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CASE REPORT

Novel Use of Long, Large-Caliber, Fenestrated Stents for Endoscopic Transpapillary Gallbladder Stenting for Therapy of Symptomatic Gallbladder Disease

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Introduction

Symptomatic gallbladder disease (SGBD) has a high prevalence in the general population, and early cholecystectomy is considered definitive therapy for patients with symptomatic cholelithiasis [1, 2]. Conservative therapy is recommended for those patients in whom surgery is contraindicated or considered high risk [3–5].

Nonsurgical gallbladder drainage methods include percutaneous and endoscopic drainage techniques [5]. While percutaneous transhepatic gallbladder catheter drainage (PCD) is efficacious, it has risks of puncture-related adverse events and tube dislodgement and results in significant patient discomfort [5, 6]. PCD is usually a temporary step until the patient is fit for surgery, symptoms resolve or drainage can be internalized by endoscopic transpapillary gallbladder stenting (ETGS) which involves placement of an internal transpapillary stent. ETGS has technical and clinical success rates comparable to PCD with the advantage of internal drainage; however, its limitations include the potential for stent migration or occlusion requiring stent exchange, cystic duct or gallbladder perforation, and recurrence of symptomatic biliary disease [5–10].

ETGS has been previously described mainly using rigid, double-pigtail polyethylene plastic stents of diameter 5–7 Fr and length 10–15 cm, with inherent limitations in drainage, flexibility, and patency [5–10]. Johlin pancreatic wedge stents (JS) (Wilson-Cook Medical, Winston-Salem, NC, USA) are made of Sof-Flex® material, which is a softer polyurethane and polyethylene blend. They are fenestrated with large, multi-side holes along the length of the stent and are available in 8.5 and 10 Fr diameters and variable lengths up to 22 cm (Fig. 1). JS for ETGS have theoretical advantages over conventional stents, including soft material with conformability to tortuous cystic ducts, the presence of side holes, and large caliber allowing potentially longer patency. We report our initial experience using JS for ETGS.

Patients and Methods

Fourteen patients presenting to a single tertiary referral center with symptomatic gallbladder disease, defined as the presence of acute cholecystitis or recurrent biliary symptoms and who were considered poor candidates for cholecystectomy and/or PCD, underwent ETGS using JS between December 2009 and October 2012. Inclusion criteria to be considered for ETGS included clinical and radiologic findings of SGBD. All patients were considered

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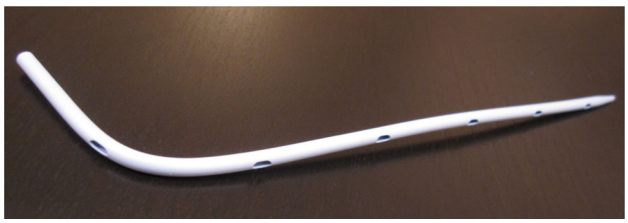

Fig. 1 Johlin pancreatic wedge stent (Wilson-Cook Medical Inc., Winston-Salem, NC, USA)

to be unfit for surgery and/or interventional radiology by those consult services. In one patient, ETGS was performed after a failed attempt at percutaneous catheter drainage. Comorbid conditions precluding surgery or a percutaneous approach included advanced liver disease, severe cardiopulmonary disease, comorbidities, metastatic cancer, presence of ascites, coagulopathy, and/or thrombocytopenia. There were no exclusion criteria. Technical success of ETGS was defined as the ability to successfully deploy the JS. Clinical response of ETGS was defined as complete resolution of the presenting clinical findings, such as abdominal pain and fever, along with laboratory improvement after successful JS placement. All adverse events (AE) were classified according to the consensus guidelines for ERCP [11]. Early AEs were defined as any procedure-related AEs occurring within 4 weeks of ETGS, and late AEs were defined as any JS-related AEs such as stent migration, occlusion, cholangitis, biliary pancreatitis, and recurrent biliary pain occurring 4 weeks post-procedure. A patent JS was assumed when there were no clinical symptoms or laboratory/radiologic evidence to indicate an AE such as cholangitis and cholecystitis. There was no scheduled stent exchange or removal however, JS exchange was performed if there was concern for stent occlusion. Stent occlusion was defined as development of abdominal pain, nausea/vomiting and/or fever with leukocytosis, and/or evidence of worsening LFTs. In the absence of these features, the stent was considered to be patent. If a patient was taken for repeat ERCP due to concerns for stent occlusion, the stent was evaluated for patency after endoscopic removal. Johlin stent patency time was defined as the interval between the time of ETGS and the time of stent exchange, cholecystectomy, death, or last follow-up. Approval for this study was obtained from the human studies committee.

ETGS Technique

All ERCP procedures were performed under general anesthesia. At ERCP, the bile duct was cannulated using standard techniques. Based on individual clinical parameters, biliary sphincterotomy, endoscopic papillary balloon dilation (EPBLD) or neither was performed. A small-caliber (4 or 5 Fr) pancreatic stent was placed for pancreatitis prophylaxis if pancreatic duct cannulation occurred or when balloon dilation of an intact biliary sphincter was performed. A balloon extraction catheter was used to obtain an occlusion cholangiogram to evaluate choledocholithiasis and to identify the cystic duct and gallbladder. Balloon sweep and stone extraction were done when choledocholithiasis was found. The cystic duct was cannulated with either a standard sphincterotome and wire or a bidirectional bending SwingTip cannula (Olympus Corp., Center Valley, PA, USA). If the above failed, SpyGlass (Boston Scientific, Natick, MA, USA) choledocoscopy was used to access the cystic duct. A guide wire, typically a 0.025-inch Visiglide (Olympus Corp., Center Valley, PA, USA), was advanced through the cystic duct and maneuvered deep into the gallbladder lumen. The access cannula was then advanced into the gallbladder, thereby dilating the cystic duct; if necessary, further dilation of the cystic duct was performed using a 4-mm Hurricane dilating balloon catheter (Boston Scientific, Matick, MA, USA). An 8.5- or 10-Fr JS was then placed as deeply into the gallbladder as possible, leaving 1–2 cm traversing the biliary orifice into the duodenal lumen (Figs. 2, 3). Additional gallbladder

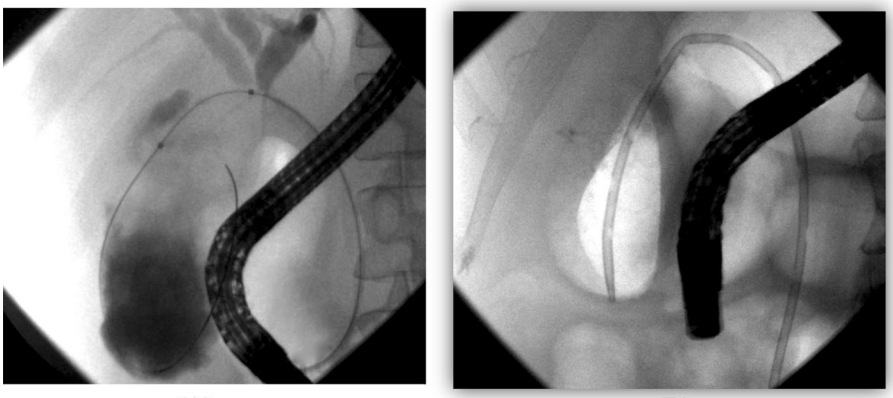

Fig. 2 **a** Cannulation of the gallbladder with wire looped within the gallbladder lumen, **b** 20 cm, 10-F Johlin stent placed in the gallbladder, with large multi-side holes clearly visible

(A) **(B)**

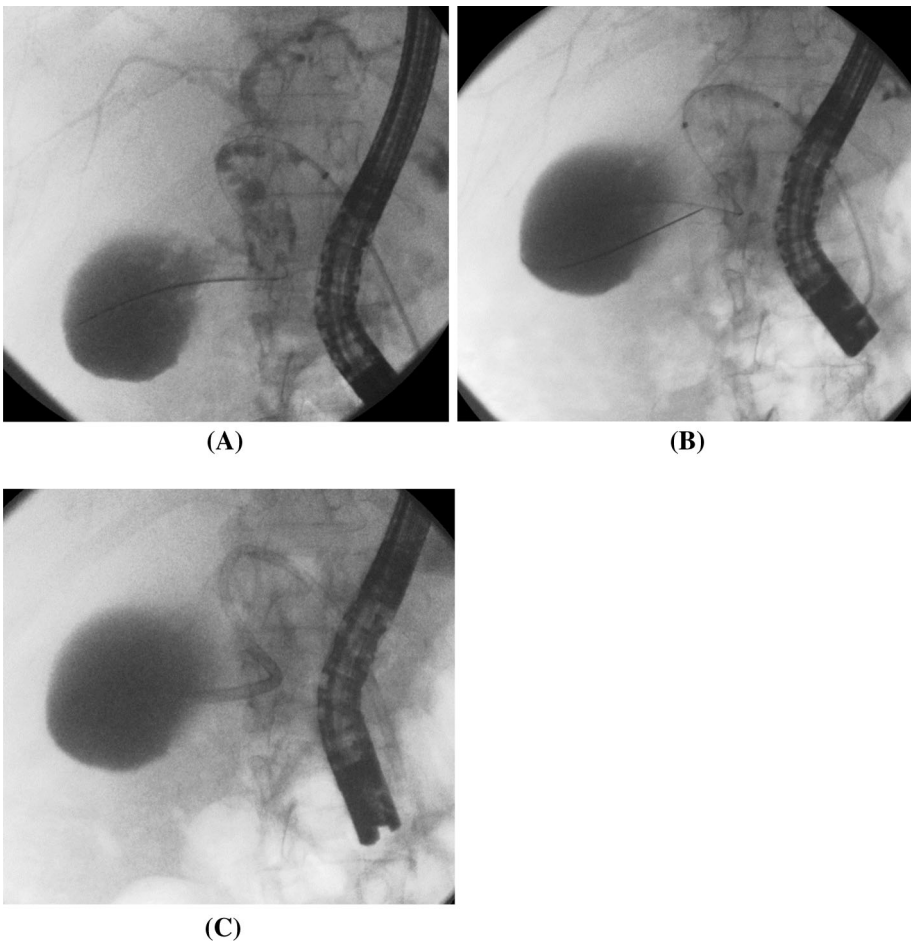

Fig. 3 **a** Balloon occlusion cholangiogram of a tortuous cystic duct, **b** Balloon dilation of the cystic duct with a 4-mm balloon dilation catheter, **c** Johlin stent placement into the gallbladder lumen with the stent following the contour of the tortuous cystic duct

lavage was performed in selected cases of suppurative cholecystitis through the stent deployment catheter system. Additional bile duct stents were placed when clinically indicated. All patients were treated with antibiotics after stent placement.

Results

Baseline demographics and clinical findings of patients who underwent ETGS are shown in Table 1. All patients except one were hospitalized at the time of their procedure, with 4 in the intensive care unit. Indications for gallbladder drainage were acute cholecystitis ($n = 13$) and recurrent biliary colic with choledocholithiasis ($n = 1$). Gallbladder stones were present in 11 patients. Comorbidities resulting in contraindication to cholecystectomy or PCD included end-stage liver disease ($n = 5$) with a mean Model for End-Stage Liver Disease (MELD) score of 34 (range 22–44), severe cardiopulmonary disease ($n = 4$), metastatic cancer ($n = 2$), post-bone marrow transplant with cytopenia ($n = 3$) and/or ascites ($n = 7$). Coagulopathy (INR > 1.5) was present in five patients and thrombocytopenia (plt $< 50{,}000$ μL) in three patients. PCD had previously failed in one patient prior to ETGS.

Procedural details for ETGS are summarized in Table 2. The median time from admission to endoscopic drainage for the 13 patients who were hospitalized was 2 days (range 1–12 days). Biliary sphincterotomy was performed in nine patients, and two had prior sphincterotomy. EPBLD was done in 1 patient with choledocholithiasis, suppurative cholecystitis, and MELD score of 35. One patient required SpyGlass choledocoscopy for access of the cystic duct. Cystic duct balloon dilation was performed in 3 patients. ETGS was technically successful in all 14 patients. JS were all 20 cm long and 8.5 Fr in 11 patients and 10 Fr in three patients. Gallbladder lavage was performed through the stent deployment catheter in three patients. This was done at the discretion of the endoscopist performing the procedure. Additional bile duct stents were placed in 4 patients and prophylactic pancreatic duct stents in eight patients.

All 14 patients had early clinical success of ETGS with improvement in clinical and laboratory and/or imaging parameters. None of the patients required PCD or urgent cholecystectomy (Table 3). There were no immediate JS-related AE, such as cystic duct perforation, stent occlusion

Table 1 Patient demographics and baseline characteristics

	ETGS
No. of patients	14
Sex, male/female	9/5
Age, median (range), years	53 (32–74)
Caucasian, *n* (%)	12 (86)
Body mass index (kg/m^2), median (range)	31.95 (16.26–42.98)
Comorbid conditions, *n* (%)	
End-stage liver disease	5 (36)
MELD, mean (range)	34 (22–44)
Severe cardiopulmonary disease	4 (29)
Metastatic cancer	2 (14)
Multiple comorbidities post-BMT	3 (21)
Ascites	7 (50)
Indications, *n* (%)	
Acute cholecystitis*	13 (93)
Recurrent symptomatic biliary disease after an initial ERCP	1 (7)
* after unsuccessful percutaneous drainage attempt in one patient	
Previous ERCP, *n* (%)	4 (29)
ETGS performed during acute hospitalization, *n* (%)	13 (93)
# in ICU, N	4
Laboratory findings at time of ETGS	
Coagulopathy (INR $\geq$ 1.5), *n* (%)	5 (36)
INR median (range)	2.03 (1.6–3.3)
Thrombocytopenia (Platelets $\leq$50), *n* (%)	3 (21)
Platelets, 10e9/L, median (range)	47 (46–49)

ETGS endoscopic transpapillary gallbladder stenting, *MELD* Model for End-Stage Liver Disease, *BMT* bone marrow transplant, *ERCP* endoscopic retrograde cholangiopancreatography, *ICU* intensive care unit

Table 2 Procedure details for endoscopic transpapillary gallbladder stenting

	n (%)
Technical successful ETGS with Johlin stent	14 (100)
8.5 Fr × 20 cm	11 (79)
10 Fr × 20 cm	3 (21)
Clinical successful ETGS with Johlin stent	14 (100)
Biliary sphincterotomy	9 (64)
Previous biliary sphincterotomy	2 (14)
Endoscopic papillary balloon dilation	1 (7)
Additional bile duct stent placed	4 (29)
Prophylactic pancreatic duct stent placed	8 (57)
Endoscopic cystic duct balloon dilation	3 (21)
Gallbladder lavage performed through stent	3 (21)

Table 3 Procedure outcomes of endoscopic transpapillary gallbladder stenting

	n (%)
Clinical successful ETGS with Johlin stent	14 (100)
Procedure-related adverse events, *n* (%)	
Post-ERCP pancreatitis	0
Post-sphincterotomy bleed	1 (7)
Cystic duct perforation	0
Cholangitis	0
Stent occlusion	0
Death	0
Delayed adverse events (>4 weeks), *n* (%)	
Stent occlusion	0
Distal migration of stent	0
Biliary pain, recurrent	0
Cholangitis	0
Biliary pancreatitis	0
Death	0
Gallbladder stent exchange, *n* (%)	2 (14)
Stent found to be occluded, *n*	0
Eventual cholecystectomy, *n* (%)	3 (21)
Time to cholecystectomy, median (range) days	43 (28–97)
Death from all-cause mortality, *n* (%)	6 (43)
Related to biliary disease	0
Sepsis	3
Multisystem organ failure	1
Fibrinolysis	1
Metastatic cancer	1
Stent present to date, *n* (%)	6 (43)
Duration of stent placement, median (range) days	242 (46–422)

or migration, and cholangitis. Additionally, there was no post-ERCP pancreatitis. The only early AE was that of post-sphincterotomy bleeding, occurring 2 days post-procedure, which was successfully treated by placement of a fully covered metal biliary stent across the major papilla, alongside the JS, for tamponade. Gallbladder stents were in place for a median of 94.5 days (range 12–422 days). Two patients underwent repeat ERCP for elevated LFTs; however, they were found to have patent gallbladder stents, with the etiology of their recurrent symptoms attributed to metastatic cancer and progressive liver disease.

Median follow-up was 242 days (range 46–422 days) with six patients still alive with JS in place. At the last patient follow-up, there were no cases of delayed AE, including stent occlusion and migration. Three patients underwent eventual cholecystectomy and JS removal after a median of 43 days (range 28–97 days) after stabilization of their cardiopulmonary disease, completion of chemotherapy and, in one case, as part of emergent surgery

for abdominal catastrophe related to surgical percutaneous gastrostomy tube placement. In the follow-up period, six patients died, including 1 patient that had cholecystectomy, at a mean of 76.5 days after ETGS, with no deaths related to biliary disease. The most common cause of death was attributed to sepsis from a nonbiliary source (bacterial peritonitis with subsequent multisystem organ failure in three patients with advanced cirrhosis and fibrinolysis syndrome resulting in one patient with advanced cirrhosis), acute respiratory failure in one patient with a hematologic malignancy post-bone marrow transplantation, and metastatic cancer in patient.

Discussion

Current nonsurgical treatment options for symptomatic gallbladder diseases center on drainage techniques [5]. PCD is the most widely established technique with technical success rates nearly 100 % and response rates 78–95 %, but associated with AEs in 0.3–12 % including hemorrhage, pneumothorax, bile peritonitis, inadvertent tube removal, and migration [5, 6]. Additionally, chronic indwelling percutaneous catheter are uncomfortable and are associated with a mortality rate as high as 17.5 % [6]. Severe coagulopathy, thrombocytopenia, and massive ascites are usually considered absolute contraindications, thereby excluding these patients from attempted PCD.

Endoscopic ultrasound (EUS)-guided transmural gallbladder drainage has been described in patients who are poor surgical candidates, most recently using a bi-flanged fully covered lumen apposing metal stent (LAMS) and one-step delivery system [12–15]. However, it requires expertise in interventional EUS and may be technically challenging due to difficult scope position and lack of a suitable transmural "window" for gallbladder access, with a potential for perforation and stent misdeployment. It is relatively contraindicated in patients with coagulopathy and ascites, and/or a gallbladder not adherent to the duodenal or gastric wall, which are often present in severely ill patients, with potential for catastrophic perforation and bile leakage. The role of a choledochoduodenostomy in patients who undergo subsequent cholecystectomy or liver transplantation is unknown, and concerns have been raised about additional need for closure of a duodenal fistula. There is also uncertainty about potential long-term complications, e.g., duodenal inflammation due to the LAMS, and whether stents should be left in place indefinitely or removed in patients in whom cholecystectomy is not anticipated in the future.

Although first reported more than 20 years ago, ETGS remains an important technique for poor surgical candidates [5–10]. In a pooled analysis of seven retrospective studies, the technical success rate of ETGS was 96 % with a pooled response rate of 88 %, compared to 80.9 % and 75.3 %, respectively, for endoscopic nasocystic gallbladder drainage (ENGBD) [6]. The benefits of ETGS include complete internal drainage with physiologic bile flow without the associated percutaneous puncture-related AE. Without a chronic indwelling catheter, there is improved patient acceptance and comfort [5–10].

Procedure-related AE, including post-ERCP pancreatitis, perforation of the cystic duct or gallbladder, cholangitis, and septic complications, have been reported in 0–14 % [7]. Potential disadvantages of ETGS, as previously described, include stent migration, occlusion, cystic duct or gallbladder perforation, and recurrence of symptomatic biliary disease. We hypothesized that the use of the Johlin stents might offer advantages over conventional polyethylene double-pigtail plastic stents. The JS is fenestrated with large, multi-side holes, thus offering numerous ports for drainage of not only the gallbladder, but also the bile duct. The softer polyurethane and polyethylene blend provides flexibility, which might decrease the risk of gallbladder and cystic duct perforation, and the extreme length and large caliber of the stent might reduce the risk of stent migration and occlusion. The stent is straight, allowing for relatively easy deployment compared to a double-pigtail design. Additionally, there is also the ability to lavage the gallbladder through the stent deployment catheter system, similar to that which can be done with ENGBD.

In our series, stents could always be placed. All patients had clinical evidence of gallbladder disease based on symptoms and imaging studies, including evidence of gallstones and/or a distended gallbladder. While cystic duct cannulation can be challenging in these settings, this was accomplished in all cases and was significantly facilitated with the use of a SwingTip cannula (Olympus Corp., Center Valley, PA, USA). There were no cases of stent occlusion, migration, or gallbladder or cystic duct injury. We did not schedule routine stent exchanges, but adopted a watchful waiting approach. At the last follow-up, 6 patients still had their original JS in place, with median stent longevity of 242 days. There are several possible explanations for the high patency rate associated with JS in this series. Firstly, since the stents are designed for use in the pancreatic duct, unlike polyethylene biliary stents, JS are fenestrated with large, multi-side holes along the length of the stent, thus offering numerous ports for drainage of not only the gallbladder but also the bile duct. Secondly, the stents are composed of a different material which may affect patency. Thirdly, patients typically did not have bile duct obstruction but rather cystic duct obstruction which tends to be focal and may resolve if edema resolves or an obstructing stone dislodges. Finally, in patients who had a

biliary sphincterotomy, there may be flow around the stent as well. There were 6 patient deaths, none of which were attributed to biliary disease.

In conclusion, ETGS using the JS appears to be a safe, effective, and feasible gallbladder drainage technique for patients with SGBD who are not surgical candidates due to severe comorbidity. ETGS with JS provides the option of a bridge to cholecystectomy as well as long-term therapy in patients at high risk of surgery and/or PCD.

Conflict of interest None of the authors have a conflict of interest to report.

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