence of complications.

EUS-HGS is performed to create a fistula between the left intrahepatic bile duct and the stomach (Figure 2). The indication for EUS-HGS is similar to that for EUS-CDS, that is, palliation of distal malignant biliary obstruction. However, EUS-HGS could be also performed in patients with altered upper gastrointestinal tract anatomy or gastric outlet obstruction. In addition, palliation of a left intrahepatic bile duct with a malignant hilar biliary obstruction is possible with EUS-HGS[23,24]. The technical success rate with EUS-HGS is 81%-100% (Table 1)[8,9,13,25]. EUS-HGS itself has serious complications, however, because the fistula traverses the peritoneum[26]. The complication rate ranges from 19% to 30%. Common complications are pneumoperitoneum, bleeding, bile leak, cholangitis, and stent migration. In particular, inward stent migration can be fatal. It is important to manage these complications[27,28]. To prevent inward stent migration, a longer stent might be better and it should be deployed not under fluoroscopic guidance but rather direct endoscopic visualization. Although some specialized SEMSs for EUS-HGS have been developed[22], highly dedicated SEMSs for EUS-HGS are necessary to reduce the complication rate. Recently, the feasibility of EUS-HGS for treating isolated right intrahepatic bile duct was reported[29,30]. Also, bilateral EUS-HGS for palliation of hilar malignant biliary obstruction could be feasible in the near future.

EUS-GBD is performed to create a fistula between the gallbladder and gastrointestinal tract (stomach or duodenum) (Figure 3). This procedure is indicated for drainage in patients with acute cholecystitis as an alternative to percutaneous transhepatic gallbladder drainage (PTGBD), and who are not suitable candidates for emergency cholecystectomy. The technical success rate is reported to be around 100% (Table 2)[31-33]. A plastic stent or nasobiliary tube is used in patients with temporary stent placement, whereas SEMSs are used for patients who are not suitable for future cholecystectomy. Jang *et al*[33] reported that the technical and clinical success rates for EUS-GBD were similar to those for PTGBD. Also, the pain scores were lower following EUS-GBD than after PTGBD in patients prior to cholecystectomy. A recent report indicated that, if a specialized SEMS is used, EUS-GBD is feasible for patients who are not suitable candidates for elective cholecystectomy[34]. In the future, EUS-GBD might be the treatment of choice for acute cholecystitis in high-risk patients.

EUS-RV

An indication for the EUS-RV is biliary cannulation in patients who have failed biliary cannulation in conventional ERCP. For EUS-RV, the bile duct is punctured and a guidewire is advanced through the

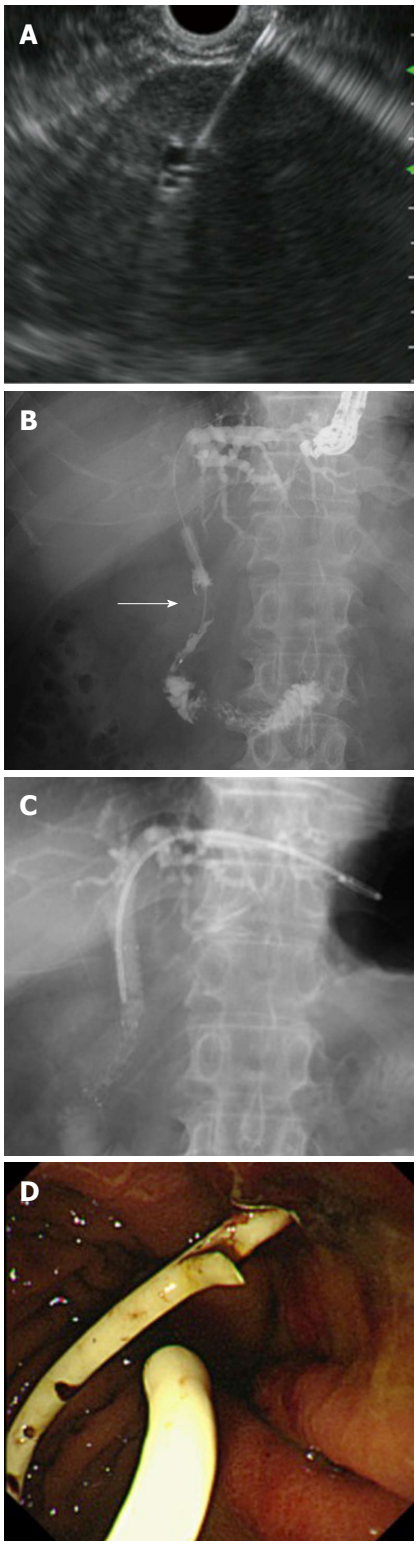

Figure 2 Endoscopic ultrasonography-guided hepaticogastrostomy. A: Left intrahepatic bile duct was punctured; B: Cholangiography showing distal malignant stricture (arrow); C: Following antegrade self-expandable metallic stent placement, a plastic stent was deployed between the intrahepatic bile duct and stomach; D: Endoscopic view showing that the distal end of the plastic stent was located at the stomach.

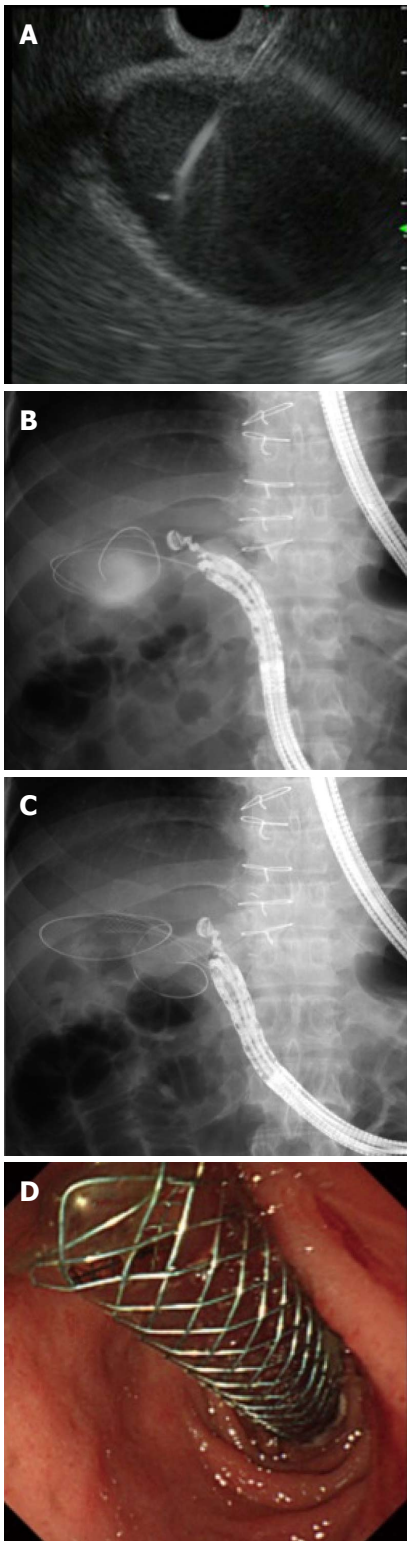

Figure 3 Endoscopic ultrasonography-guided gallbladder drainage. A: Endoscopic ultrasonography showing that the gallbladder was punctured by the needle; B: Guidewire was advanced through the needle into the gallbladder; C: A self-expandable metallic stent (SEMS) was placed between the gallbladder and the duodenum; D: Endoscopic view showing that distal end of a SEMS was located at the stomach.

Table 2 Published data of endoscopic ultrasonography-guided gallbladder drainage (n > 10)

Ref.	No. of patients	Study design	Stent	Technical success	Complication rate	Complication
Jang *et al*[33]	30	P	ENBD	97%	7%	Pneumoperitoneum
Choi *et al*[32]	63	R	MS	98%	5%	Perforation, pneumoperitoneum

P: Prospective; R: Retrospective; ENBD: Endoscopic nasobiliary drainage; MS: Metallic stent.

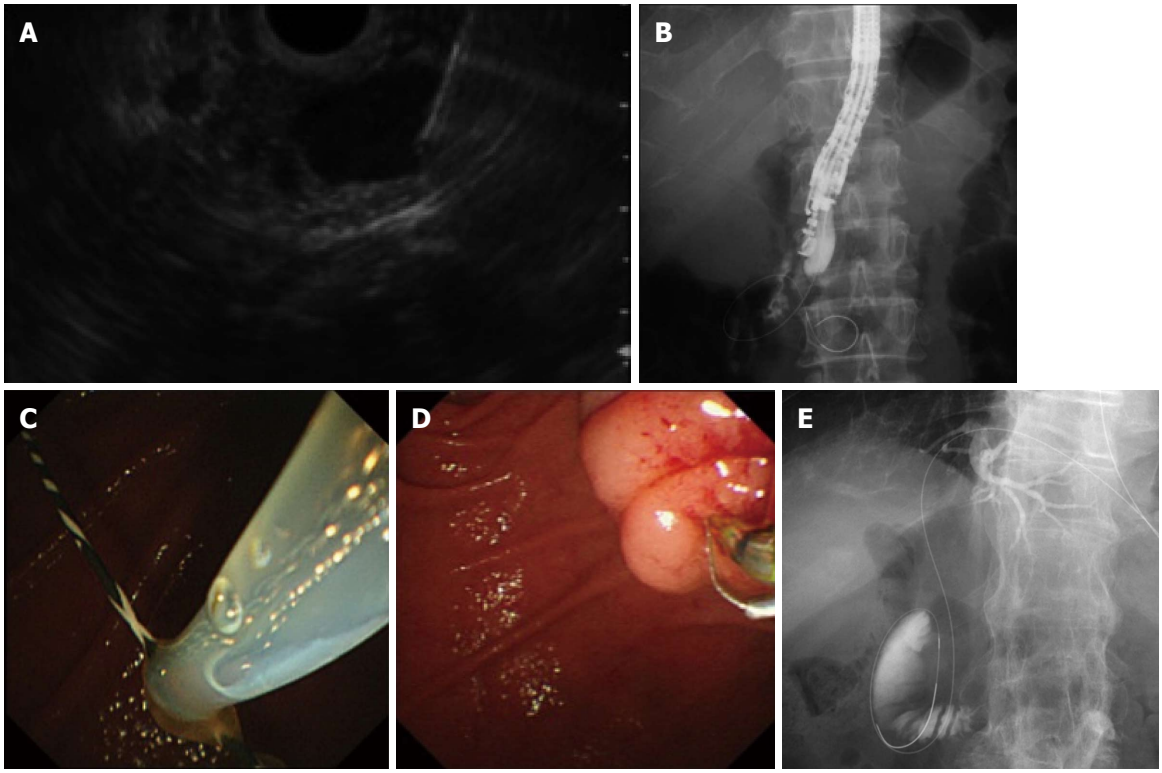

Figure 4 Endoscopic ultrasonography-guided rendezvous procedure. A: Endoscopic ultrasonography showing that extrahepatic bile duct was punctured by the needle; B: Radiography showing the guidewire was passed through the needle into the duodenum across the papilla antegradely. The endoscope was in the short position; C: Following echoendoscope withdrawal, the duodenoscopic view showed that a guidewire passing through the papilla was grasped by the snare; D: After the guidewire was pulled out through the accessary channel of the duodenoscope, a catheter was inserted into the bile duct over the existing guidewire; E: Transhepatic approach. Abdominal radiography shows that a guidewire was placed through the papilla into the duodenum.

needle to the duodenum. An ERCP-related procedure is then performed using the guidewire. EUS-RV is indicated when biliary access fails during ERCP. There are two biliary access routes depending on the site to be addressed: transhepatic and transduodenal (Figure 4). The transduodenal route is further divided according to the endoscope position: long (push) and short (pull)[35]. The short endoscopic position is referred to as the tip of the endoscope oriented in the caudal direction, while the endoscope is directed cranially in the long endoscopic position. The echoendoscope is advanced into the upper gastrointestinal tract (esophagus, stomach, duodenum and jejunum), and the bile duct is punctured by an FNA biopsy needle. The guidewire is then advanced through the needle antegradely across the papilla to the duodenum. In patients undergoing choledochojejunostomy, the guidewire is passed through the anastomosis to the jejunum. The echoendoscope is then pulled out, keeping the guidewire in place. The ERCP endoscope (duodenoscope or enteroscope) is then advanced to the papilla or the anastomosis where the guidewire has been placed. Biliary access is then achieved alongside or over the guidewire after grasping and withdrawing the instrument through the accessory channel of the endoscope. The biliary intervention is then begun. EUS-RV is indicated when biliary cannulation fails or a biliary stricture cannot be passed. The technical success rate varies from 63% to 98% (Table 3)[10,36-39]. The technical success rate for the transduodenal route is reported to be higher than that for the transhepatic route. Dhir *et al*[39] noted that the biliary cannulation success rate was higher with EUS-RV than that for the precut technique in patients with difficult ERCP cannulation. The complication rate was around 10%. The most common complications were biliary peritonitis and pancreatitis. Shah *et al*[38] reported that the transhepatic route could have a tamponade effect

Table 3 Published data of endoscopic ultrasonography-guided rendezvous procedure (n > 40)

Ref.	No. of patients	Access route	Technical success	Complication rate	Complication
Maranki *et al*[36]	49	TD, TH	63%	16%	Pneumoperitoneum, bleeding, peritonitis, aspiration pneumonia
Iwashita *et al*[37]	40	TD, TH	73%	13%	Pancreatitis, pneumoperitoneum, sepsis
Shah *et al*[38]	74	NA	74%	8%	Pancreatitis, bile leak, perforation
Dhir *et al*[39]	58	TD	98%	3%	Bile leak
Vila *et al*[10]	60	NA	68%	22%	Biloma, bleeding, Perforation, pancreatitis, cholangitis, hematoma, abscess, pseudocyst

NA: Not available; TD: Transduodenal route; TH: Transhepatic route.

Table 4 Published data of endoscopic ultrasonography-guided antegrade treatment (n > 10)

Ref.	No. of patients	Study design	Stent	Technical success rate	Complication rate	Complication
Shah *et al*[38]	16	R	MS	81%	6%	Hematoma
Park *et al*[41]	14	P	MS	57%	0%	-
Dhir *et al*[42]	35	R	MS	97%	23%	Bleeding, cholangitis, bile leak, pneumoperitoneum
Ogura *et al*[43]	12	R	MS	100%	8%	Pancreatitis

MS: Metallic stent; P: Prospective; R: Retrospective.

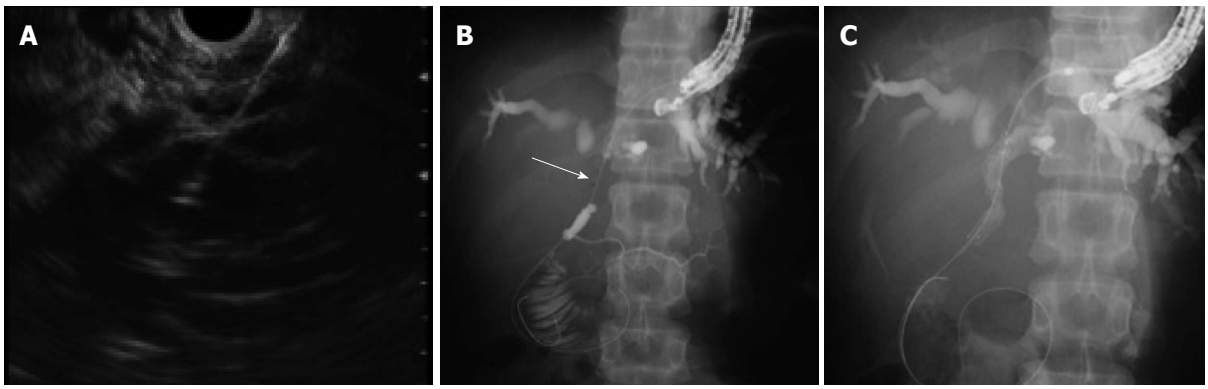

Figure 5 Endoscopic ultrasonography-guided antegrade treatment. A: Left intrahepatic bile duct was punctured; B: Guidewire was advanced through the needle across the stricture (arrow); C: A self-expandable metallic stent was placed antegradely across the stricture.

and protect against bile leakage, but a prospective study is needed to confirm their results.

EUS-AT

An indication for EUS-AT is biliary intervention in patients in whom conventional ERCP is impossible. EUS-AT is performed when it is necessary to approach the biliary intervention antegradely through a bilioenteric fistula. Antegrade is the opposite of retrograde in ERCP and is used to maintain bile flow. EUS-AT is indicated, for example, when biliary drainage is needed in patients whose upper gastrointestinal anatomy is altered, or who have malignant gastric outlet obstruction because it is impossible to perform conventional ERCP-related procedures in those patients. EUS-AT is usually performed *via* the transhepatic route (Figure 5). The echoendoscope is advanced into the upper gastrointestinal tract (esophagus, stomach and jejunum), and the left intrahepatic bile duct is punctured using an FNA biopsy needle. A cholangiogram is then obtained followed by antegrade guidewire insertion through the needle to the duodenum or jejunum across the papilla or the anastomosis. Finally, the biliary intervention is performed antegradely. It is thus possible to perform EUS-AT in patients with altered upper gastrointestinal anatomy[40]. There have been some small case series regarding the feasibility of EUS-AT to treat bile duct stones, malignant biliary obstruction, and anastomotic stricture. The technical success and complication rates for EUS-AT are 57%-100% and 0%-23%, respectively (Table 4)[38,41-43]. Although there are no large case series, the reported complications have been identified as bile leakage, pneumoperitoneum, and bleeding.

Table 5 Important features of each procedure

	EUS-BEA	EUS-RV	EUS-AT
Indication	Patients with malignant biliary obstruction after failed ERCP	Patients with failed biliary cannulation in ERCP	Patients with malignant biliary obstruction after failed ERCP
Advantage	Not traversing the malignant stricture	Leading to ERCP related procedure	Possible in patients with altered upper GI anatomy
Weak point	Necessity of fistula dilation Lack of dedicated stent	Difficult guidewire manipulation Difficulty in patient who was not accessible to the papilla	Difficult guidewire manipulation

ERCP: Endoscopic retrograde cholangiopancreatography; EUS-RV: Endoscopic ultrasonography-guided rendezvous procedure; EUS-BEA: Endoscopic ultrasonography-guided bilioenteric anastomosis; GI: Gastrointestinal; US-AT: Endoscopic ultrasonography-guided antegrade treatment.

WHICH TECHNIQUE SHOULD WE SELECT?

In patients with an accessible papilla, any EUS-BD procedure could be possible. Artifon *et al*[14] reported that the technical and clinical success rates for EUS-CDS and EUS-HGS for treating distal malignant obstruction were similar. Also, Khashab *et al*[25] reported that the clinical efficacy and safety were similar for EUS-CDS and EUS-RV. Although the complication rate for EUS-RV was relatively lower than that for EUS-BEA, more prospective studies are necessary. For patients with an inaccessible papilla, EUS-HGS and EUS-AT are possible.

There are no data concerning which procedure should be chosen. Hence, it is important to understand the characteristics of each procedure (Table 5).

FUTURE PERSPECTIVES

There are few data available that compare the clinical efficacy of EUS-BD and ERCP with regard to which is the treatment of choice. Dhir *et al*[42] reported that the short-term outcomes of EUS-BD (EUS-CDS and EUS-AT) were comparable with those achieved with ERCP. As EUS-BD is performed under direct visualization, it has the potential to substitute for ERCP. A prospective, randomized study is necessary, however, to confirm it. The future development of highly dedicated devices is mandatory.

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