Outcomes of EUS-guided transluminal gallbladder drainage in patients without cholecystitis

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Abstract

Background and Objectives: Cholecystectomy is the gold standard for most gallbladder-related disease. However, many patients with gallbladder disease are poor surgical candidates. Current nonsurgical gallbladder drainage (GBD) methods include percutaneous cholecystostomy and endoscopic ultrasound-guided transluminal GBD (EUS-GBD). Outcomes for EUS-GBD for the treatment of noncholecystitis (NC) gallbladder disease have not been defined. **Materials and Methods:** Cases were identified using procedural data from a quaternary academic hospital for endoscopic procedures from 2015 to 2020. Patients who underwent EUS-GBD for acute cholecystitis, biliary colic, gallstone pancreatitis, and secondary prevention of gallstone disease were included. **Results:** Fifty-five cases of EUS-GBD were identified over the 5-year study period. Forty-one cases were performed for acute cholecystitis, and 15 were performed for other NC indications. Indications for NC drainage included primary treatment of symptomatic biliary colic and secondary prevention of gallstone pancreatitis and choledocholithiasis. There was no statistically significant difference in complications, mortality, or reintervention requirements. There was a 13.3% rate of immediate complications in the NC group, which were all medically managed. **Conclusions:** EUS-GBD appears to be a safe and effective way to manage gallstone disease in nonsurgical candidates with NC gallbladder-related disease. Overall complications and readmissions were infrequent. Complication rates were similar to those published in patients who underwent EUS-GBD for acute cholecystitis.

Key words: biliary tract diseases, drainage, EUS, ultrasonography

INTRODUCTION

Cholecystectomy, either open or laparoscopic, has long been the gold standard for treating patients with both infectious (acute cholecystitis, cholangitis) and noninfectious (cholelithiasis, choledocholithiasis, pancreatitis, biliary colic, *etc.*) calculous gallbladder

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diseases. Many patients are not surgical candidates due to comorbidities which make surgery prohibitive. Alternative gallbladder drainage options have been employed in such patients.

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Percutaneous cholecystostomy (PC) was long considered the first-line nonoperative management for calculous gallbladder disease and is still commonly used. PC is also used as a bridge to surgery in patients with severe cholecystitis.^[1,2] The overall clinical success rates of PC are roughly 90%.^[3] However, PC has many potential downsides. These include bleeding, peritonitis, pneumothorax, decreased quality of life due to reliance on an external drainage system, high recurrence rates after tube removal, and risk of dislodgement in patients with ascites or cognitive impairment.^[4,5] Adverse event rates have been reported as high as 14%, with mortality as high as 19% for PC.^[6] The comorbidities that render patients who undergo PC poor surgical candidates contribute to their increased mortality.

Recently, EUS-guided gallbladder drainage (EUS-GBD) has emerged as an alternative method of GBD in patients with acute cholecystitis who are nonoperative candidates.^[4,5] Several studies have demonstrated technical and clinical success of EUS-GBD for acute cholecystitis in nonoperative candidates.^[7-11] This has been streamlined with the development of cautery enhanced lumen-apposing metal stents (LAMS).

EUS-GBD has demonstrated high technical and functional success rates, with low rates of recurrence of cholecystitis.^[5,6] Compared to PC, EUS-GBD has demonstrated less overall and less serious adverse events in patients with acute cholecystitis, with adverse events rates ranging from 6% to 32% compared with upward of 71% in studies evaluating PC.^[12-14] EUS-GBD also results in shorter hospital stays, less postprocedural pain, less cost, and less need for repeat interventions than PC.^[13-16] EUS-GBD has been shown to be feasible in patients with ascites, giving it another advantage over PC.^[17] With these outcomes, EUS-GBD has been increasingly utilized as a primary alternative to surgical cholecystectomy or as an alternative drainage method in patients converting from failed PC.^[18]

In addition to acute cholecystitis, cholecystectomy is recommended in patients for secondary prevention of gallstone-related disease. This includes gallstone pancreatitis, biliary colic from either cholelithiasis or choledocholithiasis, and malignant biliary obstruction without evidence of either acute cholecystitis or cholangitis. Cholecystectomy is also recommended in patients with choledocholithiasis after removal of common bile duct stones. While there are convincing data that EUS-GBD is safe and effective for the treatment of acute cholecystitis, there are not robust data on the role of EUS-GBD for secondary prevention of gallstone-related disease. To this end, this investigation seeks to determine the impact of EUS-GBD for secondary prevention of gallstone-related disease in nonoperative candidates without acute cholecystitis.

MATERIALS AND METHODS

Using procedural data generated by Provation from the Department of Gastroenterology at a Quaternary Academic Health Center between January 2015 and April 2020, all endoscopic cases that documented the use of an LAMS were identified. Cases that billed for use of an LAMS for purposes other than EUS-GBD were excluded. All EUS-GBD cases during this time were considered, regardless of technical success. Technical success was defined as successful LAMS deployment and visualization of biliary flow.

EUS-GBD was performed using a curvilinear therapeutic echoendoscope. Pentax echoendoscopes were used through April 2018, with Olympus echoendoscopes used thereafter. All procedures were performed using a cautery enhanced LAMS (10 mm Axios, Boston Scientific, Marlborough, MA, USA). The use of guidewire access was at the discretion of the endoscopist. Our institutional practice is to place a double pigtail plastic stent through the LAMS to maintain patency and prevent migration [Figure 1]. Insufflation with carbon dioxide



Figure 1. Intraprocedural images of a lumen-apposing metal stent (red arrow) placed into a distended gallbladder via EUS for gallbladder drainage and a double pigtail plastic stent (blue arrow) placed through the lumen apposing metal stent per departmental policy to prevent migration

is used to prevent risk of pneumoperitoneum. After a 1-month period, patients are brought back to endoscopy for further washout and LAMS removal; the pigtail stents remain indefinitely. Cases were performed either from a duodenal or gastric access point. LAMS was removed in 1 month and replaced with a pigtail stent if determined to be clinically feasible.

Once identified from the database, cases were stratified based on whether the indication for EUS-GBD was for primary treatment of cholecystitis (C) or for secondary prevention of gallstone-related disease, such as choledocholithiasis or gallstone pancreatitis in the absence of acute cholecystitis (noncholecystitis [NC]). The indications for EUS were determined based on chart review. Factors included in the assessment of acute cholecystitis were the presence of Murphy's sign, right upper quadrant (RUQ) abdominal pain, mass, or tenderness, fevers, elevated C-reactive protein, leukocytosis, or imaging findings characteristic of acute cholecystitis including pericholecystic fluid, gallbladder wall thickening, and/or gallstones/debris per the Tokyo criteria.^[19] Included in the NC group were all other patients who underwent EUS-GBD primarily for the treatment of biliary colic, secondary prevention of gallstone pancreatitis, and secondary prevention of gallstone-related complications of choledocholithiasis.

Each case was examined retrospectively, with primary demographic and immediate complication rates collected from review of admission notes, endoscopy reports, and discharge summaries. Any complication or adverse outcome attributed to EUS-GBD within 14 days of the initial procedure was included and defined as an immediate complication; anything occurring later than 14 days after the EUS-GBD was defined as a late complication. Readmissions, late complications, and need for reintervention or stent removal were monitored for up to 1 year following EUS-GBD. To collect outcome data, any additional admissions, endoscopic procedures, abdominal imaging (including ultrasonography, computed tomography images, and magnetic resonance imaging of the abdomen), or outpatient office visit notes within the Partners Healthcare System within 1 year of the date of the initial EUS-GBD procedure were included. When appropriate, the admission notes, endoscopy reports, radiology reports, and progress notes were examined for descriptions of indications for admission and/or repeat endoscopic intervention, as well as late complications attributed to EUS-GBD.

Results were analyzed by averaging desired data within the two groups and comparing the averages by Student's *t*-test for continuous variables. No categorical variables were assessed. The primary outcome of this study was to compare the technical and clinical success of EUS-GBD in the NC group when compared to the C group. Secondary outcomes included admission length, need for re-intervention, and readmission rates for gallstone-related complications in patients who underwent NC drainage. This study was approved by the MGH IRB (2019P002708).

RESULTS

Fifty-six cases of EUS-GBD were identified over the 5-year study period. Of these, 41 were performed for acute cholecystitis, and 15 were performed for indications other than cholecystitis (NC). Indications for NC drainage included symptomatic biliary colic, malignant biliary obstruction without cholecystitis, prevention of gallstone pancreatitis, and secondary prevention of gallstone-related complications in patients with choledocholithiasis. Basic demographic data were compared [Table 1]. The only statistically significant difference at presentation was the presence of leukocytosis in the cholecystitis group (14.3 *vs.* 8.4 K/ μ L, *P* = 0.02).

Patients who underwent NC drainage had an average admission length of 9.3 days, compared to 11.6 days among patients in the C group [P = 0.56, Table 2].

Table 1. Characteristics of patients who had EUS-GBD-NC *versus* EUS-GBD-C during the study period

	EUS-GBD-C	EUS-GBD-NC	Р
n	41	15	
Age (years)	77.0	72.7	0.29
Male (%)	53.7	46.7	0.65
BMI (kg/m ²)	24.0	26.1	0.25
Cancer history (%)	46.3	46.7	0.98
Alcohol use disorder (%)	24.4	26.7	0.86
Tobacco use history (%)	46.3	60.0	0.37
Jaundice (%)	17.1	40.0	0.07
Abdominal pain (%)	63.4	46.7	0.27
WBC (K/µL)	14.3	8.4	0.02*
Alkaline phosphatase (U/L)	269	376	0.19
Total bilirubin (mg/dL)	3.0	3.9	0.58
AST (U/L)	139	155	0.84
ALT (U/L)	92	154	0.20

*Denotes significance. Past medical history, symptom burden, and laboratory data were compared across the groups. EUS-GBD: EUS-guided gallbladder drainage; NC: Noncholecystitis; C: Cholecystitis; AST: Aspartate transaminase; ALT: Alanine aminotransferase; BMI: Body mass index; WBC: White blood cells

	EUS-GBD-C	EUS-GBD-NC	Р
n	41	15	
Admission length (days)	11.6	9.3	0.56
Patients with immediate complications (%)	6 (14.6)	2 (13.3)	0.90
Average readmissions within 1 year	1.3	0.5	0.11
Average readmissions for biliary disease within 1 year	0.1	0.2	0.57
Admissions for recurrent biliary disease within 1 year (%)	5 (12.2)	2 (13.3)	0.91
Patients with late complications (%)	4 (9.8)	0 (0)	0.22
Patients who had stent removal (%)	16 (39.0)	9 (60.0)	0.17
Average days until stent removal	98.0	43.3	0.58
Patients requiring re-intervention within 1 year (%)	8 (19.5)	4 (26.7)	0.57
Average days until re-intervention	148.5	46.5	0.96
Death within 1 year (%)	7 (17.1)	3 (20.0)	0.80

Table 2. Outcomes of EUS-GBD, with comparison between those who underwent EUS-GBD-C *versus* EUS-GBD-NC

EUS-GBD: EUS-guided gallbladder drainage; NC: Noncholecystitis; C: Cholecystitis

There was a 100% technical success rate in all patients attempted within both groups, defined as successful LAMS deployment and visualization of biliary flow. There was a 13.3% rate of immediate complications among NC patients, which were due to postprocedural fever (n = 1) and persistent RUQ pain (n = 1); the patient with fever was medically managed, though the patient with persistent RUQ pain underwent ERCP with sphincterotomy on postprocedure day 3. There was a 14.6% rate of immediate complications among C patients (P = 0.90), including fevers (n = 1), undifferentiated shock (n = 1), persistent RUQ pain (n = 1), bacteremia (n = 1), microperforation of the stomach antrum (n = 1, managed endoscopically duringthe initial procedure), and bile peritonitis (n = 1). All complications were managed medically or endoscopically as above and did not require surgical intervention.

Over the 1-year follow-up period after the initial procedure, two NC patients were re-admitted with symptoms attributable to gallstone-related diseases: one with gallstone pancreatitis and one with recurrent malignant biliary obstruction (who was readmitted twice). There were five patients requiring readmission within the C group: four with recurrent biliary obstruction and cholangitis requiring multiple readmissions and one with stent-related bacteremia. There was no statistical difference in the number of readmissions for all purposes or among those readmitted for biliary disease [Table 2].

There were no late complications in the NC group, compared to an 10.0% rate of late complications in the C group (n = 4), due to stent occlusion (n = 1), internal stent migration (n = 1), bleeding (n = 1), and

procedure-related pancreatitis (n = 1, P = 0.22). There was a stent removal rate of 60% at an average of 43.3 days postprocedure in the NC group, compared to 39% at an average of 98 days postprocedure in the C group (P = 0.17 and P = 0.58, respectively). 20% of patients died within 1 year in both groups (P = 1.00). None of the deaths were procedure related. One patient in either group died during the same admission as their procedure. Neither of the deaths were directly related to stent-induced complications.

DISCUSSION

Although EUS-GBD is increasingly utilized for management of gallstone diseases in nonoperative candidates, studies evaluating its efficacy have focused primarily on the evaluation of its use in patients with acute cholecystitis. However, there is substantial potential for the role of EUS-GBD in NC gallbladder disease as well. This study demonstrates that EUS-GBD achieves good technical and immediate clinical success in those patients presenting with biliary colic, gallstone pancreatitis, and gallbladder obstruction secondary to malignancy or choledocholithiasis without signs or symptoms of cholecystitis. There was no difference in the primary outcomes, with broad technical success in both groups and similar clinical success with few immediate or late complications. Note that this technical success rate solely captures attempted cases, and any case where EUS-GBD was thought unpractical or dangerous (decompressed gallbladder, anatomical variations, etc.) was not captured based on our use of Provation procedural data to gather cases. Although no comparison of clinical success between the two groups was significant, it is notable that there were no late complications, such as stent migration

or occlusion, in the NC group. The rates of immediate and late complications in both groups were similar to those documented in previous studies.^[12-14,20,21]

Secondary outcomes including length of hospital admission, rates of readmissions (both for all indications and recurrent biliary disease), and stent removal rates were similar between the two groups. In all cases, stent removal was a planned procedure with removal of the LAMS and replacement with plastic pigtail stents per our institutional protocol, though it is unclear whether this is a necessary step in the average patient's care. Mortality in the NC group was primarily related to underlying disease (*i.e.*, malignancy). As EUS-GBD is emerging as an alternative to surgical gallbladder decompression in the setting of acute cholecystitis, these findings suggest that EUS-GBD can be considered as an alternative decompression method in patients with NC gallbladder or biliary disease.

These data demonstrate resolution of symptoms postprocedure in NC patients, with only one patient noting persistent postprocedural pain. However, there was a 13.3% rate of recurrent biliary disease within 1 year among NC patients. Although this was statistically similar to the C group, the C patients have inherent higher risk of recurrent biliary disease than the patient population undergoing NC drainage for secondary prevention. This is well established in the literature. Previous studies have documented a wide range of recurrent biliary disease after a variety of interventions for secondary prevention of gallstone-related disease.[12-15,21-26] Patients who have no endoscopic intervention or biliary sphincterotomy demonstrate rates of recurrent biliary disease ranging from 4% to 24%.[22-25] The 13.3% rate of recurrent biliary disease found in this study falls within this range, indicating that EUS-GBD alone does not eliminate future gallstone-related complications. This could be confounded by the lack of standardization for stone removal post-EUS-GBD. Thus, further prospective studies are needed to delineate the clinical role of NC.

The data in this study are limited by the relatively small number of cases that presented over the study period, particularly for the NC group. These numbers are similar to prior EUS-GBD studies for acute cholecystitis and speak to a greater need for study of EUS-GBD, in general, with multicenter prospective trials as possible. Small differences between NC versus C groups could thus escape the power of this study. With greater generalizability of EUS-GBD, the technique can be evaluated in more patient cases for all indications to provide more data on the technique's safety and efficacy. One challenge to comparing the two cohorts is the overlap between the two groups; for instance, a patient presenting without objective evidence of cholecystitis are occasionally empirically treated with antibiotics and would be stratified to the C group despite lack of infection.

EUS-GBD itself has several limitations in clinical practice, including requirement of a skilled endoscopic ultrasonographer, difficulty distending a typically contracted gallbladder in nonobstructive cases, difficulty puncturing a thick gallbladder wall, increased risk in patients with ascites, and difficulty deploying a stent in a patient with a large gallstone due to space constraints.^[25] Early studies suggest that technical success of EUS-GBD was lower in patients with benign diseases compared with malignant diseases, potentially due to less dilated ducts or lack of fixation to surrounding tissues.^[15] Our dataset examines cases of attempted EUS-GBD, and our search method may exclude patients with decompressed gallbladders or anatomical limitations to successful EUS-GBD; however, we demonstrate a high technical success rate in cases where LAMS deployment was attempted.

As EUS-GBD is incorporated into more gastroenterology training programs and with improvements in endoscopic and stenting materials, the technique can be used in more clinical scenarios. Early cost analysis studies have demonstrated less cost associated with EUS-GBD than PC,^[15,16] primarily due to high reintervention rates in PC patients. Larger studies are needed to better understand the cost-effectiveness of EUS-GBD. PC has been associated with higher adverse events than EUS-GBD, with risks of cholangitis, hemorrhage, and biloma higher than in EUS-GBD. There are quality-of-life considerations that need further study; external drains via PC are associated with lower quality of life at 12 weeks when compared with EUS drainage of the biliary tree.^[20] Furthermore, when the two procedures are explained to patients, more choose EUS-GBD than PC.^[20] The risks and limitations to the procedure itself must be considered on a patient-by-patient basis.

EUS-GBD remains an emerging treatment for gallbladder disease in nonoperative candidates. Our study is the first to demonstrate safety and technical success in NC cases. Our study also demonstrates some risk of recurrent gallbladder disease within 1 year despite EUS-GBD. A prospective study will be needed to better define this risk and the role of EUS-GBD in patients who are not operative candidates.

CONCLUSION

Outcomes of EUS-guided transluminal gallbladder drainage in patients without cholecystitis were similar to those in patients with infectious gallbladder disease.

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Conflicts of interest

There are no conflicts of interest.

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