

# Comparison of EUS-guided choledochoduodenostomy and percutaneous drainage for distal biliary obstruction: A multicenter cohort study

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## ABSTRACT

**Background and Objectives:** Percutaneous transhepatic biliary drainage (PTBD) and EUS-guided choledochoduodenostomy (EUS-CD) are alternate therapies to endoscopic retrograde cholangiopancreatography with stent placement for biliary decompression. The primary outcome of this study is to compare the technical and clinical success of PTBD to EUS-CD in patients with distal biliary obstruction. Secondary outcomes were adverse events (AEs), need for reintervention, and survival. **Methods:** A multicenter retrospective cohort study from three different centers was performed. Cox regression was used to compare time to reintervention and survival and logistic regression to compare technical and clinical success and AE rates. Subgroup analysis was performed in patients with malignant biliary obstruction (MBO). **Results:** A total of 86 patients (58 PTBD and 28 EUS-CD) were included. The two groups were similar with respect to age, gender, and cause of biliary obstruction, with malignancy being the most common etiology (80.2%). EUS-CD utilized lumen-apposing metal stents in 15 patients and self-expandable metal biliary stents in 13 patients. Technical success was similar between EUS-CD (100%) and PTBD (96.6%;  $P = 0.3$ ). EUS-CD was associated with higher clinical success compared to PTBD (84.6% vs. 62.1%;  $P = 0.04$ ). There was a trend toward lower rates of AEs with EUS-CD 14.3% versus PTBD 29.3%, odds ratio: 0.40 (95% confidence interval [CI]: 0.12–1.33,  $P = 0.14$ ). The need for reintervention was significantly lower among patients who underwent EUS-CD (10.7%) compared to PTBD (77.6%) (hazard ratio: 0.07, 95% CI: 0.02–0.24;  $P < 0.001$ ). A sensitivity analysis of only patients with MBO demonstrated similar rate of reintervention between the groups in individuals who survived 50 days or less after the biliary decompression. However, reintervention rates were lower for EUS-CD in those with longer survival. **Conclusion:** EUS-CD is a technically and clinically highly successful procedure with

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a trend toward lower AEs compared to PTBD. EUS-CD minimizes the need for reintervention, which may enhance end-of-life quality in patients with MBO and expected survival longer than 50 days.

**Key words:** distal biliary obstruction, endoscopic ultrasound-guided choledochoduodenostomy, malignant biliary obstruction, percutaneous transhepatic biliary drainage

## BACKGROUND

ERCP with transpapillary biliary stenting is the preferred initial intervention for biliary decompression at most centers. In the uncommon scenario of ERCP failing to achieve biliary drainage, patients can undergo either percutaneous transhepatic biliary drainage (PTBD) or EUS-guided routes, including choledochoduodenostomy (EUS-CD).<sup>[1]</sup> PTBD has historically been the preferred alternative after failed ERCP given the high clinical success rate and widespread availability.<sup>[2]</sup> However, PTBD drainage is associated with morbidity including recurrent drain obstruction, displacement, and cholangitis requiring frequent exchanges and therefore negatively impacting patients' quality of life.<sup>[3]</sup>

EUS-CD has emerged as an alternative treatment modality by providing internal biliary drainage in patients with distal common bile duct (CBD) obstruction with upstream prestenotic biliary dilation. The procedure has traditionally been performed using covered self-expandable metal biliary stents (SEMSs). The development of the cautery-enhanced delivery system of lumen-apposing metal stents (LAMSs) allows simple puncture and stent delivery, potentially without the requirement for wire-guided device exchange and tract dilation, thus leading to faster procedure times and reducing the risk of losing biliary access during stent deployment.<sup>[4]</sup> Data comparing EUS-CD to PTBD are limited, including studies that utilize LAMS.<sup>[5,6]</sup> This multicenter study aims to compare EUS-CD to PTBD in patients with malignant and benign distal biliary obstruction (DBO).

## METHODS

### *Study population and outcomes*

A multicenter retrospective cohort study was performed from three centers including two from the United States (Mayo Clinic Rochester and the University of North Carolina) and one from Asia (The Chinese University of Hong Kong). The study was approved

by the Mayo Clinic institutional review board (IRB: 19-007927 on August 29, 2019) and by each individual institution IRB. Consecutive patients with malignant and benign DBO from January 2010 to July 2019 were included if they were treated by either EUS-CD or PTBD. Patients who were treated with EUS-CD or PTBD as either the first modality or after ERCP failure were included in this study.

Patients with surgically altered intestinal anatomy (*e.g.*, Roux-en-Y) were excluded. Baseline characteristics, laboratory values, and route of biliary drainage were extracted from medical records. The primary outcomes were technical and clinical success. Technical success was defined as successful placement of PTBD or EUS-CD stent. Clinical success was defined as normalization of bilirubin or a 50% reduction within 2 weeks of biliary drainage. Secondary outcomes were adverse events (AEs) (bile leak, bleeding, perforation, obstruction, cholangitis, and stent migration), number of reinterventions, recurrence of biliary obstruction requiring additional drainage, and survival. For time to reintervention, patients were censored at the time of death if they had not developed the outcome. Survival time was determined from the time of initial drainage to the time of death or last clinical follow-up.

### *EUS-CD technique*

There was some variation in the technique given the multicenter retrospective nature of the study, but overall, all endoscopists followed the same principles. Periprocedural antibiotics were administered at the time of biliary drainage. First, the linear echoendoscope was advanced into the duodenum and the optimal positioning was identified where the dilated bile duct was in close proximity to the duodenal wall. For EUS-CD using SEMS, sequential steps then involved bile duct puncture using a 19-gauge needle through a transduodenal approach, bile aspiration, contrast injection, and fluoroscopically guided cholangiography. Subsequently, a guidewire was passed retrograde through the needle, into the proximal biliary tree.

The tract was dilated by advancing the needle sheath and exchanged for a 4–8 mm balloon dilator over the guidewire. The SEMS was then deployed across the tract. The SEMS utilized either a Viabil (W.L. Gore and Associates, Inc., Flagstaff, AZ) or partially covered Wallflex stent (Boston Scientific, Marlborough, MA). Noncautery-enhanced LAMS (Axios, Boston Scientific, Marlborough, MA) was deployed in similar fashion. Cautery-enhanced LAMS delivery systems (Axios, Boston Scientific, Marlborough, MA) were deployed using either a similar technique above over the guidewire without the need for prior tract dilation (*i.e.*, over the guidewire technique) or by directly puncturing the bile duct with concurrent use of electrocautery without prior guidewire placement (*i.e.*, freehand technique). The LAMS was advanced and the distal flange deployed within the bile duct under EUS and fluoroscopic guidance. The proximal flange was then deployed in the duodenal lumen. The variation in the technique resulted from endoscopist preference and stent selection. Plastic stents were variably placed through the LAMS and SEMS.

#### *Percutaneous transhepatic biliary drainage technique*

The technique was similar to a previously described biliary access technique.<sup>17</sup> Briefly, a standard transhepatic cholangiography is performed via a right mid-axillary (right lobe) or subcostal (left lobe) puncture of the liver based on feasibility using fluoroscopic and/or ultrasound guidance using a 20–22-gauge needle with contrast injection used for confirmation. A 0.018-inch guidewire was then introduced and used to exchange the needle for a 4-French coaxial dilator. Through this dilator, a 4-French catheter and wire were used to negotiate across the ampulla into the intestinal lumen. A 0.035-inch guidewire is introduced into the intestinal lumen and the catheter and dilator are removed. The transhepatic access is dilated with a 10-French dilator, and a 10-French hydrophilic biliary drainage catheter is placed over the wire with the loop formed in the intestinal lumen and side holes extending into the biliary tree.

#### *Statistical analysis*

Baseline characteristics were compared between the two groups using Chi-square for categorical variables and Student's *t*-test for continuous ones. Clinical success, technical success, and rate of AEs were compared using crude and adjusted logistic regression model. Serum bilirubin concentration before and after drainage was compared within each group using paired *t*-test.

Time to reintervention and survival were plotted using a Kaplan–Meier curve and compared using the Cox proportional hazards model. Crude hazard ratio and adjusted hazard ratio (aHR) were calculated controlling for possible confounders. Two-sided  $P < 0.05$  was considered statistically significant. All analysis was performed using STATA 14.2 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

## RESULTS

A total of 86 patients met inclusion criteria including 58 patients who underwent PTBD and 28 who underwent EUS-CD. Baseline characteristics are compared in Table 1. The mean age of the cohort was  $66.4 \pm 14.7$  years and 48.8% were female. There was no significant difference between the two groups with respect to age and gender. Malignant biliary obstruction (MBO) was noted in 80.2% and was similar between groups, with pancreatic cancer being the most common cause of obstruction (68.1%). The mean bilirubin level at the time of drainage was similar between the EUS-CD ( $8.5 \pm 7.4$  mg/dL) and the PTBD groups ( $8.8 \pm 8.2$  mg/dL;  $P = 0.87$ ). The majority of patients failed ERCP before proceeding with EUS-CD (75%) or PTBD (74.1%),  $P = 0.93$ . The reason for proceeding with EUS-CD or PTBD as the first modality was mostly based on the clinician judgment that an ERCP would not be technically feasible or clinically successful in providing biliary drainage. The reason for ERCP failure was most commonly due to failure to reach the papilla in the EUS-CD group (66.7%), whereas the main reason for failure in the PTBD group was inability to deeply cannulate the biliary tree (60.5%;  $P = 0.04$ ).

EUS-CD was performed using either LAMS (15, 53.6%) or SEMS (13, 46.4%). The median follow-up after drainage was 164 days (interquartile range: 53–484 days). There was no significant difference in the duration of follow-up between the two groups ( $P = 0.16$ ) [Table 1].

#### *Overall cohort*

Technical success was similar between the two groups (EUS-CD 100% *vs.* PTBD 96.6%;  $P = 0.3$ ). However, patients who underwent EUS-CD had significantly higher rates of clinical success 84.6% compared to 62.1% in those who underwent PTBD, odds ratio (OR): 3.4 (95% confidence interval [CI]: 1.02–11,  $P = 0.04$ ). The mean bilirubin level decreased

from  $8.3 \pm 7.4$  mg/dl to  $3.6 \pm 3.5$  mg/dL,  $P < 0.001$  in the EUS-CD group and from  $8.8 \pm 8.2$  mg/dL to  $5.1 \pm 5.5$  mg/dL,  $P < 0.001$  within 2 weeks after biliary drainage [Figure 1]. EUS-CD had lower AEs 14.3% compared to PTBD 29.3% without reaching a statistical significance, OR: 0.4 (95% CI: 0.12–1.33,  $P = 0.14$ ). The need for reintervention was only 10.7% in the EUS-CD group compared to 77.6% in the PTBD group; HR: 0.07 (95% CI: 0.02–0.24,  $P < 0.001$ ) [Figure 2]. The need for reintervention remained significantly lower in the EUS-CD group even after controlling for age, gender, and etiology of biliary obstruction (malignant *vs.* benign) aHR:

0.07 (95% CI: 0.02–0.23,  $P < 0.001$ ). Since routine PTBD exchange is expected, the data were reanalyzed to include only unplanned reinterventions, which were also lower in the EUS-CD group compared to PTBD group but not statistically significant, HR: 0.2 (95% CI: 0.05–1.05,  $P = 0.06$ ) and aHR: 0.24 (95% CI: 0.05–1.06,  $P = 0.06$ ).

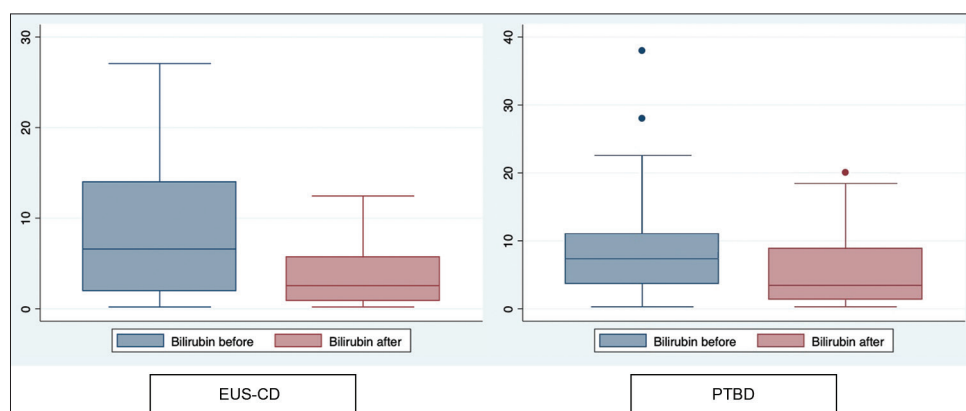
### Malignant biliary obstruction

The majority of patients in our cohort had MBO ( $n = 69$ ). Pancreatic adenocarcinoma was the most common cause of MBO in 47 (68%) followed by metastatic disease in 9 (13.1%), gastric and duodenal

**Table 1. Baseline characteristics comparing patients who underwent EUS-CD to those who underwent percutaneous transhepatic biliary drainage ( $n=86$ )**

|  | EUS-CD ( $n=28$ ) | PTBD ( $n=58$ )   | <i>P</i> | Total ( $n=86$ ) |
|--|-------------------|-------------------|----------|------------------|
| Age (years), mean $\pm$ SD                             | 67.4 $\pm$ 13.7   | 65.8 $\pm$ 15.1   | 0.64     | 66.4 $\pm$ 14.7  |
| Female, <i>n</i> (%)                                   | 16 (57.1)         | 26 (44.8)         | 0.28     | 42 (48.8)        |
| Cause of biliary obstruction, <i>n</i> (%)             |                   |                   |          |                  |
| Malignant  | 23 (82.1)         | 46 (79.3)         | 0.09     | 69 (80.2)        |
| Benign   | 5 (17.9)          | 12 (20.7)         |          | 17 (19.8)        |
| Type of malignancy, <i>n</i> (%)                       |                   |                   |          |                  |
| Pancreatic cancer                                      | 12 (52.2)         | 35 (76.1)         |          | 47 (68)          |
| Cholangiocarcinoma                                     | 1 (4.4)           | 3 (6.5)           |          | 4 (5.8)          |
| Gastric or duodenal adenocarcinoma                     | 4 (17.4)          | 5 (10.9)          |          | 9 (13.1)         |
| Metastases   | 6 (26)            | 3 (6.5)           |          | 9 (13.1)         |
| Failed ERCP, <i>n</i> (%)                              | 21 (75)           | 43 (74.1)         | 0.93     | 64 (74.4)        |
| Reason for ERCP failure, <i>n</i> (%)                  |                   |                   |          |                  |
| Failed to reach the papilla                            | 14 (66.7)         | 17 (39.5)         | 0.04     | 31 (48.4)        |
| Failed cannulation                                     | 7 (33.3)          | 26 (60.5)         |          | 33 (51.6)        |
| Stent type, <i>n</i> (%)                               |                   |                   |          |                  |
| SEMS   | 13 (46.4)         | -                 |          |                  |
| LAMS 15 mm $\times$ 10 mm                              | 3 (10.7)          | -                 |          |                  |
| LAMS 10 mm $\times$ 10 mm                              | 12 (35.7)         | -                 |          |                  |
| Bilirubin before drainage (mg/dl), mean $\pm$ SD       | 8.5 $\pm$ 7.4     | 8.8 $\pm$ 8.2     | 0.87     | 8.7 $\pm$ 7.9    |
| Bilirubin after drainage (mg/dl), mean $\pm$ SD        | 3.6 $\pm$ 3.5     | 5.1 $\pm$ 5.5     | 0.23     | 4.6 $\pm$ 4.9    |
| Time to last follow-up or death (mg/dl), mean $\pm$ SD | 291 $\pm$ 339     | 500.1 $\pm$ 734.1 | 0.16     | 433.9 $\pm$ 641  |

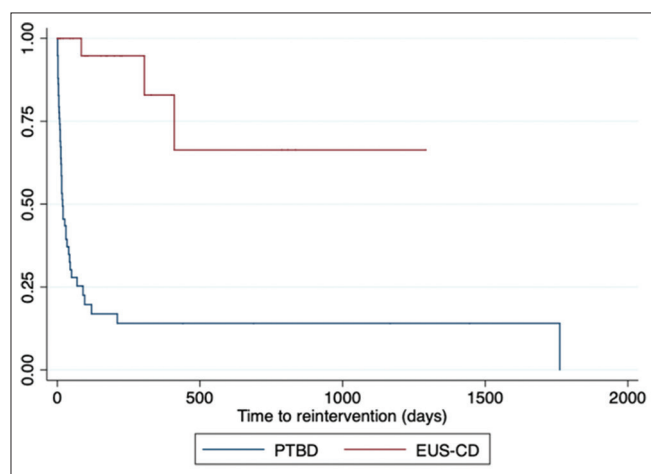
EUS-CD: EUS-guided choledochoduodenostomy; LAMS: Lumen-apposing metal stent; PTBD: Percutaneous transhepatic biliary drainage; SEMS: Self-expandable metal stent; SD: Standard deviation



**Figure 1.** Box plot comparing bilirubin level before drainage and 2 weeks after in EUS-CD and PTBD. EUS-CD: EUS-guided choledochoduodenostomy, PTBD: Percutaneous transhepatic biliary drainage



adenocarcinoma in 9 (13.1%), and cholangiocarcinoma in 4 (5.8%) [Table 1]. There was no significant difference in technical success between EUS-CD (100%) and PTBD groups (97.8%,  $P = 0.48$ ) for distal MBO [Table 2]. Clinical success was higher in patients with MBO who were treated with EUS-CD (81%) compared to PTBD (69.6%) but did not reach statistical significance, OR: 1.86 (95% CI: 0.53–6.5,  $P = 0.33$ ). There was no significant difference in rate of AE between EUS-CD (13%) and PTBD (28.3%, OR: 0.38, 95% CI: 0.1–1.5,  $P = 0.17$ ). The need for reintervention was significantly lower among patients with MBO who underwent EUS-CD (8.7%) compared to PTBD (76.1%; HR: 0.05 [95% CI: 0.01–0.23,  $P < 0.001$ ]) [Figure 2].



**Figure 2.** Kaplan-Meier curve comparing time to reintervention in days between EUS-CD and PTBD in the overall cohort. EUS-CD: EUS-guided choledochoduodenostomy, PTBD: Percutaneous transhepatic biliary drainage

The need for reintervention remained significantly lower in the EUS-CD even after controlling for age, gender and malignancy type, aHR: 0.03 (95% CI: 0.006–0.16,  $P < 0.001$ ). Unplanned reintervention due to AEs were also lower in the EUS-CD compared to PTBD, HR: 0.13 (95% CI: 0.02–1,  $P = 0.05$ ) and aHR: 0.12 (95% CI: 0.01–0.99,  $P = 0.049$ ). Among patients with MBO who survived 3 months or less ( $n = 26$ ), the need for reintervention was still lower for EUS-CD (0%), compared to PTBD (55%;  $P = 0.02$ ). Only for patients with MBO who survived 50 days or less ( $n = 20$ ) was the need for reintervention similar between EUS-CD (0%) and PTBD (46.7%;  $P = 0.06$ ). Mortality in MBO was significantly lower in the EUS-CD group compared to in the PTBD group (65.2% vs. 97.8%;  $P < 0.001$ ). However, there was no significant difference in survival time between the two groups, HR: 0.59 (95% CI: 0.32–1.06,  $P = 0.08$ ) and aHR: 0.57 (95% CI: 0.3–1.06,  $P = 0.07$ ) controlling for age, gender, and malignancy type.

#### *Lumen-apposing metal stents versus percutaneous transhepatic biliary drainage*

EUS-CD was performed in 15 patients using LAMS using either 10 mm × 10 mm (12 patients) or 15 mm × 10 mm (3 patients). Technical and clinical success with LAMS was 100% and 84.6%, respectively. There was no significant difference between EUS-CD with LAMS and PTBD in technical success (OR: Not estimated,  $P = 0.4$ ) or clinical success OR: 3.3 (95% CI: 0.67–15.7,  $P = 0.14$ ). There was also no significant difference in rate of AEs between EUS-CD with

**Table 2. Outcome summary comparing EUS-CD to percutaneous transhepatic biliary drainage in the overall cohort ( $n=86$ ) and in the subgroup of patients with malignant distal biliary obstruction ( $n=69$ )**

| Outcomes                                 | Overall cohort ( $n=86$ ) |                 |        | Malignant distal biliary obstruction only ( $n=69$ ) |                 |        |
|--|---------------------------|-----------------|--------|--|-----------------|--------|
|  | EUS-CD ( $n=28$ )         | PTBD ( $n=58$ ) | $P$    | EUS-CD ( $n=23$ )                                    | PTBD ( $n=46$ ) | $P$    |
| Technical success, $n$ (%)               | 28 (100)                  | 56 (96.6)       | 0.3    | 23 (100)   | 45 (97.8)       | 0.48   |
| Clinical success, $n$ (%)                | 22 (84.6)                 | 36 (62.1)       | 0.04   | 17 (81)  | 32 (69.6)       | 0.33   |
| Adverse events, $n$ (%)                  | 4 (14.3)                  | 17 (29.3)       | 0.1    | 3 (13)   | 13 (28.3)       | 0.16   |
| Occlusion                                | 1 (3.6)                   | 6 (10.3)        | 0.3    | 1 (4.3)  | 6 (13)          | 0.26   |
| Cholangitis                              | 3 (10.7)                  | 7 (12.1)        | 0.85   | 2 (8.7)  | 5 (10.9)        | 0.78   |
| Migration                                | 0                         | 4 (6.9)         | 0.16   | 0  | 4 (8.7)         | 0.15   |
| Perforation                              | 0                         | 1 (1.7)         | 0.49   | 0  | 1 (2.2)         | 0.48   |
| Bile leak                                | 2 (7.1)                   | 2 (3.5)         | 0.45   | 2 (8.7)  | 1 (2.2)         | 0.2    |
| Bleeding                                 | 0                         | 3 (5.2)         | 0.2    | 0  | 2 (4.4)         | 0.31   |
| Need for reintervention, $n$ (%)         | 3 (10.7)                  | 45 (77.6)       | <0.001 | 2 (8.7)  | 35 (76.1)       | <0.001 |
| Time for reintervention (days), mean±SD* | 268 (315)                 | 64 (261)        | <0.001 | 357.5 (74.2)   | 74 (295)        | <0.001 |
| Number of reinterventions, mean±SD       | 0.14 (0.45)               | 1.9 (2.1)       | <0.001 | 0.13 (0.45)  | 2 (2.3)         | <0.001 |
| Death, $n$ (%)                           | 16 (57.1)                 | 47 (81)         | 0.02   | 15 (65.2)  | 45 (97.8)       | <0.001 |

\*Among patients with malignant obstruction. EUS-CD: EUS-guided choledochoduodenostomy; PTBD: Percutaneous transhepatic biliary drainage; SD: Standard deviation

LAMS (20%) and PTBD (26.6%, OR: 0.7 [95% CI: 0.18–2.7;  $P = 0.6$ ]). Reintervention was significantly lower in the EUS-CD group with LAMS (20%) compared to PTBD (73.4%, OR: 0.13 [95% CI: 0.04–0.43,  $P = 0.001$ ]) and adjusted OR: 0.12 (95% CI: 0.04–0.4,  $P = 0.001$ ) controlled for age, gender, and cause of biliary obstruction. There was no significant difference in mean duration of follow-up between LAMS ( $329 \pm 331$  days) and PTBD ( $446 \pm 664$  days;  $P = 0.51$ ).

## DISCUSSION

In this multicenter cohort retrospective study, we compared EUS-CD to PTBD for achieving biliary drainage in patients with DBO. Both techniques had similar rates of technical success, but EUS-CD was associated with higher rates of clinical success and significantly lower need for reintervention and a trend to lower rates of AEs. AEs were less common in EUS-CD without reaching statistical significance, which is most likely due to the fact that the study was underpowered to detect a difference in AEs. Among patients with MBO, both techniques were equally technically and clinically successful. However, there was a trend toward higher clinical success with EUS-CD. Achieving biliary drainage with EUS-CD in MBO was significantly associated with lower need for reintervention and a trend toward lower AEs. Furthermore, mortality was lower among patients with MBO who underwent EUS-CD. However, survival time was not significantly different as our study was not powered to detect survival benefits.

ERCP with transpapillary biliary stenting is the primary modality for decompressing the biliary tree in patients with biliary obstruction. Uncommonly, ERCP fails either due to the inability to reach the papilla in the setting of gastric outlet or duodenal obstruction or failure to achieve deep biliary cannulation. Although PTBD often achieves adequate biliary drainage, the main limitation remains the significant reduction in quality of life.<sup>[3]</sup> In addition, percutaneous drains require a frequent exchange, as they tend to obstruct, dislodge, or leak.<sup>[3,8]</sup> These challenges have inspired endoscopists to devise alternative internal biliary drainage through an array of EUS-guided approaches. Since initially described in 2001,<sup>[9]</sup> EUS-CD has progressed from using plastic stents<sup>[9,10]</sup> to biliary SEMS<sup>[11]</sup> and now includes the use of LAMS.<sup>[11,12]</sup> The proposed advantages of EUS-CD over PTBD include the ability for the procedure to

be performed during the index (failed) ERCP session without the need for a second session and decreased morbidity from recurrent drain malfunction experienced with external drains. Several studies have compared EUS-guided biliary drainage using SEMS to PTBD.<sup>[13–15]</sup> A meta-analysis of 9 studies including 483 patients with failed ERCP compared EUS-guided biliary drainage through different techniques using SEMS or plastic stents to PTBD.<sup>[1]</sup> The study demonstrated no differences between EUS-guided biliary drainage and PTBD with regard to technical success but EUS-guided biliary drainage were associated with better clinical success, fewer AEs, and less need for reintervention compared to PTBD. In contrast to our comparison study, this meta-analysis included a variety of EUS-guided biliary drainage techniques and was conducted before the widespread adoption of LAMS.

A significant AE of EUS-CD with covered SEMS that may result in considerable morbidity is early stent migration before adequate fistula tract maturation between the bile duct and the duodenum. While this may be overcome with the placement of plastic double pigtail stents placed through the SEMS, the invention of a specially designed, cautery-enhanced wide flange LAMS has made a significant impact on EUS-CD technique and safety. Our results and previously published data have demonstrated high technical and clinical success of EUS-CD using LAMS.<sup>[4,11,12]</sup> Multiple studies, including a meta-analysis, reported both technical and clinical success of EUS-CD with LAMS close to 96%.<sup>[16–18]</sup> A single-center retrospective case series study<sup>[12]</sup> reported EUS-CD using LAMS in 46 patients with inoperable malignant DBO. In this study, technical and clinical success (defined as serum bilirubin level reduction by 50% at 2 weeks) was 93.5% and 97.7%, respectively. AEs were reported in 11.6%. Similarly, a multicenter retrospective study of 67 patients with MBO and failed ERCP demonstrated high technical success of 95.5% and clinical success of 100% with EUS-CD using LAMS in patients with MBO after unsuccessful ERCP.<sup>[4]</sup> The need for reintervention in that study was 17.5% which is close to the 20% that was experienced with LAMS in this study cohort. A meta-analysis of 7 studies including 84 patients with DBO regardless of the etiology reported a pooled technical success of 95.5% and a pooled clinical success of 95.5% with EUS-CD using LAMS, which is similar to our study findings.<sup>[16]</sup> The definition of clinical success in the studies included in this meta-analysis varied

significantly between resolution of jaundice, 50% bilirubin reduction, 90% bilirubin reduction, or decrease in bilirubin level to less than 3 mg/dl. However, a 50% bilirubin reduction was the most common used definition. The pooled risk of AEs in this meta-analysis was only 5.2%. The reported AEs were only periprocedural and did not include stent occlusion or delayed stent migration. The pooled risk of jaundice recurrence was 8.7% which was either due to stent occlusion or migration. In addition, unlike our study where we compared EUS-CD to PTBD, these studies were all case series and did not compare EUS-CD to alternate modalities, including PTBD.

One intriguing observation in our study was the difference between in the cause of ERCP failure between the two groups. Difficult cannulation was the main reason behind ERCP failure in the PTBD group, whereas failure to reach the major papilla was the main reason behind ERCP failure in the EUS-CD cohort. Although the exact cause behind this difference is unclear, several plausible explanations could be the procedural duration and risk of AEs. Once reaching the papilla is deemed unfeasible, the endoscopist may quickly proceed with EUS-CD. However, difficult biliary cannulation may result in prolonged attempts prior to deeming ERCP a failure and an increased risk for post-ERCP pancreatitis (PEP). Thus, proceduralists may suggest proceeding with PTBD given the procedural duration and increased risk for PEP.

The major advantages of EUS-CD over PTBD from this study cohort were higher rates of clinical success and the need for fewer reinterventions. One plausible explanation for the higher rate of clinical success with EUS-CD is that the larger caliber metal stent may provide better drainage compared to plastic PTBD catheters, which are typically 7–10 Fr. In addition, with EUS-CD, the metal stents are usually placed into the CBD and allow for drainage into the duodenum. In contrast to PTBD, where bile may drain outside the body, EUS-CD allows natural drainage into the small intestine and preserves the enterohepatic cycle and regulation of bile acid. Internalization of the PTBD similarly allows for drainage into the small intestine but is not routinely performed at most centers. Given the increased need for reintervention with PTBD, one approach has been proposed is to perform PTBD in patients with short life expectancy <3 months and reserve EUS-guided biliary drainage for patients

with longer expected survival (>3 months).<sup>[19]</sup> Our data showed that this threshold might even need to be shorter than 3 months. Among patients who lived <3 months, EUS-CD had a significantly lower need for reintervention. Only among patients who lived 50 days or less, did EUS-CD and PTBD demonstrate similar rates of reintervention. However, it is prudent for endoscopists to bear in mind some disadvantages of EUS-CD before proceeding with this route. First, EUS-CD can only be performed in patients with DBO and dilated CBD. While there is no absolute cutoff, an ongoing RCT comparing EUS-CD *versus* ERCP for biliary drainage has limited enrollment for EUS-CD to a minimum CBD diameter of 1.2 cm.<sup>[20]</sup> Second, EUS-CD often needs to be combined with a luminal bypass procedure in those with severe gastric outlet obstruction; otherwise, bile can reflux into the stomach, a condition poorly tolerated by patients.

The major strengths of this study were the multicenter and the comparative design. Although multiple previous studies have reported EUS-CD with LAMs, comparative data to PTBD are lacking. There are several limitations of our study. First, the retrospective design of the study might have resulted in residual confounders. Second, deciding the method of biliary drainage could have been influenced by unaccounted factors. One specific factor was the cause of ERCP failure which significantly differed between the two groups and could have influenced the decision behind subsequent biliary drainage. Other possible unaccounted factors may include the availability of PTBD and EUS-CD at that time, the overall condition of the patient (critically ill *vs.* elective), and the patient's preference. However, both groups were similar in terms of age, gender, cause of biliary obstruction, type of malignancy, and rates of prior ERCP failure. Besides, all these cases were from referral centers where both EUS-CD and PTBD were available. Third, this study may be subject to referral bias as all participating centers were high-volume tertiary care centers. Nonetheless, this caveat reflects the reality of these complex cases, which are usually performed in centers with expertise in interventional EUS techniques. However, one must also note that PTBD is widely available and is likely a more favorable option in facilities with lower ERCP or interventional EUS volume. Finally, the multicenter design of this study meant that different endoscopists performed EUS-CD which resulted in some variation in the technique. However, all endoscopists were experienced and followed the general techniques described in the methods section.

In conclusion, ERCP failure for biliary drainage is uncommon. EUS-CD is a technically and clinically highly successful procedure without an increased risk and possibly fewer AEs compared to PTBD in patients with DBO. EUS-CD minimizes the need for reintervention, which enhances end-of-life quality in patients with advanced malignancy. Based on our reported experience, EUS-CD may be the preferred method of biliary drainage in patients with life expectancy longer 50 days and further cost analysis for this indication is needed.

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### Conflicts of interest

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