Thieme

US multicenter outcomes of endoscopic ultrasound-guided gallbladder drainage with lumen-apposing metal stents for acute cholecystitis

Authors

Yakira David[1], Gaurav Kakked[2], Bradley Confer[3], Ruchit Shah[4], Harshit Khara[4], David L Diehl[3], Matthew Richard Krafft[5], Sardar M Shah-Khan[6], John Y Nasr[7], Petros Benias[8], Arvind Trindade[9], Thiruvengadam Muniraj[10], Harry Aslanian[11], Prabhleen Chahal[12], John Rodriguez[12], Douglas G Adler[13], Jason Dubroff[14], Rabi De Latour[15], Demetrios Tzimas[16], Lauren Khanna[15], Gregory Haber[15], Adam J Goodman[17], Nicholas Hoerter[18], Nishi Pandey[19], Mena Bakhit[20], Thomas E. Kowalski[21], David Loren[22], Austin Chiang[23], Alexander Schlachterman[24], Jose Nieto[25], Ameya Deshmukh[26], Yervant Ichkhanian[27], Mouen A. Khashab[28], Maan El Halabi[29], Richard S. Kwon[30], Anoop Prabhu[31], Ariosto Hernandez-Lara[32], Andrew Storm[32], Tyler M. Berzin[33], John Poneros[34], Amrita Sethi[35], Tamas A Gonda[36], Vladimir Kushnir[37], Natalie Cosgrove[38], Daniel Mullady[37], Abdullah Al-Shahrani[39], Lionel D'Souza[40], Jonathan Buscaglia[41], Juan Carlos Bucobo[42], Vineet Rolston[43], Prashant Kedia[44], Franklin Kasmin[45], Satish Nagula[46], Nikhil A Kumta[47], Christopher DiMaio[48]

Institutions

1 Gastroenterology, Mayo Clinic College of Medicine and Science, Rochester, United States
2 Rush University Medical Center, Chicago, United States
3 Gastroenterology and Nutrition, Geisinger Medical Center, Danville, United States
4 Geisinger Medical Center, Danville, United States
5 Digestive Diseases, Ruby Memorial Hospital, Morgantown, United States
6 Gastroenterology, Rutgers Robert Wood Johnson Medical School New Brunswick, New Brunswick, United States
7 Digestive Diseases, West Virginia University School of Medicine, Morgantown, United States
8 Rutgers University, New Brunswick, United States
9 North Shore Long Island Jewish Medical Center, New Hyde Park, United States
10 Yale University, New Haven, United States
11 Department of Medicine, Section of Digestive Diseases, Yale University School of Medicine, New Haven, United States
12 Cleveland Clinic, Cleveland, United States
13 Gastroenterology, University of Utah School of Medicine, Salt Lake City, United States
14 University of Utah Health, Salt Lake City, United States
15 NYU Langone Health, New York, United States
16 Northwell Health, New Hyde Park, United States
17 Gastroenterology, NYU Langone Medical Center, New York, United States
18 Icahn School of Medicine at Mount Sinai, New York, United States
19 Bayonne Medical Center, Bayonne, United States
20 Brown University Warren Alpert Medical School, Providence, United States
21 Gastroenterology, Thomas Jefferson University - Center City Campus, Philadelphia, United States
22 Fox Chase Cancer Center, Philadelphia, United States
23 Thomas Jefferson University Hospital JeffSTAT Education Center, Philadelphia, United States
24 Division of Gastroenterology, Hepatology & Nutrition, University of Florida, Gainesville, United States
25 Gastroenterology, Borland-Groover Clinic, Jacksonville, United States
26 Saint Louis University, St Louis, United States
27 Indiana University, Bloomington, United States
28 Gastroenterology, Johns Hopkins Hospital, Baltimore, United States
29 Tufts Medical Center, Boston, United States
30 Internal Medicine, Univ Michigan, Ann Arbor, United States
31 Roswell Park Comprehensive Cancer Center, Buffalo, United States
32 Mayo Foundation for Medical Education and Research, Rochester, United States
33 Gastroenterology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, United States
34 Digestive and Liver Diseases, Columbia University Medical Center, New York, United States
35 Columbia Presbyterian Medical Center, New York, United States
36 Digestive and Liver Diseases, Columbia University Medical Center, NYC, United States
37 Washington University in St Louis, St Louis, United States
38 Gastroenterology & Hepatology, Thomas Jefferson University, Philadelphia, United States
39 CU Anschutz Medical Campus, Aurora, United States

40 Stony Brook University Hospital, Stony Brook, United States
41 Division of Gastroenterology, State University of New York, Stony Brook, United States
42 North Shore University Hospital, Manhasset, United States
43 Memorial Sloan Kettering Cancer Center, New York, United States
44 Gastroenterology, Methodist Dallas Medical Center, Dallas, United States
45 HCA Florida Aventura Hospital and Medical Center, Aventura, United States
46 Medicine, Icahn School of Medicine at Mount Sinai, New York, United States
47 Dr. Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, United States
48 Catholic Health St Francis Hospital & Heart Center, Roslyn, United States

Key words
Endoscopic ultrasonography, Intervention EUS, Biliary tract, Quality and logistical aspects, Performance and complications

received 14.7.2024
accepted after revision 25.11.2024

Bibliography
Endosc Int Open 2025; 13: a24955542
DOI 10.1055/a-2495-5542
ISSN 2364-3722

Georg Thieme Verlag KG, Oswald-Hesse-Straße 50, 70469 Stuttgart, Germany

Corresponding author
MBBS Yakira David, Mayo Clinic College of Medicine and Science, Gastroenterology, 200 First Street SW , 55905-0001 Rochester, United States
yakiradavid@gmail.com

Supplementary Material is available at https://doi.org/10.1055/a-2495-5542

ABSTRACT

Background and study aims EUS-guided gallbladder drainage (EUS-GBD) using lumen apposing metal stents (LAMS) has excellent technical and short-term clinical success for acute cholecystitis (AC). The goals of this study were to determine the long-term clinical outcomes and adverse events (AEs) of EUS-GBD with LAMS.

Patients and methods A multicenter, retrospective study was conducted at 18 US tertiary care institutions. Inclusion criteria: any AC patient with attempted EUS-GBD with LAMS and minimum 30-day post-procedure follow-up. Long-term clinical success was defined as absence of recurrent acute cholecystitis (RAC) > 30 days and long-term AE was defined as occurring > 30 days from the index procedure.

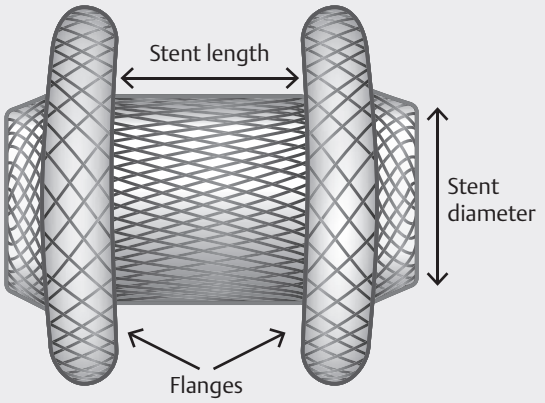
Results A total of 109 patients were included. Technical success was achieved in 108 of 109 (99.1%) and initial clinical success in 106 of 109 (97.2%). Long-term clinical success was achieved in 98 of 109 (89.9%) over a median follow-up of 140 days (range 30–1188). On multivariable analysis (MVA), acalculous cholecystitis (odds ratio [OR] 15.93, 95% confidence interval [CI] 1.22–208.52, $P = 0.04$) and the occurrence of a LAMS-specific AE (OR 63.60, 95% CI 5.08–799.29, $P < 0.01$) were associated with RAC. AEs occurred in 38 of 109 patients (34.9%) at any time, and in 10 of 109 (9.17%) > 30 days from the index procedure. Most long-term AEs (7 of 109; 6.42%) were LAMS-specific. No technical or clinical factors were associated with occurrence of AEs. LAMS were removed in 24 of 109 patients (22%). There was no difference in RAC or AEs whether LAMS was removed or not.

Conclusions EUS-GBD with LAMS has a high rate of long-term clinical success and modest AE rates in patients with AC and is a reasonable destination therapy for high-risk surgical candidates.

Introduction

Cholecystectomy is recommended for definitive management of acute cholecystitis (AC) [1, 2]. However, in patients who are critically ill with multiple comorbidities there is increased morbidity and mortality with surgical intervention [3]. Percutaneous gallbladder drainage (PT-GBD) is safe and efficacious but is associated with pain, discomfort, and recurrent biliary events often due to tube dislodgement [3, 4, 5, 6]. PT-GBD may also result in increased surgical complications in patients who subsequently undergo cholecystectomy [7].

Endoscopic ultrasound (EUS)-guided gallbladder drainage (EUS-GBD) is an alternative means of endoscopic gallbladder drainage. Initial EUS-GBD procedures using plastic and luminal self-expanding metal stents were technically and clinically successful but were often complicated by stent migration or occlusion [8]. The procedure has been refined through use of lumen-apposing metal stents (LAMS) (▶ **Fig. 1**), which allow for techni-



▶ **Fig. 1** Lumen-apposing metal stent.

cal ease of deployment and fewer risks of migration or occlusion [9]. In addition, due to the size and stability of LAMS, adjunctive procedures such as per-oral cholecystoscopy, gallstone lithotripsy, and removal are also facilitated [10, 11, 12]. Prior studies have demonstrated high rates of technical and short-term clinical success with EUS-GBD as well as low rates of adverse events (AE) compared with both PT-GBD and endoscopic transpapillary gallbladder drainage [13, 14, 15, 16, 17, 18]. Long-term data from Asian and European cohorts suggest good long-term outcomes [19, 20].

Technical details such as site of placement, use of wire guidance, stent size, use of coaxial plastic stents, and interval removal of stents vary by provider and it is unknown whether these variables affect procedure outcomes. There are also limited data on the effect of EUS-GBD or presence of a gallbladder LAMS on subsequent cholecystectomy.

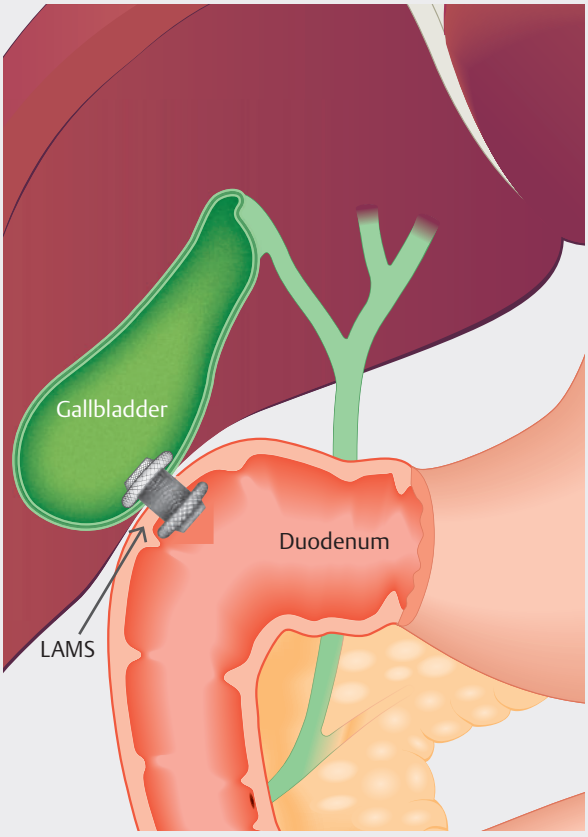
This study aimed to expand on existing data and determine long-term clinical success and AE of EUS-GBD with LAMS among United States institutions. It further sought to determine clinical and technical factors that influence clinical success and AEs as well as the impact of EUS-GBD with LAMS on interval cholecystectomy.

Patients and methods

Study design and population

This was a retrospective multicenter study conducted at 18 US tertiary institutions. Approval was granted by the Icahn School of Medicine at Mount Sinai Institutional Review Board (IRB-19–02464) as well as all participating institutions. Data use agreements were obtained from collaborating institutions as necessary.

Patients older than age 18 years old with AC who underwent attempted EUS-GBD with a LAMS between January 2013 to December 2019 and had a minimum of 30 days follow-up from the index procedure were included in this study. AC was defined using the Tokyo 2018 guidelines as presence of right upper quadrant pain/positive Murphy's sign accompanied by either fever, leukocytosis, elevated C reactive protein, or white blood cell count and/or radiologic evidence of AC [21].



▶ **Fig. 2** Choledochoduodenostomy with lumen-apposing metal stent.

Patient demographics and clinical features of presentation data were collected.

Endoscopic procedures

Endosonography using a curvilinear echoendoscope was performed on all patients. The gallbladder was identified and examined by the endosonographer to determine suitability for EUS-GBD. EUS-GBD was performed by either a transgastric or transduodenal route at endoscopist discretion. All patients underwent attempts at EUS-GBD with a LAMS (Axios, Boston Scientific, Marlborough, Massachusetts, United States). Decisions regarding stent diameter (10 mm × 10 mm, 15 mm × 10 mm, 20 mm × 10 mm), placement of LAMS over a guidewire, and use of an electrocautery-enhanced deployment system were at endoscopist discretion.

The LAMS was placed using standard techniques, with transmural puncture across the gastric or duodenal wall into the gallbladder lumen, followed by stepwise deployment of the distal and then proximal flange (▶ **Fig. 2**). The decision about whether the LAMS was balloon-dilated and/or if a coaxial plastic stent was placed was at endoscopist discretion.

Data pertaining to other procedure-related factors were recorded, including whether cystic duct interrogation, per-oral cholecystoscopy, gallstone extraction, and same-session endoscopic retrograde cholangiopancreatography were performed.

Outcomes

The primary outcome was to determine long-term clinical success and AEs of EUS-GBD with a LAMS. Technical success was defined as successful deployment of the LAMS in the gallbladder.

Recurrent acute cholecystitis (RAC) was defined as return of typical features of AC in patients who had initial resolution of symptoms after the index procedure. There are no established guideline criteria for long-term clinical success. For the purposes of this study, long-term clinical success was defined as absence of RAC ≥ 30 days after the index procedure.

Non-LAMS AE were classified according to the American Society of Gastrointestinal Endoscopy (ASGE) Lexicon for AE [22]. LAMS-specific AEs were defined as LAMS food impaction, LAMS misdeployment, LAMS migration in the gastrointestinal lumen or gallbladder, bleeding due to the LAMS, or buried LAMS. These were also evaluated in both the short term (< 30 days) and in the long term (≥ 30 days).

The secondary outcome was to determine technical and clinical factors associated with clinical success and AE

Statistical analysis

Descriptive analysis was performed on all demographic, technical, clinical, and outcome variables. Categorical variables were presented as percentages. Continuous variables were presented as median with interquartile ranges (IQRs). The relationship between technical and clinical factors and RAC and AE was explored using a univariate logistic regression. Significant associations were further explored using multivariable logistic regression. $P < 0.05$ was considered significant. All statistical analysis was conducted using IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, New York, United States: IBM Corp.

Results

A total of 140 cases were submitted by 18 institutions across the United States. Thirty-one cases had less than 30 days follow-up from the procedure and were excluded from analysis. The final sample used for analysis included 109 cases. Four of these cases have previously been published as part of a multicenter study on short-term outcomes of EUS-GBD in cirrhotic patients and were included because this study had different endpoints [23]. Median follow-up in the current study was 140 days (IQR 76–330, range 30–1188).

Demographics and clinical features

Demographics and clinical features are detailed in ▶ **Table 1**. Median age of the study population was 73 years (IQR 61.5–82) and 56% were male. Median Charlson comorbidity index was 7 and most patients had an American Society of Anesthesiologist (ASA) physical status classification of III or IV (96.2%).

▶ **Table 1** Demographics and clinical features of study population.

Parameter	Value (n = 109)
Demographics	
Median age/years (IQR)	73 (61.5–82)
Female n (%)	48 (44)
Median Charlson Comorbidity Index (IQR)	7 (5–8)
Clinical features	
ASA III + IV, n (%)	103 (96.2)
Ascites present, n (%)	28 (25.7)
Acalculous cholecystitis, n (%)	29 (26.6)
CBD stones present at index procedure, n (%)	27 (24.8)
Pre-procedure bilirubin (mg/dL) (IQR)	1.6 (0.7–3.8)
Pre-procedure platelets (x103/uL)(IQR)	225 (147–287.3)
Pre-procedure INR (IQR)	1.2 (1.1–1.4)
Pre-procedure antibiotics, n (%)	97 (89)
Pre-procedure anticoagulation, n (%)	37 (33.9)
Prior PT-GBD attempt, n (%)	10 (9.6)
Prior transpapillary GBD attempted, n (%)	6 (5.5)

ASA, American Society of Anesthesiologist physical status classification; CBD, common bile duct; IQR, interquartile range; PT-GBD, percutaneous gallbladder drainage.

Most cases were performed under general anesthesia (81.3%). Most patients (97/109, 89%) were on antibiotics pre-procedure.

A minority of patients (26.6%) had acalculous cholecystitis. Common bile duct (CBD) stones were present in 24.8% of patients and ascites was present in 25.7%. PT-GBD was attempted initially in 10 cases (9.6%) and failed in nine of them. Endoscopic transpapillary gallbladder drainage was attempted initially in six patients (5.5%) and all were unsuccessful.

Procedure details

Technical details of the procedures are detailed in ▶ **Table 2**. Most LAMS were placed using a transduodenal approach (73.4%). Electrocautery-enhanced LAMS was used in the majority of cases (90.8%). The most common stent diameters were 15 mm (59.8%) and 10 mm (38.3%). Wire guidance was utilized in 27.5%. Immediate balloon dilation of the LAMS was performed in 35.8% of cases. A coaxial plastic stent was placed in 33.9% of patients; the majority of these were 7F double pigtail plastic stents (78.4%).

At the index procedure, the cystic duct was interrogated in 31.2% of cases and was patent in 50% of these cases. Gallbladder stone extraction was performed in 13.8% of patients and per-oral cholecystoscopy was performed in 11% during the index procedure. No patients underwent lithotripsy of gallbladder stones via the LAMS. An ERCP was also performed during the index procedure in 30.3% of patients with biliary sphincter-

▶ **Table 2** Technical details of index procedure.

Parameter	Value, n (%)
Anesthesia	
General anesthesia	87 (81.3)
MAC	19 (17.8)
LAMS specifics	
Approach for LAMS	
Transgastric	29 (26.6)
Transduodenal	80 (73.4)
LAMS diameter (mm)	
10 mm	41 (38.3)
15 mm	64 (59.8)
20 mm	2 (1.9)
LAMS type	
Electrocautery-enhanced	99 (90.8)
Adjunctive procedures	
Over the wire LAMS placement	30 (27.5)
Stent dilation	39 (35.8)
Cystic duct interrogation	34 (31.2)
Cystic duct patent	17 (15.6)
Per-oral cholecystoscopy	12 (11)
Gallbladder stone extraction	15 (13.8)
ERCP performed at index procedure	33 (30.3)
CBD stones extraction	17 (15.6)
Biliary sphincterotomy	21 (19.3)
Biliary stent placed	16 (14.5)
Coaxial double pigtail plastic stent (DPPS) placed	37 (33.9)
▪ 7F	29 (26.6)
▪ 10F	8 (7.3)
Median # of coaxial DPPSs (IQR)	1 (1–1)

DPPS, double pigtail plastic stent; IQR, interquartile range; LAMS, lumen-apposing metal stent; MAC, monitored anesthesia care.

otomy performed in 19.3%, CBD stone extraction performed in 15.6%, and biliary stent placement in 19.3%.

Clinical outcomes

▶ **Table 3** shows the outcomes of EUS-GBD.

Technical success

Technical success was achieved in 108 of 109 cases (99.1%). The lone unsuccessful case was attempted using a transduodenal approach and failed due to stent misdeployment.

▶ **Table 3** Short- and long-term clinical outcomes in patients undergoing EUS-GBD (n = 109).

Parameter	Value
Short-term outcomes	
Technical success, n (%)	108 (99.1)
Short-term clinical success, n (%)	106 (97.2)
Median time to clinical success, days (IQR)	1 (1–3)
Discharged from hospital, n (%)	107 (98.2)
Median time to hospital discharge, days (IQR)	3 (2–7)
RAC < 30 days, n (%)	4 (3.7)
Interval development of cholangitis < 30 days, n (%)	2 (1.8)
Interval development of choledocholithiasis < 30 days, n (%)	4 (3.7)
Interval development of gallstone pancreatitis < 30 days, n	0
Long-term outcomes	
RAC ≥ 30 days, n (%)	4 (3.7)
Long-term clinical success, n (%)	98 (92.5)
Median time to long-term RAC, days (IQR)	100.5 (88.75–122.25)
Interval development of cholangitis ≥ 30 days, n (%)	3 (2.8)
Interval choledocholithiasis ≥ 30 days, n (%)	3 (2.8)
Interval gallstone pancreatitis ≥ 30 days, n (%)	1(0.9)

EUS-GBD, endoscopic ultrasound gallbladder drainage; RAC, recurrent acute cholecystitis.

Short-term clinical outcomes

Initial clinical success was achieved in 106 of 109 cases (97.2%) and median time to success was 1 day (IQR 1–3). The technically unsuccessful case accounted for one of the clinically unsuccessful cases. The other two clinical failures were technically successful with LAMS placed using a transgastric approach. One clinical failure was due to stent migration 2 days after placement and clinical success was then achieved via percutaneous drainage. The other case had no obvious explanation for its clinical failure. That patient's cholecystitis was subsequently managed supportively.

Most patients (98.2%) were discharged from the hospital and median time to discharge was 3 days. Within the first 30 days from the index procedure, there were four of 109 cases (3.7%) of recurrent cholecystitis. Thus, overall short-term clinical success was 93.6% (102/109). Three of the RAC cases were associated with food impactions of the LAMS and were managed endoscopically. Two of these were placed transduodenally and the third was transgastric. The fourth case was placed

transduodenally and was not associated with any LAMS AEs. It was managed supportively.

Additional gallstone complications occurred in four patients (3.7%) within 30 days of EUS-GBD. Four patients developed interval choledocholithiasis and two (1.8%) of them developed cholangitis.

Long-term clinical outcomes

When examining outcomes more than 30 days following EUS-GBD, RAC occurred in four of 109 patients (3.7%); these occurred at 61, 98, 103, and 180 days. Thus, the overall long-term clinical success rate for all attempted cases was 89.9% (98/109). Two of the long-term RAC cases had transduodenal LAMS placement. One developed a LAMS food impaction and was managed endoscopically while the other was not associated with any LAMS complication and was managed supportively. The other two long-term RAC cases had transgastric LAMS placements. One was complicated by a buried LAMS and was managed endoscopically while the other was complicated by LAMS migration and was managed supportively.

Additional gallstone complications occurred in four patients (3.7%) ≥ 30 days after EUS-GBD. Three patients developed interval choledocholithiasis and all of them developed cholangitis. One patient (0.9%) developed gallstone pancreatitis.

Adverse events

AEs are shown in ▶ **Table 4**. Thirty-eight (34.9%) patients had a total of 50 AEs (12 patients had more than one AE). There were 17 of 109 (15.6%) LAMS-specific AEs.

Short-term AEs

During the index procedure, there was one non-LAMS duodenal perforation (0.92%). There were also three LAMS misdeployments (2.75%) All of these were attempted via a transduodenal approach. Two of these were due to distal flange deployment in the peritoneum and one was due to immediate migration of the distal flange out of the gallbladder into the peritoneum after it was deployed. All of these were managed endoscopically with subsequent correct positioning.

All other AEs occurred in the post procedure period. Within the first 30 days post procedure, seven of 109 patients (6.42%) had a LAMS-specific AE with median time to occurrence of 10 days (IQR 1–15). Food impactions of the LAMS six of 109 (5.5%) were the most common LAMS-specific AE and all were managed endoscopically. The majority, five of six were placed with a transduodenal approach.

During this time, 21 patients had a total of 27 non-LAMS AE (6 patients had 2 non-LAMS AE). Median time to occurrence was 8 days (IQR 1.25–14.75). The most common non-LAMS AE in this timeframe were fever in eight of 109 (7.34%) and abdominal pain in seven of 109 (6.42%). A transgastric approach was utilized for five of eight cases and a transduodenal approach for three of eight cases with fever. Fever was managed supportively in six of eight cases, endoscopically in one of eight and by interventional radiology in one of eight cases. A transduodenal approach was used in six of seven cases with abdominal pain and transgastric for one of seven cases. Supportive

▶ **Table 4** Adverse events in patients undergoing EUS-GBD (n = 109).

Parameter	Value, n (%)
Intra-procedure adverse events	
Total intra-procedure adverse events	4 (3.7)
LAMS misdeployment	3 (2.8)
Non-LAMS perforation	1 (0.9)
Short-term adverse events < 30 days	
Total short-term adverse events	34 (31.2)
Fever	8 (7.34)
Abdominal pain	7 (6.42)
Food Impactions	6 (5.5)
Hypotension	2 (1.8)
Dysrhythmia	2 (1.8)
Infection	2 (1.8)
LAMS migration into the gastrointestinal lumen	1 (0.9)
Non-LAMS-associated bleeding	1 (0.9)
Non-LAMS perforation	1 (0.9)
Hypopnea	1 (0.9)
Hypoxia	1 (0.9)
Deep vein thrombosis	1 (0.9)
Pneumonia	1 (0.9)
Short-term adverse event severity	
Mild	14
Moderate	16
Severe	4
Long-term adverse events ≥ 30 days	
Total long-term adverse events	12 (11)
Food impactions	2 (1.8)
LAMS migration into the gastrointestinal lumen	2 (1.8)
Abdominal pain	2 (1.8)
Buried LAMS	1 (0.9)
LAMS migration into the gallbladder lumen	1 (0.9)
Biliary obstruction secondary to LAMS	1 (0.9)
Fever	1 (0.9)
Pneumonia	1 (0.9)
Non-LAMS-associated bleeding	1 (0.9)
Long-term adverse event severity	
Mild	3 (2.8)
Moderate	8 (7.3)
Severe	1 (0.9)

EUS-GBD, endoscopic ultrasound gallbladder drainage; LAMS, lumen-apposing metal stent

▶ **Table 5** Significant factors on univariate and multivariable analysis of associated with long-term clinical success and adverse events.

Parameter	Univariate			Multivariable		
	OR	CI	*P* value	OR	CI	*P* value
Recurrent acute cholecystitis						
ASA III vs ASA II	0.08	0.01–0.70	0.02	0.24	0.01–7.52	0.42
ASA IV vs ASA II	0.03	0.00–0.47	0.01	0.02	0.00–1.42	0.07
Acalculous vs calculous cholecystitis	5.35	1.19–24.03	0.03	**15.93**	**1.22–208.52**	**0.04**
Over the wire placement vs Direct Placement	5.07	1.13–22.73	0.04	5.05	0.61–41.67	0.13
LAMS AE	24.55	4.40–136.86	< 0.01	**63.70**	**5.08–799.29**	**< 0.01**
Any adverse event						
Coaxial plastic stent placement	2.89	1.16–7.19	0.022	2.34	0.90–6.10	0.082
Time to clinical resolution of AC	1.21	1.03–1.43	0.021	1.20	1.02–1.42	0.27

AC, acute cholecystitis; ASA, American Society of Anesthesiologist physical status classification; CI, confidence interval; OR, odds ratio.

management was used in six of seven cases of abdominal pain cases and endoscopic management for one of seven cases.

Long-term AEs

Ten patients (9.17%) had a total of 12 AEs occurring 30 days or later from the index procedure (2 patients had > 1 AE)

There were seven of 109 (6.42%) LAMS-specific AEs > 30 days from the index procedure. Median time to occurrence was 85 days (IQR 62–150). There were two LAMS food impactions (transduodenal placement), two LAMS migrations into the gastrointestinal lumen (1 transduodenal, 1 transgastric placement), one buried LAMS (transgastric placement), one LAMS migration into the gallbladder lumen (transgastric placement), and one developed inflammatory changes around the LAMS which caused biliary obstruction (transduodenal placement). LAMS migrations into the gastrointestinal lumen were managed supportively. All other LAMS complications were managed endoscopically.

Long-term non-LAMS AE occurred in three of 109 patients (2.8%). Two of these patients each had two long-term non-LAMS AEs. Median time to these long-term non-LAMS AE was 180 days (IQR 64.5–254). One patient had abdominal pain, one had pneumonia and non-LAMS associated bleeding, and one had fever and abdominal pain. The abdominal pain and non-LAMS-associated bleeding were managed endoscopically whereas the other non-LAM AEs were managed supportively.

Factors influencing clinical success and AEs

▶ **Table 5** shows univariate and multivariable analysis of statistically significant clinical and technical factors and occurrence of RAC and AEs. On univariate analysis, RAC was less common in patients with ASA III (odds ratio [OR] 0.08, 95% confidence interval [CI] 0.01–0.70, $P = 0.02$) or IV (OR 0.03, 95% CI 0.00–0.47, $P = 0.01$) compared with those with ASA II. RAC was also associated with acalculous compared with calculous cholecystitis (OR 5.35, 95% CI 1.19–24.03, $P = 0.03$), over-the-wire LAMS placement (OR 5.07, 95% CI 1.13–22.73, $P = 0.04$), and having a LAMS-specific AE (OR 24.55, 95% CI 4.40–136.86, $P < 0.01$). When controlled for each other on multivariable analysis, only acalculous cholecystitis (OR 15.93, 95% CI 1.22–208.52 $P = 0.04$) and LAMS-specific AEs (OR 63.70, 95% CI 5.08–799.29, $P < 0.01$) remained associated with an increased risk of AC.

On univariate analysis, placement of a coaxial plastic stent (OR 2.89, 95%CI 1.16–7.19, $P = 0.02$) and increased time to resolution of AC (OR 1.21, 95%CI 1.03–1.43, $P = 0.02$) were associated with increased incidence of AE. However, when controlled for each other, neither of these remained significant.

No other clinical or technical factors were associated with occurrence of RAC and AE.

Outcomes of LAMS removal

LAMS were removed in 24 of 109 patients (22%). Median time to removal was 38 days (IQR 32–61). Removal was elective in 22 of 24 (91.7%). Removal was uncomplicated in all cases except one (transgastric placement), in which there was a buried LAMS and tract dilation was required for exposure and removal. RAC occurred in one of 24 cases (4.2%) in which LAMS was removed, compared with seven of 85 cases (8.2%; $P = 0.68$) in which LAMS was not removed. At the time of LAMS removal, the cystic duct was noted to be patent in 18 (75%), not patent in one (4.2%), and not evaluated in five (20.8%). The fistula was intentionally left open in most cases (19/24; 79.2%). Fistula closure was performed in the other five patients by over-the-scope clips (OVESCO) (n = 3), endoscopic suturing (n = 1), and surgically during an interval cholecystectomy (n = 1). The lone case of RAC occurred in one of the patients in whom the cystic duct was not evaluated and the fistula was closed with an OVESCO.

LAMS impact on cholecystectomy

Five patients (4.6%) underwent interval elective cholecystectomy Median time to cholecystectomy was 36 days (IQR 32–61). Two (40%) were laparoscopically performed, whereas the

other three (60%) ultimately required an open procedure. One case that was converted from laparoscopic to open required an antrectomy and Billroth II anastomosis due to RAC, which became complicated by a gallbladder abscess despite repeat endoscopic attempts at evacuating the gallbladder and PT-GBD. In the other two patients who underwent open cholecystectomies, the treatment was done as part of a Whipple procedure for duodenal and pancreatic adenocarcinoma. The need for an open procedure was not influenced by the time from the EUS-GBD procedure to interval cholecystectomy. There were no other perioperative AEs.

Death

Twenty-six patients (23.9%) died during the study period with median time to death of 150 days (IQR = 83–283.5). Based on the criteria outlined in the ASGE Lexicon for reporting AE, none of these deaths were attributed to the EUS-GBD procedure by the proceduralists. Median Charlson Comorbidity Index for the patients who died was 7 and for those who survived was 6 ($P = 0.083$).

Discussion

EUS-GBD with LAMS was associated with excellent long- term clinical success and low rates of major AEs in this study, with few patients going on to have interval cholecystectomy. Initial acalculous cholecystitis and occurrence of a LAMS-specific AE were associated with RAC. Neither leaving in place nor removal of the LAMS increased risk of RAC

EUS-GBD technique is not standardized. Variations include use of electrocautery-enhanced vs standard LAMS, stent diameter, over-the-wire versus free-hand techniques, and dilation of the fistula tract and stent [9, 24, 25, 26]. In addition, some advocate placement of coaxial plastic stents to prevent bleeding secondary to pressure injury from the distal LAMS flange, or to minimize risk of stent migration or food impaction [25]. In this study, none of these variable practices impacted technical or clinical success or AEs. This may help guide endosonographers in terms of technical decision making. However, our study was not sufficiently powered nor designed to truly evaluate the impact of these variables.

Site of LAMS placement has been thought to influence clinical success and AEs. It is hypothesized that due to gastric motility, transgastric placement may be more subject to stent migration, tissue ingrowth, and food impaction whereas LAMS removal may be more complicated from a transduodenal approach [20, 27, 28]. Other studies indicate that site of placement does not affect clinical success or incidence of AEs and similar findings were noted in our study [29, 30]. The decision for transgastric or transduodenal approach is likely dictated in part by the suitability of the puncture window. However, in cases in which a suitable drainage window is present in both locations, the ultimate decision is left to endoscopist discretion. Future studies should specifically address this issue because it remains a current debate among endoscopists.

Gallbladder drainage has traditionally been intended as a bridge to definitive treatment of AC with a cholecystectomy [2, 5]. In this study, few patients underwent interval cholecystectomy, and after follow-up of up to 3 years, there were only eight cases of RAC. Thus, it is reasonable to consider EUS-GBD as destination therapy for high surgical risk candidates.

In this study, patients with acalculous cholecystitis had higher rates of recurrence, which would suggest that this subgroup of patients may benefit more from interval cholecystectomy. This finding, however, contrasts with other studies of PT-GBD in which there were lower rates of recurrence in acalculous cholecystitis, which obviated the need for an interval cholecystectomy [10, 31, 32, 33]. The explanation for this contrary finding is unclear. Poor drainage in acalculous cholecystitis is driven by bile stasis due to gallbladder dysmotility and gallbladder ischemia in the setting of critical illness as opposed to cystic duct occlusion [34, 35]. It is possible that this can recur even in the presence of an alternative drainage route. Further study is needed to validate this finding and to investigate factors that influence recurrence after EUS-GBD.

RAC was not associated with LAMS removal, but was associated with LAMS dysfunction, either due to migration, occlusion from food, or tissue ingrowth. Similarly, in other studies, LAMS occlusion with food debris was the most likely cause of RAC [36]. Some centers routinely remove the LAMS after resolution of AC for this reason as well as the concern that prolonged dwelling increases risk of stent erosion, causing bleeding and migration [9, 11, 28]. Leaving the LAMS in situ did not, however, increase risk of these AEs in this study. Similar studies with LAMS used for gallbladder drainage also noted no increased risk of AE with longer dwell times [20, 24, 27]. In addition, if RAC occurs, it is likely due to LAMS dysfunction, which in most cases, was amenable to either endoscopic therapy or supportive care. Thus, in these patients who are at high surgical risk, using LAMS as destination therapy is likely a safe and effective treatment option.

There are a number of strengths and limitations to this study. A major strength is that data were collected from 18 large, US, academic/tertiary-referral centers. EUS-GBD is still relatively new, and the technique has not yet been standardized. Inclusion of large centers provides data from a broad range of technique practices. As such, these findings start to provide some clarity about which clinical and specific technical factors of EUS-GBD have an impact on outcomes. It appears that factors such as use of a wire, use of electrocautery-enhanced LAMS, balloon dilation of LAMS, placement of a coaxial stent, diameter of LAMS, location of deployment, and whether it is left in situ or removed have no major impact on clinical outcomes. A major limitation of this study is its retrospective nature, which is limited to accuracy of data provided in patient charts and its single-arm nature, which did not allow for comparisons of a matched population with either cholecystectomy or PT-GBD. In addition, all participating endoscopists were experienced and at tertiary centers, which may limit generalizability of the results to other practice settings.

Conclusions

In conclusion, EUS-GBD with LAMS has excellent long-term clinical success for management of AC regardless of technique used or LAMS dwell time. The few cases that recur are usually due to LAMS malfunction and can usually be managed nonsurgically. Given these findings, it is reasonable to consider this technique as destination therapy for high-risk surgical candidates.

Conflict of Interest

Harry Aslanian: Olympus (consultant), Boston Scientific (consultant). Prabhleen Chahal: Advisory council Medtronic, Boston Scientific (consultant). Rabia DeLatour: Ambu (consultant). David L. Diehl: Boston Scientific (consultant). Christopher J. DiMaio: Boston Scientific (consultant, speaker), Medtronic (consultant, speaker). Tamas A. Gonda: Boston Scientific (Research support). Thomas Kowalski: Boston Scientific (consultant), Medtronic (consultant). Nikhil A. Kumta: Boston Scientific (consultant, speaker), Olympus (consultant), Apollo Endosurgery (consultant, speaker). Dan Mullady: Boston Scientific (consultant), Cook (consultant). John Y. Nasr: Boston Scientific (consultant). Jose Nieto: Boston Scientific (consultant). Alexander Schlachterman: Lumendi (consultant), ConMed (consultant), Olympus (consultant), Medtronic (consultant), FujiFilm (consultant). Andrew Storm: Apollo Endosurgery (consultant and research grants), ERBE (consultant), Boston Scientific (research grants). All other authors: No conflicts of interest

References

[1] Ansaloni L, Pisano M, Coccolini F et al. 2016 WSES guidelines on acute calculous cholecystitis. World J Emerg Surg 2016; 11: 25 doi:10.1186/s13017-016-0082-5

[2] Okamoto K, Suzuki K, Takada T et al. Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis. J Hepatobiliary Pancreat Sci 2018; 25: 55–72 doi:10.1002/jhbp.516

[3] Endo I, Takada T, Hwang TL et al. Optimal treatment strategy for acute cholecystitis based on predictive factors: Japan-Taiwan multicenter cohort study. J Hepatobiliary Pancreat Sci 2017; 24: 346–361 doi:10.1002/jhbp.456

[4] Alvino DML, Fong ZV, McCarthy CJ et al. Long-term outcomes following percutaneous cholecystostomy tube placement for treatment of acute calculous cholecystitis. J Gastrointest Surg 2017; 21: 761–769 doi:10.1007/s11605-017-3375-4

[5] Mori Y, Itoi T, Baron TH et al. Tokyo Guidelines 2018: management strategies for gallbladder drainage in patients with acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci 2018; 25: 87–95

[6] Yun SS, Hwang DW, Kim SW et al. Better treatment strategies for patients with acute cholecystitis and American Society of Anesthesiologists classification 3 or greater. Yonsei Med J 2010; 51: 540–545 doi:10.3349/ymj.2010.51.4.540

[7] Altieri MS, Bevilacqua L, Yang J et al. Cholecystectomy following percutaneous cholecystostomy tube placement leads to higher rate of CBD injuries. Surg Endosc 2019; 33: 2686–2690 doi:10.1007/s00464-018-6559-4

[8] Anderloni A, Buda A, Vieceli F et al. Endoscopic ultrasound-guided transmural stenting for gallbladder drainage in high-risk patients with acute cholecystitis: a systematic review and pooled analysis. Surg Endosc 2016; 30: 5200–5208

[9] Itoi T, Binmoeller KF, Shah J et al. Clinical evaluation of a novel lumen-apposing metal stent for endosonography-guided pancreatic pseudocyst and gallbladder drainage (with videos). Gastrointest Endosc 2012; 75: 870–876

[10] Bhatt MN, Ghio M, Sadri L et al. Percutaneous cholecystostomy in acute cholecystitis-predictors of recurrence and interval cholecystectomy. J Surg Res 2018; 232: 539–546 doi:10.1016/j.jss.2018.06.051

[11] Chan SM, Teoh AYB, Chiu PWY et al. Advanced gallbladder interventions after endoscopic ultrasonography-guided gallbladder drainage. Techniq Innov Gastrointest Endosc 2020; 22: 24–26

[12] Tan YY, Zhao G, Wang D et al. A new strategy of minimally invasive surgery for cholecystolithiasis: calculi removal and gallbladder preservation. Dig Surg 2013; 30: 466–471 doi:10.1159/000357823

[13] Higa JT, Sahar N, Kozarek RA et al. EUS-guided gallbladder drainage with a lumen-apposing metal stent versus endoscopic transpapillary gallbladder drainage for the treatment of acute cholecystitis (with videos). Gastrointest Endosc 2019; 90: 483–492

[14] Luk SW, Irani S, Krishnamoorthi R et al. Endoscopic ultrasound-guided gallbladder drainage versus percutaneous cholecystostomy for high risk surgical patients with acute cholecystitis: a systematic review and meta-analysis. Endoscopy 2019; 51: 722–732

[15] Mohan BP, Khan SR, Trakroo S et al. Endoscopic ultrasound-guided gallbladder drainage, transpapillary drainage, or percutaneous drainage in high risk acute cholecystitis patients: a systematic review and comparative meta-analysis. Endoscopy 2020; 52: 96–106 doi:10.1055/a-1020-3932

[16] Oh D, Song TJ, Cho DH et al. EUS-guided cholecystostomy versus endoscopic transpapillary cholecystostomy for acute cholecystitis in high-risk surgical patients. Gastrointest Endosc 2019; 89: 289–298 doi:10.1016/j.gie.2018.08.052

[17] Siddiqui A, Kunda R, Tyberg A et al. Three-way comparative study of endoscopic ultrasound-guided transmural gallbladder drainage using lumen-apposing metal stents versus endoscopic transpapillary drainage versus percutaneous cholecystostomy for gallbladder drainage in high-risk surgical patients with acute cholecystitis: clinical outcomes and success in an International, Multicenter Study. Surg Endosc 2019; 33: 1260–1270

[18] Teoh AYB, Kitano M, Itoi T et al. Endosonography-guided gallbladder drainage versus percutaneous cholecystostomy in very high-risk surgical patients with acute cholecystitis: an international randomised multicentre controlled superiority trial (DRAC 1). Gut 2020; 69: 1085–1091

[19] Dollhopf M, Larghi A, Will U et al. EUS-guided gallbladder drainage in patients with acute cholecystitis and high surgical risk using an electrocautery-enhanced lumen-apposing metal stent device. Gastrointest Endosc 2017; 86: 636–643

[20] Walter D, Teoh AY, Itoi T et al. EUS-guided gall bladder drainage with a lumen-apposing metal stent: a prospective long-term evaluation. Gut 2016; 65: 6–8

[21] Yokoe M, Hata J, Takada T et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci 2018; 25: 41–54

[22] Cotton PB, Eisen GM, Aabakken L et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc 2010; 71: 446–454 doi:10.1016/j.gie.2009.10.027

[23] James TW, Krafft M, Croglio M et al. EUS-guided gallbladder drainage in patients with cirrhosis: results of a multicenter retrospective study. Endosc Int Open 2019; 7: E1099–E1104

[24] Cho DH, Jo SJ, Lee JH et al. Feasibility and safety of endoscopic ultrasound-guided gallbladder drainage using a newly designed lumen-apposing metal stent. Surg Endosc 2019; 33: 2135–2141 doi:10.1007/s00464-018-6485-5

[25] James TW, Baron TH. EUS-guided gallbladder drainage: A review of current practices and procedures. Endosc Ultrasound 2019; 8: S28–S34 doi:10.4103/eus.eus_41_19

[26] Ogura T, Higuchi K. Endoscopic ultrasound-guided gallbladder drainage: Current status and future prospects. Dig Endosc 2019; 31: 55–64 doi:10.1111/den.13334

[27] Boregowda U, Umapathy C, Nanjappa A et al. Endoscopic ultrasound guided gallbladder drainage - is it ready for prime time? World J Gastrointest Pharmacol Ther 2018; 9: 47–54 doi:10.4292/wjgpt.v9.i6.47

[28] Chan SM, Teoh AYB, Yip HC et al. Feasibility of per-oral cholecystoscopy and advanced gallbladder interventions after EUS-guided gallbladder stenting (with video). Gastrointest Endosc 2017; 85: 1225–1232

[29] Teoh AYB, Serna C, Penas I et al. Endoscopic ultrasound-guided gallbladder drainage reduces adverse events compared with percutaneous cholecystostomy in patients who are unfit for cholecystectomy. Endoscopy 2017; 49: 130–138

[30] Tyberg A, Saumoy M, Sequeiros EV et al. EUS-guided versus percutaneous gallbladder drainage: isn't it time to convert? J Clin Gastroenterol 2018; 52: 79–84 doi:10.1097/MCG.0000000000000786

[31] Kim SB, Gu MG, Kim KH et al. Long-term outcomes of acute acalculous cholecystitis treated by non-surgical management. Medicine (Baltimore) 2020; 99: e19057 doi:10.1097/MD.0000000000019057

[32] Noh SY, Gwon DI, Ko GY et al. Role of percutaneous cholecystostomy for acute acalculous cholecystitis: clinical outcomes of 271 patients. Eur Radiol 2018; 28: 1449–1455 doi:10.1007/s00330-017-5112-5

[33] Abbas SH, Ghazanfar MA, Gordon-Weeks AN et al. Acalculous Cholecystitis: Is an elective interval cholecystectomy necessary. Dig Surg 2018; 35: 171–176 doi:10.1159/000477780

[34] Barie PS, Eachempati SR. Acute acalculous cholecystitis. Gastroenterol Clin North Am 2010; 39: 343–357 doi:10.1016/j.gtc.2010.02.012

[35] Huffman JL, Schenker S. Acute acalculous cholecystitis: a review. Clin Gastroenterol Hepatol 2010; 8: 15–22 doi:10.1016/j.cgh.2009.08.034

[36] Cho SH, Oh D, Song TJ et al. Comparison of the effectiveness and safety of lumen-apposing metal stents and anti-migrating tubular self-expandable metal stents for EUS-guided gallbladder drainage in high surgical risk patients with acute cholecystitis. Gastrointest Endosc 2020; 91: 543–550