

# Endoscopic ultrasound-guided gallbladder drainage as a rescue therapy for unresectable malignant biliary obstruction: a multicenter experience

## Authors

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## ABSTRACT

**Background** Endoscopic retrograde cholangiopancreatography (ERCP) is often unsuccessful in patients with duodenal stenosis or malignant ampullary infiltration. While endoscopic ultrasound-guided biliary drainage (EUS-BD) has been proposed as an alternative, EUS-guided gallbladder drainage (EUS-GBD) is an attractive option when both approaches fail. We aimed to assess the effectiveness and safety of EUS-GBD as rescue therapy for malignant distal bile duct obstruction.

**Methods** A multicenter retrospective study was performed on patients with unresectable malignant distal bile duct obstruction who underwent EUS-GBD between 2014 and 2019 after unsuccessful ERCP and EUS-BD. Clinical success was defined as a decrease in serum bilirubin of >50% within 2 weeks.

**Results** 28 patients were included, with a lumen-apposing metal stent used in 26 (93%) and a self-expandable metal stent in two (7%). The technical success rate was 100%. The clinical success rate was 93%, with an improvement in bilirubin (7.3 [SD 5.4] pre-procedure vs. 2.8 [SD 1.1] post-procedure;  $P=0.001$ ). Delayed adverse events included food impaction of the stent ( $n=3$ ), with a further two patients developing cholecystitis and bleeding.

**Conclusion** This study demonstrates the feasibility of gallbladder drainage to relieve malignant distal bile duct obstruction in patients with failed ERCP and EUS-BD.

## Introduction

Transpapillary drainage of the bile ducts through endoscopic retrograde cholangiopancreatography (ERCP) is the standard treatment for malignant distal bile duct obstruction [1, 2]. Up to 25% of patients with pancreatic cancer and biliary obstruction have concurrent duodenal stenosis, which makes ERCP challenging and often unsuccessful [3]. Multiple studies have reported the usefulness of endoscopic ultrasound-guided bile duct drainage (EUS-BD) as an alternative treatment to achieve biliary drainage [4, 5]. Although EUS-BD has a high technical success rate and an acceptable risk profile, EUS-BD can fail for multiple reasons [4–6].

EUS-guided gallbladder drainage (EUS-GBD), commonly used in treating acute cholecystitis in patients who are not surgical candidates, is an attractive salvage therapy when both ERCP and standard EUS-BD techniques are unsuccessful [7, 8]. A previous single-center study reported a clinical success rate of 91% for EUS-GBD in 12 patients who failed ERCP and EUS-BD, with an adverse event rate of 16.7% [9].

We aimed to assess the effectiveness and safety of EUS-GBD as a rescue therapy for biliary drainage after failed endoscopic interventions for unresectable malignant distal bile duct obstruction.

## Methods

### Study design and patient characteristics

This was a multicenter retrospective study from four tertiary care medical centers in the USA involving patients with obstructive jaundice secondary to an unresectable malignant distal biliary stricture. We included patients between 2014 and 2019 who underwent failed attempts at ERCP and EUS-BD followed by EUS-GBD (► Fig. 1). None of the included patients in this series have previously been published. Institutional review board (IRB) approval was granted at all four institutions.

### EUS-GBD technique

The therapeutic linear-array echoendoscope was positioned in the distal antrum or duodenal bulb, from where the gallbladder was adequately visualized. Color flow Doppler was used to ensure the absence of interposed blood vessels in the chosen access window. The endoscopist then chose one of two techniques – freehand or wire-guided – using either a cautery-enhanced lumen-apposing metal stent (LAMS) or self-expandable metal stent (SEMS).

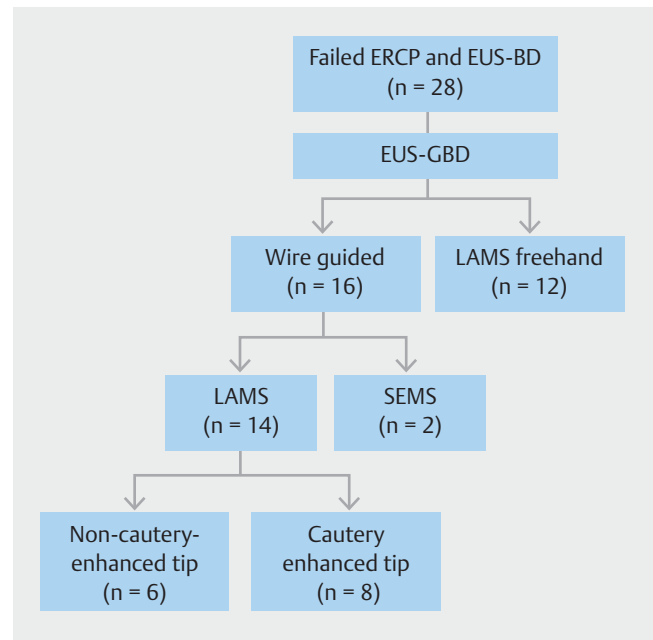
In the freehand technique, the gallbladder wall was punctured under EUS guidance with a cautery-enhanced LAMS (► Fig. 2; ► Video 1). The distal flange was deployed inside the gallbladder under EUS guidance, and this was followed by retraction of the delivery system to create apposition prior to deployment of the proximal flange under endoscopic and fluoroscopic guidance. The waist of the LAMS was dilated using a balloon dilator, and a double-pigtail plastic stent (DPS) was placed within the LAMS at the discretion of the endoscopist.

In the wire-guided technique, a 19-gauge fine-needle aspiration (FNA) needle was used to puncture the gallbladder wall, and this was followed by contrast injection to confirm the needle positioning. A 0.025-inch hydrophilic-tipped guidewire was advanced and coiled in the gallbladder. The tract was dilated with a 4-mm dilating balloon. Subsequently, a stent was advanced over the wire into the lumen of gallbladder. The stent used was either a non-cautery-enhanced LAMS or a fully covered SEMS (FCSEMS) (► Fig. 3 and ► Fig. 4). An anchoring DPS was placed at the discretion of the endoscopist.

## Results

Of a total of 24 720 ERCPs performed at all institution between 2014 and 2019 for malignant distal biliary obstruction, 1.6% (n = 384) underwent EUS-BD. Among those, 28 patients (7%) failed EUS-BD and underwent EUS-GBD. Their mean age was 68 years (standard deviation [SD] 13 years) and 46% were women; they had multiple etiologies. Reasons for the failure for EUS-BD included inadequate window for puncture, inability to pass the wire and form a tract, and inability to pass a stent.

EUS-GBD was transduodenal in 15 patients (54%) and transgastric in 13 patients (46%). The type of stent used included: LAMS with a cautery-enhanced tip in 20 patients (71%), of these 12 were inserted freehand; LAMS with a non-cautery-enhanced tip in six patients (21%); and a SEMS in two patients (7%). Stent



► Fig. 1 Flow chart of patients with malignant distal biliary obstruction after failed endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound-guided bile duct drainage (EUS-BD). EUS-GBD, EUS-guided gallbladder drainage; LAMS, lumen-apposing metal stent; SEMS, self-expandable metal stent.

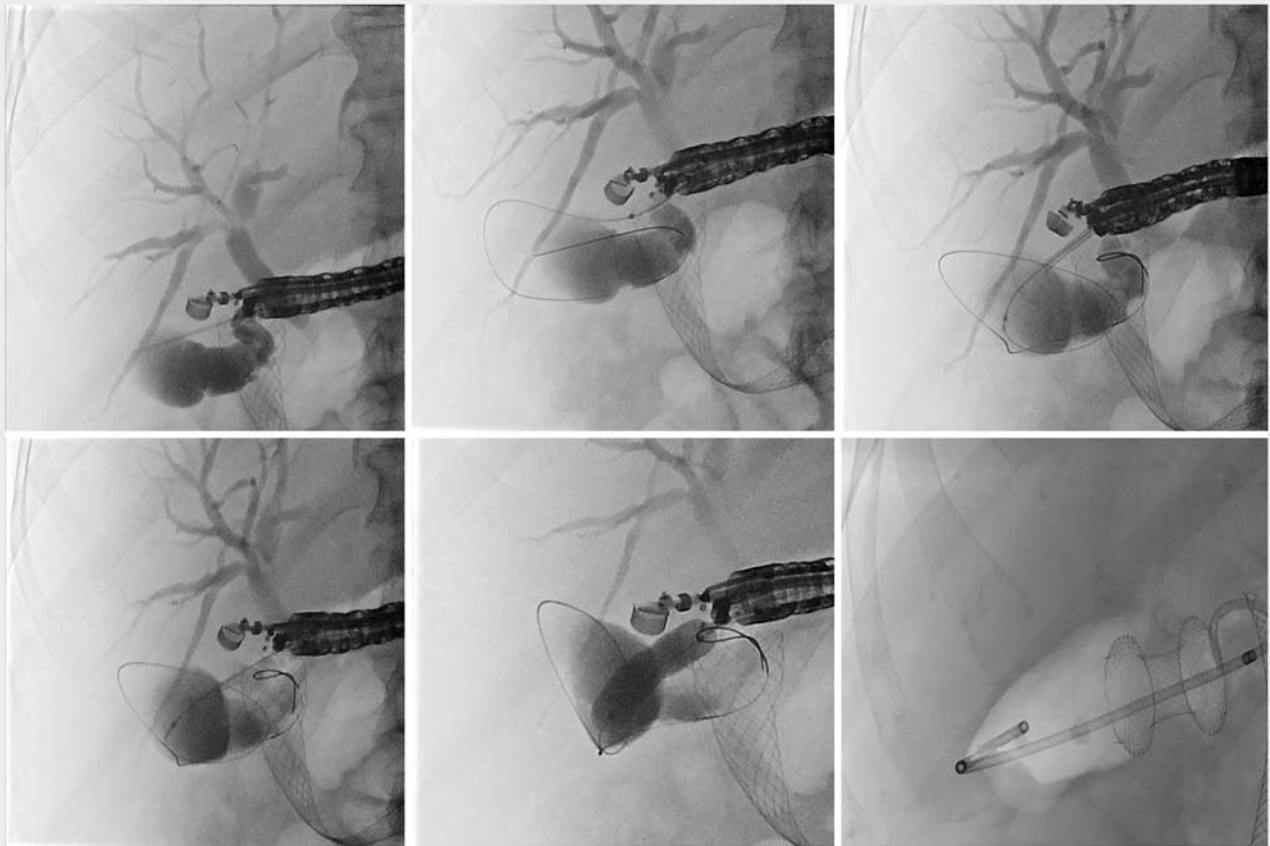


► Video 1 Endoscopic ultrasound-guided gallbladder drainage with the placement of a lumen-apposing metal stent for rescue therapy of malignant distal bile duct obstruction. Online content viewable at: <https://doi.org/10.1055/a-1259-0349>

diameters were either 10 mm (n = 13) or 15 mm (n = 15). Anchoring DPSs were used in 19 patients (68%).



► **Fig. 2** Endoscopic ultrasound views of lumen-apposing metal stent placement for gallbladder drainage using the freehand technique.



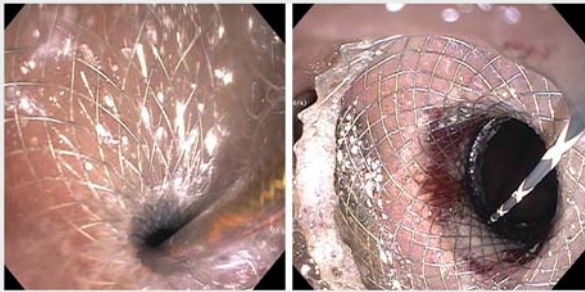
► **Fig. 3** Fluoroscopic views of lumen-apposing metal stent placement for gallbladder drainage using the wire-guided technique.

## Outcomes

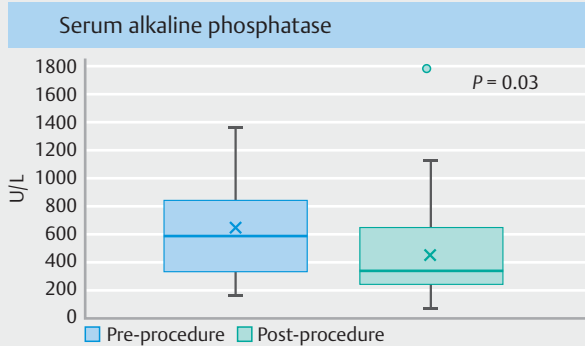
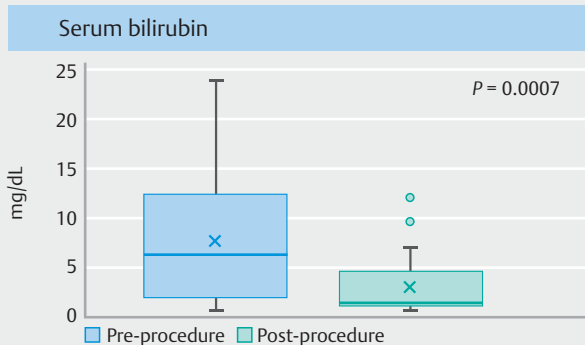
### Primary outcome

Clinical success was achieved in 26 patients (93%). The mean serum bilirubin decreased significantly 2 weeks after the procedure compared with before the procedure (2.8 [SD 1.1] vs. 7.3

[SD 0.54], respectively;  $P=0.001$ ). There was a concomitant decrease in mean serum alkaline phosphatase (454 [SD 321] vs. 623 [SD 324], respectively;  $P=0.03$ ) (► **Fig. 5**).



► **Fig. 4** Endoscopic views of the lumen-apposing metal stent immediately following placement.



► **Fig. 5** Graphical comparisons of the serum bilirubin and alkaline phosphatase before and after endoscopic ultrasound-guided gallbladder drainage.

### Secondary outcomes

Technical success, defined as successful stent deployment, was achieved in all patients (100%). The median procedure time was 55 minutes (range 3–77 minutes). The median length of hospital stay post-intervention was 5 days (range 1–35 days). At the time of writing this manuscript, 10 patients (36%) had died. None of the deaths were due to the procedure.

### Adverse events

The rate and severity of adverse events were defined according to the American Society for Gastrointestinal Endoscopy (ASGE) lexicon [10]. There were no immediate adverse events. Delayed adverse events (after 24 hours post-procedure) occurred in five

patients (18%), all of which were graded as moderate according to the ASGE lexicon. The adverse events included three cases of food impaction in the stent requiring revision of the anchoring plastic stents; this was complicated by acute cholecystitis in all three patients, which resolved with revision of the anchoring stents and antibiotics. Two patients developed delayed bleeding, both patients were on anticoagulation, but this resolved without the need for radiological or surgical intervention. One patient had an ulcer with a visible vessel inside the gallbladder on EGD thought to have been caused by irritation from the edge of the metal stent. A hemoclip was placed with no recurrent bleeding. The second patient had an endoscopy where clots were removed from the stent, but no bleeding lesion was seen and there was no recurrent bleeding. There were no episodes of perforation or stent migration.

### Long-term follow-up and need for reintervention

Patients were followed for a median of 33 months (range 3–64 months). Apart from the five patients (18%) with delayed adverse events who needed reintervention, as described above, no other patient needed reintervention for recurrent jaundice or other adverse events. Stent patency at >30 days was 82%.

### Discussion

This is the first multicenter study evaluating EUS-GBD as a rescue therapy for malignant distal bile duct obstruction when both ERCP and EUS-BD have failed. Our results show excellent technical and clinical success rates for EUS-GBD. Although EUS-GBD was associated with moderate adverse events and the need for reintervention in about 18% of patients, there were no severe or fatal adverse events. The adverse event rate should be considered in the context of the complexity of these patients and the lack of less invasive options for such patients, who are typically not surgical candidates and have already failed ERCP and EUS-BD. EUS-GBD achieved successful resolution of biliary obstruction and jaundice in 93% of these patients.

ERCP has been the standard of care for relieving biliary obstruction since 1990 [2]. EUS-BD has emerged as a salvage therapy for failed ERCP [5]. Reported clinical success and adverse event rates of this procedure vary from 67% to 100% and 0% to 46%, respectively [4–6]. EUS-BD failures occur owing to a variety of reasons: inability to access the bile duct, either due to anatomical reasons, intervening vasculature, or small ducts; difficulty in passing the guidewire; failure to advance endoscopic accessories including the stent; and unstable scope position.

Surgical drainage methods, such as biliary-enteric bypass, are rarely performed owing to their very high rates of morbidity and mortality. Percutaneous drainage of the gallbladder is associated with increased morbidity, which can be up to 16%, and adverse events in up to 41% of patients, including pleural effusion, pneumothorax, bile leak, peritonitis, pericatheter leak, bleeding, and fistula formation [11, 12].

To date, only two single-center studies and a case report have reported the use of EUS-GBD as a rescue therapy [9, 13, 14]. The first series included 12 patients with reported technical and clinical success rates of 100% and 92%, respectively.

Adverse events were reported in 16% of patients, including stent dysfunction in 8% [9]. The second study included nine patients with pancreatic cancer and distal biliary obstruction, and similar technical and clinical success rates (100% and 78%, respectively) were reported. One patient (11%) required reintervention using percutaneous biliary drainage [13].

It is important to note that cystic duct patency (as the only communication between the biliary tree and gallbladder) is required for EUS-GBD to be effective for the treatment of biliary obstruction. Tumor involvement of the cystic duct precludes the usefulness of gallbladder drainage. Therefore, patency of the cystic duct needs to be confirmed before proceeding. This can be achieved by review of the cross-sectional imaging during the pre-procedure planning and careful EUS examination before drainage is attempted. The location of the tumor in relation to the proximal or distal bile duct is a useful indicator of cystic duct involvement [15].

This study has several limitations. The sample size is small, despite being from four centers. This should be considered in the context of the EUS-GBD procedure as a rescue therapy in a small subset of patients. EUS-GBD remains limited to large referral centers given its technical complexities. All procedures in this study were performed in centers with experience in therapeutic EUS, so the results of the study are not generalizable to other medical settings.

In conclusion, this multicenter study shows that EUS-GBD is an effective rescue therapy to relieve malignant distal bile duct obstruction after failed ERCP and EUS-BD. The procedure is technically feasible with an acceptable safety profile. This procedure should be considered as an alternative to percutaneous and surgical techniques, and as part of a multidisciplinary approach.

## Competing interests

S.Irani has provided consultancy to Boston Scientific; R. Law has provided consultancy to Olympus America; S. Mahadev has provided consultancy to Dilumen (Lumendi); D. Carr-Locke has provided consultancy to Boston Scientific and US endoscopy; M. Khashab has provided consultancy to Boston Scientific, Medtronic, and Olympus; R. Sharaiha has provided consultancy to Olympus, Cook, Boston, and Dilumen (Lumendi). The remaining authors declare that they have no conflict of interest.

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