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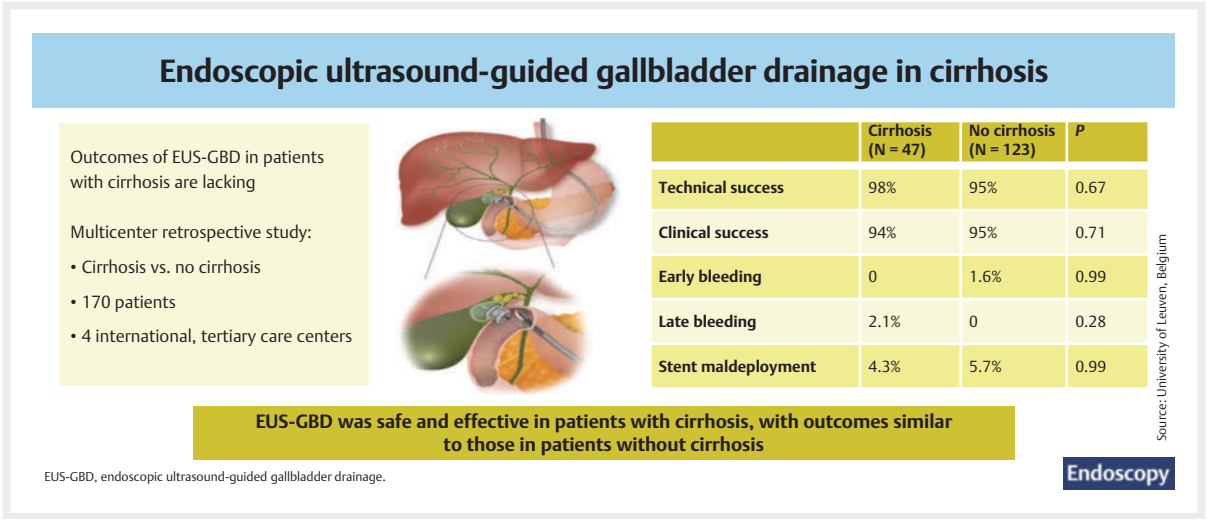
Safety and effectiveness of endoscopic ultrasound-guided gallbladder drainage in patients with cirrhosis: an international multicenter experience

GRAPHICAL ABSTRACT



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ABSTRACT

Background Endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) for symptomatic gallbladder disease has been shown to be safe and effective in patients with high surgical risk, but data are lacking for patients with cirrhosis. We investigated the safety and effectiveness of EUS-GBD in patients with and without cirrhosis.

Methods This retrospective review included patients who underwent EUS-GBD at four (three US and one Spanish) international tertiary care centers. Outcomes, including technical success, clinical success, and procedure-related adverse events, were compared between patients with and without cirrhosis.

Results 170 patients (47 with cirrhosis, 123 without cirrhosis) were included. There was no difference in age, sex, race, comorbidities, antiplatelet use, hemoglobin, or international normalized ratio between the two groups (P>0.05 for all). The most common etiology of cirrhosis was alcohol (42.6%) with mean Model of End-stage Liver

Disease-Sodium (MELD-Na) score of 16.2 (SD 8.8). Acute cholecystitis was more common in patients with cirrhosis (74.5% vs. 56.9%; $P=0.02$). Technical (cirrhosis 97.9% vs. no cirrhosis 95.1%; $P=0.67$) and clinical (93.6% vs. 94.9%; $P=0.71$) success rates were similar in the two groups. Adverse events were infrequent and similar between groups, the most common being stent maldeployment (cirrhosis 4.3% vs. no cirrhosis 5.7%; $P=0.99$). Survival rates were similar at the end of follow-up.

Conclusion EUS-GBD was safe and effective in patients with cirrhosis, with outcomes similar to patients without cirrhosis when performed by experienced echoendoscopists. Patients with cirrhosis and symptomatic gallbladder disease can be considered for EUS-GBD.

Introduction

Symptomatic gallbladder disease, including biliary colic, calculous cholecystitis, and acalculous cholecystitis, represents a significant healthcare burden in the USA, affecting approximately 10%–15% of US adults [1]. The treatment of choice for symptomatic gallbladder disease has been surgical resection, performed via an open or preferably a laparoscopic approach [2]. However, for patients who are high-risk surgical candidates due to malignancy, underlying cirrhosis, severe cardiac disease, or other significant comorbid conditions, clinicians have searched for alternative, less invasive therapeutic options.

Percutaneous transhepatic gallbladder drainage (PTGBD) has been traditionally done for these poor operative patients. However, the utility of PTGBD is limited by patient discomfort and the need for external appliances but also by higher rates of adverse events, ranging from 50% to 75%, such as catheter dislodgment, fistula leaks, cellulitis, infection, and recurrent cholecystitis [3, 4]. Endoscopic techniques for managing symptomatic gallbladder disease include endoscopic ultrasound (EUS)-guided transmural drainage (EUS-GBD), or endoscopic retrograde cholangiography-based transpapillary drainage (ETP-GBD); however, EUS-GBD has higher technical success and similar safety profile [2, 5, 6]. In addition, ETP-GBD does not allow for treatment of gallstones. In 2022, The European Society of Gastrointestinal Endoscopy guidelines also recommended EUS-GBD over ETP-GBD and PTGBD for patients at high surgical risk for cholecystectomy [7].

EUS-GBD is reported to have high rates of technical and clinical success in multiple studies; however, data for patients with cirrhosis are lacking. Cirrhosis complicated by coagulopathy, thrombocytopenia, and intervening ascites is considered a relative, if not absolute, contraindication for EUS-GBD. An American Gastroenterological Association practice update also listed ascites and coagulopathy as contraindications to EUS-GBD [8]. Existing literature on the outcomes of EUS-GBD in patients with cirrhosis is limited, with only a small series of 15 patients reported; therefore, additional data are needed in this population [5]. In addition, patients with cirrhosis are frequently not surgical candidates, so alternative modalities are needed to treat gallbladder disease in this population. Therefore, we aimed to study and compare the safety and effectiveness of EUS-GBD for symptomatic gallbladder disease in patients with and without cirrhosis.

Methods

Study design

We conducted a multicenter retrospective study comparing outcomes of EUS-GBD at four centers. The institutional review boards at each center approved the study. All adult patients (≥18 years) who underwent EUS-GBD for any indication at the four participating institutions up to 2022 were identified. The four participating institutions were Cleveland Clinic (Ohio), University of North Carolina in Chapel Hill, Mayo Clinic in Rochester (Minnesota), and Hospital General University Dr. Balmis in Alicante (Spain). We performed a retrospective chart review to extract data elements at each institution. The decision to perform EUS-GBD was individualized based on standard of care at each center after patient and physician(s) discussion. Patients were included if they underwent EUS-GBD for any indication and had procedure-related data available. We excluded any pediatric patient or any patient with missing procedure data. Patients were then divided into patients with cirrhosis and patients without cirrhosis at the time of EUS-GBD. Prespecified coding and a standardized data collection form were used between July 2022 and January 2023 to collate the data.

Demographics and baseline data were collected for the following variables: age, sex, body mass index, race, smoking, alcohol use, comorbidities including coronary artery disease, cerebrovascular accident, chronic obstructive pulmonary disease, prior abdominal surgeries, number of surgeries, malignancy, anticoagulation use including heparin, enoxaparin, rivaroxaban, warfarin, and apixaban, antiplatelet use such as aspirin and clopidogrel, and interventional radiology and surgery consultation prior to the procedure. Laboratory parameters including hemoglobin, platelets, albumin, international normalized ratio, and partial thromboplastin time were also collected within 1 week prior to the procedure. For patients with cirrhosis, data pertaining to etiology of cirrhosis, presence of ascites, need for pre-procedural large volume paracentesis, Model of End-stage Liver Disease-Sodium (MELD-Na), Child–Turcotte–Pugh class, transplant candidacy, and eventual transplantation were also collected. Procedural data including indications for the procedure, pre-procedural antibiotics, initial puncture site (gastric, duodenum, or jejunum), stent type, stent size, coaxial pigtail stent, and length of stay were collected. Post-procedure data including adverse events, technical success, clinical success, stent indwelling time, stent exchange, mortality, and total follow-up time were also collected.

▶ **Table 1** Demographics, comorbidities, and baseline laboratory characteristics of patients undergoing endoscopic ultrasound-guided gallbladder drainage.

Factor	Cirrhosis (N = 47)	No cirrhosis (N = 123)	*P* value
Age, mean (SD), years	66.5 (13.5)	71.3 (17.0)	0.08
Female, n (%)	18 (38.3)	55 (44.7)	0.45
Race, n (%)			0.35
▪ White	36 (76.6)	92 (74.8)	
▪ African American	6 (12.8)	24 (19.5)	
▪ Others	5 (10.6)	7 (5.7)	
Current smoker, n (%)	8 (17.0)	8 (6.5)	0.04
Current alcohol use, n (%)	12 (25.5)	8 (6.5)	0.001
Body mass index, mean (SD), kg/m2	29.5 (7.6)	27.1 (7.4)	0.07
Coronary artery disease, n (%)	13 (27.7)	39 (31.7)	0.58
Cerebrovascular accident, n (%)	3 (6.4)	10 (8.1)	0.69
Chronic obstructive pulmonary disease, n (%)	6 (12.8)	13 (10.6)	0.69
History of abdominal surgeries, n (%)	6 (12.8)	37 (30.1)	0.02
History of malignancy, n (%)	19 (40.4)	61 (49.6)	0.28
Anticoagulant use, n (%)	3 (6.4)	34 (27.6)	0.003
Antiplatelet use, n (%)	10 (21.3)	32 (26.0)	0.55
Antibiotics use, n (%)	16 (34.0)	34 (27.6)	0.43
Hemoglobin, mean (SD), g/dL	10.9 (1.9)	10.6 (1.9)	0.44
International normalized ratio, mean (SD)	1.4 (0.52)	1.3 (0.41)	0.16
Albumin, mean (SD), g/dL	2.8 (0.69)	2.9 (0.64)	0.52
Platelet count, mean (SD), platelets/microliter	134 (98)	234 (129)	<0.001
Partial thromboplastin time, mean (SD), seconds	40.8 (17.5)	43.6 (42.7)	0.78
Pre-procedure total bilirubin, mean (SD), g/dL	6.7 (7.7)	5.1 (7.8)	0.3

Outcomes

Our outcomes of interest were technical success, clinical success, and adverse events. Technical success was defined as the ability to successfully complete the procedure. Clinical success was defined as resolution of acute cholecystitis symptoms (fever, abdominal pain) and/or >10% decline in bilirubin level within 48–72 hours of hospitalization depending on indication for EUS-GBD. If there was no resolution of symptoms in the setting of cholecystitis, it was not considered as clinical success. However, if the indication for EUS-GBD was malignant biliary obstruction in the absence of fever or abdominal pain, then decline in bilirubin level was used as the indicator of clinical success. Adverse events were further categorized into postprocedural bleeding (early within 48 hours and late after 48 hours), postprocedural pancreatitis, stent maldeployment, stent dislodgment, biliary leak, or peritonitis. We considered initial maldeployment as an adverse event; however, if the procedure could still be completed successfully, it was considered technically successful. The adverse events were classified according to the AGREE classification [9]. In addition, stent indwelling time, further stent exchanges, gallstone clearance after initial procedure, food impaction in the stent, mortality rate, time to death, and total follow-up time were also compared between the two groups.

Statistical analysis

Baseline demographics and outcomes of interest were compared between the cirrhosis and no cirrhosis group. Categorical variables were expressed as percentages and compared by the Pearson's chi-squared test. Continuous variables were expressed as median (interquartile range) or mean with SD, and compared by Kruskal–Wallis test and independent *t* test, respectively. Two-sided *P* values were reported with a significance level of 0.05. Kaplan–Meier analysis with stratification by cirrhosis was run for time to stent removal or first exchange and time to death. Log rank was used to assess differences in survival outcomes by cirrhosis group. The statistical analyses were performed using SPSS version 24 (IBM Corp. Armonk, New York, USA).

▶ **Table 2** Etiology and characteristics of cirrhosis.

	N = 47[1]
Alcohol	20 (42.6)
Viral	4 (8.5)
MASLD	16 (34.0)
Other	7 (14.9)
Ascites	20 (42.6)
Large volume paracentesis	20 (42.6)
Child–Turcotte–Pugh class	
▪ A	9 (19.1)
▪ B	14 (29.8)
▪ C	3 (6.4)
MELD-Na, mean (SD)	16.2 (8.8)
Transplant candidate	4 (8.5)
▪ Underwent transplantation	1 (2.1)

MASLD, metabolic dysfunction-associated steatotic liver disease; MELD-Na, Model of End-stage Liver Disease-Sodium.
[1]Data are n (%), unless otherwise stated.

Results

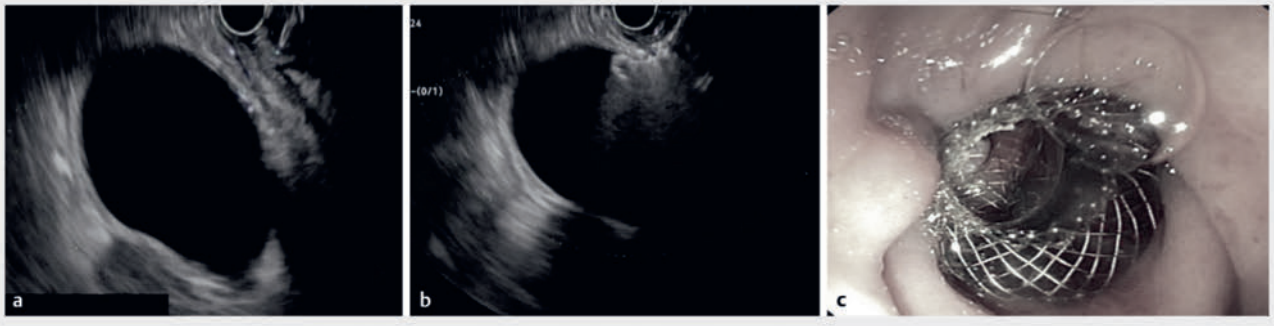
Demographics and baseline factors

A total of 170 patients were included in our study. Among the 170 patients, 47 had cirrhosis and 123 did not have cirrhosis. The mean age in patients with cirrhosis was 66.5 (SD 13.5) years compared with 71.3 (SD 17.0) years in patients without cirrhosis ($P = 0.08$). There were no statistically significant differences in terms of race, female sex (38.3% vs. 44.7%), mean body mass index (29.5 [SD 7.6] vs. 27.1 [SD 7.4] kg/m^2), coronary artery disease (27.7% vs. 31.7%), cerebrovascular accident (6.4% vs. 8.1%), and chronic obstructive pulmonary disease (12.8% vs. 10.6%) between the two groups ($P > 0.05$ for all). There were significantly higher rates of current smokers (17.0% vs. 6.5%; $P = 0.04$) and alcohol users (25.5% vs. 6.5%; $P = 0.001$) in the cirrhosis group than in the no cirrhosis group. Patients without cirrhosis also had significantly higher rates of prior abdominal surgeries (30.1% vs. 12.8%; $P = 0.02$).

Patients without cirrhosis had significantly higher use of anticoagulants (27.6% vs. 6.4%; $P = 0.003$) compared with patients with cirrhosis. There were no differences in the use of antiplatelet agents, pre-procedure surgical or interventional radiology consultation, or antibiotic use between the groups ($P > 0.05$ for all). Laboratory parameters including pre-procedure mean hemoglobin (10.9 [SD 1.9] vs. 10.6 [SD 1.9] g/dL), international normalized ratio (1.4 [SD 0.52] vs. 1.3 [SD 0.41]), albumin (2.8 [SD 0.69] vs. 2.9 [SD 0.64] g/dL), bilirubin, and partial thromboplastin time (40.8 [SD 17.5] vs. 43.6 [SD 42.7] seconds) were not significantly different between patients with and without cirrhosis ($P > 0.05$ for all). Mean bilirubin levels pre-procedure (6.7 [SD 7.7] vs. 5.1 [SD 7.8] g/dL; $P = 0.3$) and post-procedure (6.1 [SD 7.6] vs. 3.5 [SD 4.9] g/dL; $P = 0.1$) were not significantly different in patients with and without cirrhosis. In addition, median percentage change in bilirubin after EUS-GBD was not significantly different between the cirrhosis and no cirrhosis groups (15.6% vs. 27.3%; $P = 0.17$). Mean platelet count was significantly lower in patients with cirrhosis (134 [SD 98] per microliter) compared with patients without cirrhosis (234 [SD 129] per microliter; $P < 0.001$). All demographics, comorbidities, and laboratory parameters are summarized in ▶ **Table 1**.

Cirrhosis characteristics

The etiology of cirrhosis was alcohol in 42.6% (n = 20), metabolic dysfunction-associated steatotic liver disease in 34.0% (n = 16), viral in 8.5% (n = 4), and autoimmune in 14.9% (n = 7). Overall, 42.6% (n = 20) of patients had ascites and required frequent large-volume paracentesis prior to the procedure. The mean MELD-Na score in the cirrhosis group was 16.2 (SD 8.8). The Child–Turcotte–Pugh class was available for 26 patients, and was class A in 19.1%, class B in 29.8%, and class C in 6.4% of patients with cirrhosis. Four patients (8.5%) were deemed transplant candidates, and one eventually underwent transplantation during the study follow-up period. The characteristics of cirrhosis are summarized in ▶ **Table 2**.

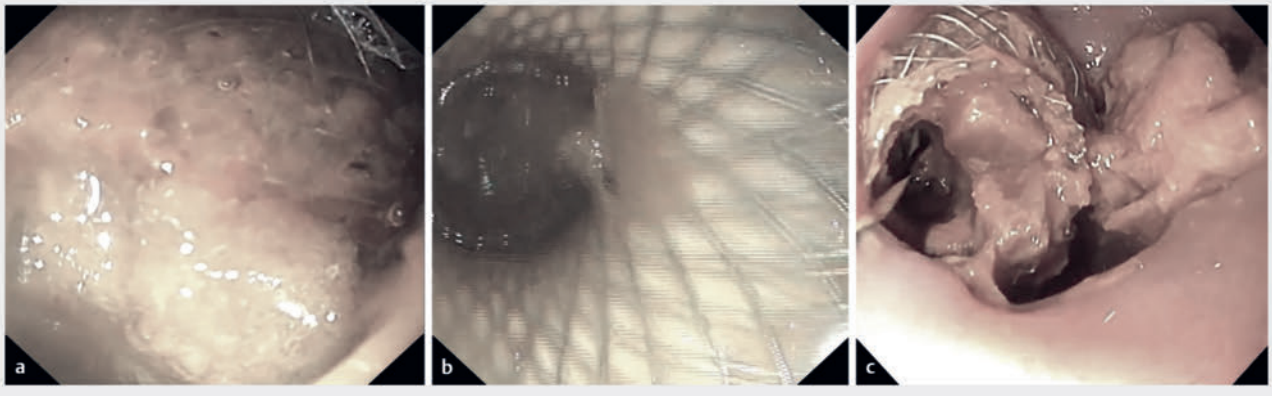


▶ **Fig. 1** Endoscopic ultrasound (**a**,**b**) and endoscopy (**c**) images. **a** The dilated gallbladder. **b** Deployment of the distal flange of the lumen-apposing metal stent in the gallbladder. **c** After deployment of the proximal flange in the gastric antrum, creating a cholecystogastrostomy.

▶ **Table 3** Procedure-related data in patients undergoing endoscopic ultrasound-guided gallbladder drainage.

Factor	Cirrhosis n = 47	No cirrhosis N = 123	*P* value
Indication, n (%)			0.02
▪ Acute cholecystitis	35 (74.5)1	70 (56.9)1	
▪ Chronic cholecystitis	2 (4.3)	4 (3.3)	
▪ Gallstone pancreatitis	1 (2.1)	5 (4.1)	
▪ Others	9 (19.1)[1]	44 (35.8)1	
Cautery-enhanced LAMS (N = 156), n (%)	46 (97.9)	110 (89.4)	0.07
Initial puncture site, n (%)[2]			0.12
▪ Gastric	2 (4.5)	20 (16.8)	
▪ Duodenum	41 (93.2)	96 (80.7)	
▪ Jejunum	1 (2.3)	3 (2.5)	
Same session ERCP	4 (8.5)	21 (17.1)	0.16
LAMS size, n (%)[3]			0.24
▪ 10×10 mm	36 (78.3)	86 (75.4)	
▪ 10×15 mm	5 (10.9)	8 (7.0)	
▪ 15×15 mm	4 (8.7)	7 (6.1)	
▪ Others	1 (2.2)	13 (11.4)	
Coaxial pigtail, n (%)[4]	37 (82.2)	94 (80.3)	0.78

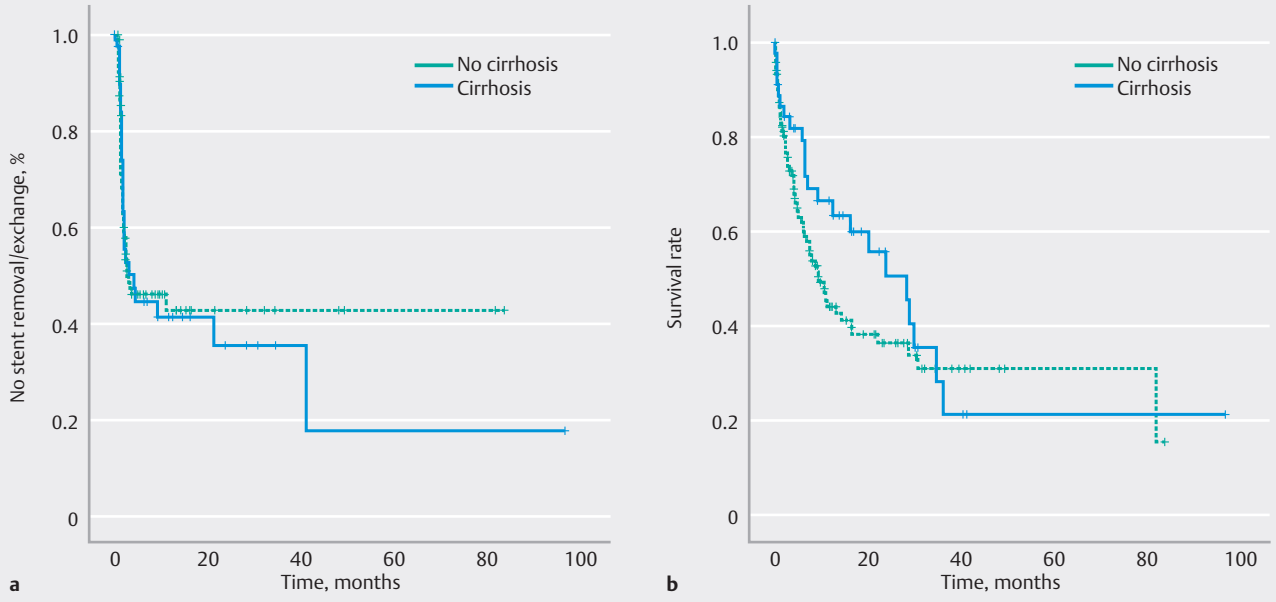
ERCP, endoscopic retrograde cholangiopancreatography; LAMS, lumen-apposing metal stent.
[1]Significant difference between groups.
[2]Cirrhosis N = 44; No cirrhosis N 119.
[3]Cirrhosis N = 46; No cirrhosis N = 114.
[4]Cirrhosis N = 45; No cirrhosis N = 117



▶ **Fig. 2** Endoscopic image of food in the gallbladder.

Procedure-related data

The indications for EUS-GBD were most commonly acute cholecystitis in both groups, but the proportion of patients with acute cholecystitis undergoing EUS-GBD was significantly higher in patients with cirrhosis (74.5% vs. 56.9%; $P = 0.02$), whereas patients with other indications such as malignancy (19.1% vs. 35.8%; $P = 0.02$) were more common in the group without cirrhosis. A minority of patients underwent EUS-GBD for chronic cholecystitis and gallstone pancreatitis. In the majority of patients, cholecystoduodenostomy was performed (93.2% vs. 80.7%; $P = 0.12$) with some undergoing cholecystogastrostomy (4.5% vs. 16.8%) and cholecystojejunostomy (2.3% vs. 2.5%) in patients with and without cirrhosis ($P = 0.12$). A cautery-enhanced lumen-apposing metal stent (LAMS) (AXIOS; Boston

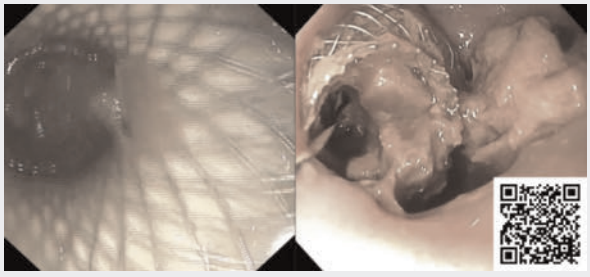


▶ **Fig. 3** Kaplan–Meier curves. **a** Time to stent removal or exchange. **b** Survival rate. There were no significant differences in times to stent removal or exchange (Log rank P = 0.21) or survival rate (Log rank P = 0.15).

Scientific Corp., Marlborough, Massachusetts, USA) was most commonly used in 91.8% (n = 156) of patients, with 14 patients undergoing use of other LAMSs such as NAGI (Taewoong Medical Co., Ltd, Gimpo, South Korea) or SPAXUS (Taewoong Medical Co., Ltd). A representative image of EUS-GBD procedure is shown in ▶ **Fig. 1**. There were no significant differences in LAMS size of 10×10 mm (78.3% vs. 75.4%), 10×15 mm (10.9% vs. 7.0%), or 15×15 mm (8.7% vs. 6.1%) in patients with or without cirrhosis (P = 0.24). Coaxial pigtail stents were placed in 82.2% and 80.3% of patients with and without cirrhosis, respectively (P = 0.78). Overall, 8.5% and 17.1% of patients with and without cirrhosis, respectively, underwent same-session endoscopic retrograde cholangiopancreatography (ERCP) with EUS-GBD (P = 016). Procedure-related data are summarized in ▶ **Table 3**.

Outcomes

The technical success rate was 97.9% and 95.1% in patients with and without cirrhosis, respectively (P = 0.67). Similarly, there was no significant difference in clinical success rates in patients with and without cirrhosis (93.6% vs. 94.9%; P = 0.71). The mean length of hospital stay after the index procedure was 7.91 (SD 15.4) days in the cirrhosis group and 7.72 (SD 13.1) days in patients without cirrhosis (P = 0.93). There were no differences in terms of adverse events including early bleeding (0 vs. 1.6%; P = 0.99), late bleeding (2.1% vs. 0; P = 0.28), pancreatitis (0 vs. 0.8%; P = 0.99), stent maldeployment (4.3% vs. 5.7%; P = 0.99), and perforation (0 vs. 1.6%; P = 0.99). Bile leak (0 vs. 3 [2.4%]; P = 0.56) and peritonitis (1 [2.1%] vs. 1 [0.8%]; P = 0.47) were infrequent and similar in patients with and without cirrhosis. The adverse events were classified into Grade I in seven patients and Grade IIIb in three patients according to the AGREE classification. The three severe adverse events were: maldeployment of LAMS, which could not be retrieved and the patient was treated with cholecystectomy; stent maldeployment leading to duodenal perforation, which was treated with duodenal stent placement and ERCP; and bleeding, which was treated with embolization of the gastroduodenal artery. Stent exchanges were performed in 36.2% and 33.9% of patients with and without cirrhosis, respectively (P = 0.78). Gallstone clearance was performed in 22.0% of patients without cirrhosis and 10.6% of patients with cirrhosis after LAMS placement (P = 0.09). Food impaction was only noted in one patient without cirrhosis (▶ **Fig. 2, Video 1**). The total mean follow-up time was 19.3 (SD 23.1) months and 11.7 (SD 15.5) months in patients with and without cirrhosis, respectively (P = 0.04).



▶ **Video 1** Food in the gallbladder after cholecystogastrostomy, clearance of food with a Roth net, and placement of a coaxial pigtail stent to prevent stent occlusion.
Online content viewable at:
https://doi.org/10.1055/a-2517-0927

▶ **Table 4** Clinical outcomes and adverse events in patients undergoing endoscopic ultrasound-guided gallbladder drainage.

Factor	Cirrhosis N = 47	No cirrhosis N = 123	P value
Technical success, n (%)	46 (97.9)	117 (95.1)	0.67
Clinical success, n (%)	44 (93.6)	112 (94.9)1	0.71
Length of stay, mean (SD), days	7.91 (15.4)	7.72 (13.1)	0.93
Early bleeding, n (%)	0	2 (1.6)	0.99
Late bleeding, n (%)	1 (2.1)	0	0.28
Pancreatitis, n (%)	0	1 (0.8)	0.99
Stent maldeployment, n (%)	2 (4.3)	7 (5.7)	0.99
Perforation, n (%)	0	2 (1.6)	0.99
Bile leak, n (%)	0	3 (2.4)	0.56
Peritonitis, n (%)	1 (2.1)	1 (0.8)	0.47
Post-procedure total bilirubin, mean (SD), g/dL	6.1 (7.6)	3.5 (4.9)	0.1
Median change in bilirubin, mean (SD), g/dL	15.6 (53)	27.3 (48)	0.17
Gallstone clearance, n (%)	5 (10.6)	27 (22.0)	0.09
Food impaction on follow-up, n (%)	0	1 (0.8)	0.99
Stent exchange, n (%)	17 (36.2)	40 (33.9)[1]	0.78
Stent indwelling time, mean (SD), weeks[2]	19.4 (38)	7.6 (6.2)	0.14
Eventual cholecystectomy, n (%)	2 (4.3)	11 (9.1)[3]	0.51
Total follow-up, mean (SD), months	19.3 (23.1)	11.7 (15.5)	0.04
Death, n (%)	23 (50.0)[4]	66 (53.7)	0.67
Time to death, mean (SD), months[5]	9.5 (10.9)	7.0 (11.7)	0.39

[1]No cirrhosis N = 118.
[2]Cirrhosis N = 24; No cirrhosis N = 52.
[3]No cirrhosis N = 121.
[4]Cirrhosis N = 46.
[5]Cirrhosis N = 20; No cirrhosis N = 60.

On Kaplan–Meier analysis, there was no statistically significant difference between the groups for time to stent removal or first stent exchange (Log rank $P = 0.21$, ▶ **Fig. 3a**). By the end of follow-up, 4.3% with cirrhosis and 9.1% without cirrhosis had undergone cholecystectomy ($P = 0.51$). There were no differences in mortality rates (50.0% vs. 53.7%; $P = 0.67$) or mean time to death (9.5 [SD 10.9] vs. 7.0 [SD 11.7] months; $P = 0.39$) between the groups. There was no significant difference in time to mortality (Log rank $P = 0.15$) between the two groups (▶ **Fig. 3b**). The outcomes are summarized in ▶ **Table 4**.

Discussion

In this large, international, multicenter study, we found that EUS-GBD was safe and effective in patients with cirrhosis. To the best of our knowledge, this is the largest study reporting safety and effectiveness of EUS-GBD in patients with cirrhosis. Compared with patients without cirrhosis, EUS-GBD in patients with cirrhosis had similar rates of technical and clinical success, and was not associated with any higher rates of adverse events.

EUS-GBD has been reported to have high rates of technical and clinical success, ranging from 90% to 100% in multiple studies [10]. In a recent meta-analysis of EUS-GBD with LAMS, the technical success rate was 94.65% (95%CI 91.54–96.67) and clinical success rate was 92.06% (95%CI 88.65–94.51) [2]. On subgroup analysis comparing PTGBD with EUS-GBD, EUS-GBD had similar rates of technical success and clinical success but was associated with a lower rate of reinterventions (odds ratio [OR] 0.05) [2]. Compared with the ETP-GBD approach, however, EUS-GBD was associated with significantly higher rates of technical success (OR 3.914) and clinical success (OR 4.59), with a lower rate of recurrence (OR 0.17) [2]. In a recent study comparing EUS-GBD with ETP-GBD, technical success rates were significantly higher with EUS-GBD (96.7% vs. 78.9%; $P<0.001$) compared with ETP-GBD [11]. With such promising data, on August 18, 2023, the United States Food and Drug Administration approved EUS-GBD as a treatment option for acute cholecystitis in patients who are poor surgical candidates (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?id = DEN230019) [12]. However, published data on

EUS-GBD have excluded patients with cirrhosis and literature remains scarce in this population. Our study reports high technical and clinical success rates of 97.9% and 93.6%, respectively, and contributes to existing literature on effectiveness of EUS-GBD, particularly in patients with cirrhosis.

The adverse events after EUS-GBD range from 10% to 16%, with the most common being LAMS occlusion leading to recurrent cholecystitis [2,13]. Other adverse events, including bleeding, stent migration, maldeployment, and self-limited pneumoperitoneum, have also been reported [14,15]. In our study, patients with cirrhosis did not have a significantly higher risk of adverse events compared with patients without cirrhosis. At the end of the follow-up period, mortality rates were around 50%, suggesting poor surgical candidacy of our study population and high likelihood of perioperative complications with cholecystectomy. The risk of recurrent cholecystitis due to LAMS obstruction may be decreased by placement of coaxial plastic stents and intraduodenal stents [16,17]. Stent maldeployment can also be treated with clip closure of punctured wall if the gallbladder wall is not punctured [7,16,17]. Another study reported significantly lower mean hospital stay with EUS-GBD compared with ETP-GBD and PTGBD (16 vs. 18 vs. 19 days; $P=0.01$), along with significantly lower rates of adverse events (1.9% vs. 4.8% vs. 19.8%; $P<0.001$) [6]. The American Gastroenterological Association clinical practice update also recommended ETP-GBD in patients who have ascites and are future surgical candidates [8]. However, EUS-GBD does not prohibit subsequent cholecystectomy nor increase surgical complexity and complications [18,19].

Our study has several important implications. Patients with cirrhosis pose a unique challenge when faced with symptomatic gallbladder disease; the vast majority of these patients are poor surgical candidates due to underlying coagulopathy, thrombocytopenia, and risk of hepatic decompensation after cholecystectomy. In addition, percutaneous cholecystostomy tube placement is also associated with higher rates of complications, ranging from 50% to 75% and including leaking ascites, bile leak, and peritonitis, which may induce hepatic encephalopathy and further overall decompensation. It is this population that requires a better alternative to surgery and PTGBD. ETP-GBD is typically attempted first but often fails and has low rates of technical success compared with EUS-GBD. Cirrhosis, especially decompensated cirrhosis with ascites, is typically considered a contraindication to EUS-GBD. EUS-GBD can fill that therapeutic gap and be an effective option for this patient population. In addition, EUS-GBD also provides an opportunity to perform cholecystoscopy through the stent to achieve complete stone clearance, if elected. In our study, we did not observe higher rates of adverse events in patients with cirrhosis, and EUS-GBD was associated with high rates of clinical and technical success, similar to those in patients without cirrhosis. Only one patient with autoimmune hepatitis eventually underwent liver transplantation after EUS-GBD, and this patient did not have any surgical complications. Our study adds to the evidence supporting the role of EUS-GBD in patients with cirrhosis when performed by expert echoendoscopists.

EUS-GBD should not be performed in patients who are potential transplant candidates to decrease surgical complexity and should only be performed after multidisciplinary discussion between surgeons and advanced endoscopists. Follow-up after EUS-GBD typically involves removing and/or exchanging the LAMS with permanent pigtail stents after 4–6 weeks to maintain fistula patency. An alternative strategy is to leave the LAMS indefinitely in frail patients with limited life expectancy and in those who refuse second procedures [20]. Patients who did not undergo scheduled exchange after index EUS-GBD still had significantly lower rates of long-term adverse events (5% vs. 16.4%; $P=0.002$) compared with patients who underwent ETP-GBD [11]. In another study, a 3-year stent patency rate of 86% was found, with a low adverse event rate, suggesting this as a durable approach in selected patients [21].

Our study has several limitations. This retrospective chart review introduces potential biases including confounding by indication. We attempted to mitigate this by collecting as many baseline variables as possible and to identify baseline differences in both groups along with data from multiple studies. All patients underwent procedures at tertiary care centers with expert echoendoscopists, which limits the generalizability of our results; however, EUS-GBD is typically performed at tertiary centers by expert endoscopists after discussion with the surgery team. We were unable to perform subgroup analyses in patients with cirrhosis and ascites owing to the small sample size and low rate of outcome of interest. Only 42.6% of our study population with cirrhosis had ascites, which also adds to the limitations of the study. Further limitations include variations in technique, practice patterns, and stents used, the issue of multiple statistical testing, and the longer follow-up in patients with cirrhosis.

Our study also has several strengths, including a large sample size, multicenter data, relevant outcomes of interest, mortality rate, and follow-up data. This is the largest multicenter study reporting outcomes of EUS-GBD in patients with cirrhosis.

In conclusion, our international, multicenter experience suggests that EUS-GBD is safe and effective in patients with cirrhosis, with outcomes similar to those of patients without cirrhosis when performed by experienced echoendoscopists. Patients with cirrhosis and symptomatic gallbladder disease can be considered for EUS-GBD. Further large studies are required for its widespread adoption and applicability in patients with cirrhosis and ascites.

Conflict of Interest

The authors declare that they have no conflict of interest.

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