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Original Article

Conversion of percutaneous cholecystostomy to transmural endoscopic ultrasound-guided gallbladder drainage in malignant biliary obstruction

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ABSTRACT

Background: In patients with distal malignant biliary obstruction, it is a challenge to manage acute cholecystitis secondary to cystic duct obstruction associated with tumor progression or stent compression. Percutaneous transhepatic gallbladder drainage (PTGBD) has been used as the treatment option of choice, because of its ease of performance and safety, but because of the use of an external drainage tube, some patients experience a decreased quality of life. We report the technical success and clinical success of conversion from PTGBD to endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) for the treatment of acute cholecystitis in patients with unresectable malignant biliary obstruction.

Methods: We included the patients with cholecystitis secondary to unresectable malignant biliary obstruction who underwent conversion from PTGBD to EUS-GBD in the study. After PTGBD for the treatment of acute cholecystitis, we performed EUS-GBD and a plastic stent or a self-expandable metal stent (SEMS) was placed for fistulostomy.

Results: Fourteen patients (median age, 69 years; 9 males and 5 females) underwent conversion to EUS-GBD after clinical improvement of cholecystitis by PTGBD. The technical success rate of the conversion from PTGBD to EUS-GBD was 100% (14/14). EUS-GBD was performed in a median of 9.5 days (range, 3–51 days) after PTGBD procedure, using mainly a plastic stent (13 patients) and a covered SEMS in one patient. The early (within 24 hours) adverse events rate was 14.3% (2/14), and the late (after 24 hours) adverse events rate was 7.1% (1/14). The rate of recurrence of cholecystitis was 28.6% (4/14). These patients underwent endoscopic re-intervention and there were no cases of further recurrence of cholecystitis.

Conclusion: Conversion of PTGBD to EUS-GBD demonstrated a feasible and safe technique for acute cholecystitis in non-surgical candidates with malignant biliary obstruction.

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Keywords: Cholecystitis; Endosonography; Fistula and drainage

Introduction

Acute cholecystitis refers to acute inflammation of the gallbladder, and usually manifests with abdominal pain, vomiting and fever. Severe acute cholecystitis can lead to life-threatening conditions such as gangrene and empyema of the gallbladder. The major predisposing factors to acute cholecystitis include gallstones or some ERCP-related procedures, malignant cystic obstruction, critical illnesses, ischemia, due to surgery, trans-arterial embolization, and total parental nutrition.^{1–5} According to

the Tokyo 13 guideline of acute cholecystitis, surgical cholecystectomy is recommended as the therapeutic option of first choice for cases with mild to moderate acute cholecystitis.⁶ Percutaneous transhepatic gallbladder drainage (PTGBD) or endoscopic drainage are the recommended therapeutic options for patients with severe cholecystitis or advanced-stage cancer, and also for high-risk surgical candidates, such as those with multiple comorbidities.⁷ PTGBD has been used as the treatment option of choice, because of its ease of performance and safety, but because of the use of an external drainage tube, some patients experience pain, discomfort,

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cosmetic disfigurement, and a decreased quality of life.

Endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) has recently been reported as an emerging therapeutic option for gallbladder drainage. Kwan et al⁸ first reported performing EUS-GBD for three patients with advanced malignancy presenting with severe acute cholecystitis. Since then, a number of studies have shown the clinical safety and efficacy of EUS-GBD using a transluminal stent for acute cholecystitis.⁹

In patients with distal malignant biliary obstruction, it is a challenge to manage acute cholecystitis secondary to cystic duct obstruction associated with tumor progression or stent compression by transpapillary self-expandable metal stent (SEMS) placement. As acute cholecystitis requires urgent drainage in patients with unresectable malignancy, we initially prefer to perform PTGBD as an external drainage, because it is a quick, simple and easy procedure with few complications. PTGBD improves acute cholecystitis with a favorable response rate, but after removal of the external tube, the cholecystitis sometimes flares up, necessitating repeat PTGBD. For this reason, after clinical resolution of cholecystitis following PTGBD, we often proceed to EUS-GBD as an internal drainage method and then remove the PTGBD tube. Only a few studies of conversion of PTGBD to EUS-GBD have been performed,^{10,11} and all have shown favorable technical success rates and low complication rates in patients with acute calculous cholecystitis. However, the clinical efficacy and safety of this technique is still uncertain for acute cholecystitis in patients with unresectable malignant biliary obstruction. We report the clinical usefulness of conversion from PTGBD to EUS-GBD for the treatment of acute cholecystitis in patients with unresectable malignant biliary obstruction. Our study was aimed at evaluating the efficacy and safety of conversion of PTGBD to EUS-GBD for the treatment of acute cholecystitis in patients with malignant biliary obstruction.

Methods

Patients and aims

Between April 2015 and April 2018, 14 cholecystitis patients with unresectable malignant biliary obstruction underwent conversion from PTGBD to EUS-GBD at National Cancer Center Hospital East (Kashiwa, Japan). The patients' medical records and endoscopy reports were retrospectively reviewed in terms of the procedural details, technical success, clinical course, follow-up period, complications and re-intervention. The main outcome of the study was to assess technical success and clinical success of conversion from PTGBD to EUS-GBD.

Our institutional review board approved the retrospective study and the patients' records.

Technical aspects

EUS-GBD was performed by one expert endoscopist (Y.H.) and experienced trainees under supervision after the informed consent. An oblique-viewing therapeutic curvilinear array echoendoscope, GF-UCT260 (Olympus Medical System, Tokyo, Japan) was used for the procedures with EU-ME1 (Olympus Medical System) as the ultrasound apparatus. After the patients were sedated with intravenous midazolam and pethidine hydrochloride and given intravenous antibiotics, the echoendoscope was introduced and positioned in the gastric antrum or the duodenal bulb to identify the gallbladder. Normal saline was injected through the PTGBD tube into the gallbladder, to facilitate visualization of the gallbladder. A standard 19-gauge fine-needle aspiration needle (Expect; Boston Scientific, Natick, MA, USA) was used to puncture the gallbladder wall. After injecting contrast into the gallbladder, a 0.025-inch or 0.035-inch guidewire (VisiGlide2 [Olympus Medical System] or Jagwire [Boston Scientific]) was inserted through the needle and coiled in the gallbladder. A fistula was created between the luminal wall of the stomach or duodenum and gallbladder using a 6-Fr coaxial electric cautery cystotome (Cysto-gastro-set; ENDO-FLEX, Voerde, Germany), and in some cases, additional dilatation with a 4 to 6 mm balloon dilator was performed to facilitate stent placement. Finally, an indwelling straight plastic stent, a double pig-tail plastic stent or a SEMS was placed for fistulostomy. After the function of the internal tube was checked by injection of contrast into the gallbladder, we removed the external PTGBD tube a few days or a week after the EUS-GBD to secure the internal drainage of it. The conversion procedure from PTGBD to EUS-GBD is demonstrated in Fig. 1.

Results

A total of 14 patients underwent conversion to EUS-GBD after clinical improvement of cholecystitis by PTGBD. The baseline characteristics of the patients are shown in Table 1. The median age of the patients was 69 years old (range, 32–83). There were 9 males (64.3%) and 5 females (35.7%). The primary underlying disease was hilar cholangiocarcinoma in 6 patients, pancreatic cancer in 4 patients, distal cholangiocarcinoma in 1 patient, intrahepatic cholangiocarcinoma in 1 patient, gallbladder cancer in 1 patient, and rectal cancer with multiple liver metastases and periportal adenopathy in 1 patient. Imaging revealed direct tumor invasion of the cystic duct in 2 patients (14.3%), prior placement

Fig. 1. The procedure of conversion from percutaneous transhepatic gallbladder drainage (PTGBD). The gallbladder was collapsed by PTGBD (A) and filled by injection of normal saline (B). (C) The guidewire was coiled inside the gallbladder. (D) After a fistula was created between the luminal wall of the stomach or duodenum and the gallbladder with a 6-Fr cauterizing cystotome, a double pigtail stent was inserted.

Table 1 Baseline Characteristics

Patient no.	Age (yr)	Sex	Primary disease	Etiology of cholecystitis	Gallstone	Interval to EUS-GBD from the onset of cholecystitis (day)	Interval to EUS-GBD from the start of PTGBD (day)
1	32	M	Rectal cancer with multiple liver metastases and periportal adenopathy	After SEMS placement	–	36	34
2	74	M	Intrahepatic cholangiocarcinoma	Calculous cholecystitis	+	51	51
3	80	F	Hilar cholangiocarcinoma	After SEMS placement	–	21	7
4	74	M	Hilar cholangiocarcinoma	Direct invasion of the cystic duct by the tumor	–	27	26
5	63	M	Hilar cholangiocarcinoma	After SEMS placement	+	9	8
6	80	M	Hilar cholangiocarcinoma	After SEMS placement	–	37	3
7	67	F	Hilar cholangiocarcinoma	After SEMS placement	–	50	46
8	79	M	Distal cholangiocarcinoma	Direct invasion of the cystic duct by the tumor	–	26	19
9	69	F	Pancreatic cancer	After SEMS placement	–	11	11
10	82	F	Pancreatic cancer	After SEMS placement	+	6	3
11	68	M	Pancreatic cancer	After SEMS placement	–	4	4
12	83	M	Pancreatic cancer	Calculous cholecystitis	+	6	4
13	69	M	Gallbladder cancer	After SEMS placement	+	8	6
14	69	F	Hilar cholangiocarcinoma	Calculous cholecystitis	+	22	19

M, male; F, female; SEMS, self-expandable metal stent; EUS-GBD, endoscopic ultrasound-guided gallbladder drainage; PTGBD, percutaneous transhepatic gallbladder drainage.

Table 2 The Procedure Description and the Adverse Events

Patient no.	Procedure time (min)	Stent type	Adverse event	Recurrence of cholecystitis	Mean duration of follow-up (mo)
1	49	Plastic stent (straight type)	None	None	1.6
2	48	Plastic stent (straight type)	None	None	6.2
3	26	Plastic stent (double pigtail type)	None	None	10.9
4	21	Plastic stent (straight type)	None	None	6.9
5	24	Plastic stent (straight type)	None	None	3.5
6	16	Plastic stent (straight type)	None	None	6.1
7	59	Plastic stent (straight type)	Bleeding	Day 14 from EUS-GBD (migration)	6.7
8	42	Plastic stent (double pigtail type)	Bile leak	None	0.3
9	23	Covered SEMS 7-Fr ENBD	None	None	0.9
10	15	Plastic stent (double pigtail type)	None	Day 68 from EUS-GBD (clogging tube stent)	2.8
11	20	Plastic stent (straight type)	None	None	2.7
12	15	Plastic stent (double pigtail type)	None	Day 6 from EUS-GBD (clogging tube stent)	2.0
13	27	Plastic stent (double pigtail type)	Bile leak	Day 1 from EUS-GBD (clogging tube stent)	2.0
14	44	Plastic stent (double pigtail type)	None	None	2.0

SEMS, self-expandable metal stent; ENBD, endoscopic nasobiliary drainage; EUS-GBD, endoscopic ultrasound-guided gallbladder drainage.

of SEMS in 9 patients (64.3%), and gallstones in 6 patients (42.9%). The procedure and the complications are shown in Table 2. The technical success rate of the conversion from PTGBD to EUS-GBD was 100% (14/14). EUS-GBD was performed a mean of 21.5 days (range, 4–51 days) after the onset of cholecystitis, and a mean of 9.5 days (range, 3–51 days) after the start of PTGBD. The stent type used was mainly a plastic stent (13 patients) and a covered SEMS in 1 patient. The median procedure time for EUS-GBD was 25 minutes (range, 15–59 minutes). In regard to the complications, the early (within 24 hours) adverse events rate was 14.3%

(2/14), with bile leak in 1 patient and bleeding in 1 patient. The late (after 24 hours) adverse events rate was 7.1% (1/14), with stent migration in 1 patient. The rate of recurrence of cholecystitis was 28.6% (4/14), caused by stent migration in 1 patient and inadequate drainage due to a clogged tube stent in 3 patients. One patient with stent migration developed recurrent cholecystitis at 14 days after EUS-GBD; the EUS-GBD was successfully repeated, and subsequently functioned well, with no further recurrence. Three patients with a clogged tube stent developed relapse of cholecystitis on 1, 6 and 68 days, respectively, after EUS-GBD. In

Fig. 2. The re-intervention for clogged plastic stent. An indwelling clogged double pigtail stent was placed through the duodenum into the gallbladder. The guidewire was coiled inside the gallbladder beside the stent (A) and a fully-covered self-expandable metal stent was inserted through the cholecystoduodenal fistula alongside the indwelling plastic stent (B, C).

cases of endoscopic reintervention, the plastic stent was removed and exchanged with a covered SEMS (cSEMS), or a cSEMS was placed alongside the indwelling plastic stent (Fig. 2). There were no cases of further recurrence of cholecystitis. The PTGBD tubes were finally removed in 13 patients (92.9%) in a median of 14 days (range, 2–61 days) after PTGBD procedure and in a median of 4.5 days (range, 2–15 days) after EUS-GBD. We did not remove the clamped PTGBD tube in only one patient because the patient died of the primary disease in rapid progression, although the clinical success rate was 100% (14/14) because all the patients of our study finally achieved internal drainage by EUS-GBD.

Discussion

PTGBD is often selected as the initial procedure for acute cholecystitis, in particular, for emergency cases. Removal of a PTGBD tube often results in a flare-up of cholecystitis, especially in cases with cystic duct obstruction caused by an indwelling biliary SEMS or tumor invasion. EUS-GBD is an interventional EUS-guided procedure for internal gallbladder drainage. Internal drainage provides a better quality of life to patients, both in terms of esthetics and ease of tube management, than PTGBD in the long term. One meta-analysis revealed that the technical and clinical success rates of EUS-GBD were equivalent to those of PTGBD, whereas the frequency of adverse events, pain score, and re-intervention rate were lower than those of PTGBD.¹² This meta-analysis study suggested that EUS-GBD is advantageous over PTGBD for the treatment of acute cholecystitis. However, the incidence of peritonitis from bile leak as an adverse event is reported to be higher in the case of EUS-GBD. Conversion of PTGBD to EUS-GBD may minimize the risk of leak of infectious bile, because the bile juice is initially drained by PTGBD and cleared by the time of EUS-GBD. In our study, the technical success rate of conversion of PTGBD to EUS-GBD was high (100%) with the low incidence of uneventful adverse events and the clinical success rate was also high (100%) by finally internalized gallbladder drainage. These results suggest that conversion of PTGBD to EUS-GBD is both feasible and safe in patients with malignant biliary obstruction.

It will improve the clinical outcomes if we address some technical points in this conversion procedure. The first is in regard to the choice of internal stent. Our results showed that a plastic tube is sufficient for complete drainage of purulent fluid as initial stent, because recurrence of cholecystitis due to stent dysfunction was observed in only 3 patients (21.4%), all of which had gallstones or gallbladder sludge predisposing to the relapse of cholecystitis. Taking it into consideration, cSEMS may be a better choice than a plastic tube in the presence of gallstones or gallbladder sludge. Recent preliminary studies of EUS-GBD showed favorable efficacy and safety of lumen-apposing metal stents (LAMS's),^{13,14} but trials of LAMS's are still ongoing and these stents are still not approved in Japan. Especially in emergent situations, PTGBD provides bet-

ter accessibility to acute treatment of cholecystitis than EUS-guided treatment because of limited EUS-guided intervention experts, although EUS-guided gallbladder drainage directly enabled an internal drainage. Therefore, we routinely adopt conversion from PTGBD to EUS-GBD using an inexpensive plastic tube as the initial internal stent. The second point is the optimal timing of the conversion. Excessively early conversion is considered not safe, because it takes several days to drain by PTGBD and resolve infection with antibiotic treatment. On the other hand, excessively late conversion would also seem to be disadvantageous, because the gallbladder wall can become thickened and stiff with the development of chronic cholecystitis by repeated external tube clogging in the long-term PTGBD management, which makes more difficult to perform endoscopic intervention. Although there is no clear evidence yet, we think that best timing of conversion may be 1 to 2 weeks from onset of cholecystitis. The third point is for endoscopic reintervention. In our present study, 4 patients needed endoscopic re-intervention. Clogging stent led to recurrent cholecystitis. Reintervention was performed mainly by adding or exchanging a stent. Exchanging a stent from plastic tube to cSEMS was successful over the short term, with no further recurrence of cholecystitis during the follow-up after endoscopic reintervention.

There were some limitations of our study. First of all, it was a retrospective study with a small number of cases, although the clinical outcomes were satisfactory, with no necessity for percutaneous drainage over the short term. Second, we adopted this conversion technique particularly for patients with malignant biliary obstruction. We are still not certain whether this technique is feasible and safe over the long term in patients with acute calculus cholecystitis unrelated to malignant biliary obstruction. We obtained favorable results, even in patients with unresectable malignant biliary obstruction. Thirdly, we successfully performed EUS-GBD using an inexpensive plastic stent in 64.3% of patients (9/14). cSEMS are more expensive than plastic tubes, but may preclude the need for re-intervention, because it is a widely opened stent that allows more effective drainage. We have no data on the benefits of cSEMS over a plastic stent.

In conclusion, conversion of PTGBD to EUS-GBD was demonstrated to be a feasible and safe procedure for non-surgical candidates with malignant biliary obstruction. Endoscopic reintervention was performed successfully with no further requirement for percutaneous drainage during the follow-up. Further study is awaited to determine if such conversion to EUS-GBD could be the treatment strategy of first choice for patients with acute cholecystitis.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Isayama H, Kawabe T, Nakai Y, Tsujino T, Sasahira N, Yamamoto N, et al. Cholecystitis after metallic stent placement in patients with malignant distal biliary obstruction. *Clin Gastroenterol Hepatol*. 2006;4:1148-53.
2. Miyayama S, Yamashiro M, Takeda T, Aburano H, Komatsu T, Sanada T, et al. Acute cholecystitis caused by malignant cystic duct obstruction: treatment with metallic stent placement. *Cardiovasc Intervent Radiol*. 2008;31 Suppl 2:S221-6.
3. Laurila J, Syrjälä H, Laurila PA, Saarnio J, Ala-Kokko TI. Acute acalculous cholecystitis in critically ill patients. *Acta Anaesthesiol Scand*. 2004;48:986-91.
4. Hagino RT, Valentine RJ, Clagett GP. Acalculous cholecystitis after aortic reconstruction. *J Am Coll Surg*. 1997;184:245-8.
5. Hatada T, Kobayashi H, Tanigawa A, Fujiwara Y, Hanada Y, Yamamura T. Acute acalculous cholecystitis in a patient on total parenteral nutrition: case report and review of the Japanese literature. *Hepatogastroenterology*. 1999;46:2208-11.
6. Miura F, Takada T, Strasberg SM, Solomkin JS, Pitt HA, Gouma DJ, et al. TG13 flowchart for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci*. 2013;20:47-54.
7. Tsuyuguchi T, Itoi T, Takada T, Strasberg SM, Pitt HA, Kim MH, et al. TG13 indications and techniques for gallbladder drainage in acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci*. 2013;20:81-8.
8. Kwan V, Eisendrath P, Antaki F, Le Moine O, Devière J. EUS-guided cholecystenterostomy: a new technique (with videos). *Gastrointest Endosc*. 2007;66:582-6.
9. Widmer J, Singhal S, Gaidhane M, Kahaleh M. Endoscopic ultrasound-guided endoluminal drainage of the gallbladder. *Dig Endosc*. 2014;26:525-31.
10. Law R, Grimm IS, Stavas JM, Baron TH. Conversion of percutaneous cholecystostomy to internal transmural gallbladder drainage using an endoscopic ultrasound-guided, lumen-apposing metal stent. *Clin Gastroenterol Hepatol*. 2016;14:476-80.
11. Chantarojanasiri T, Matsubara S, Isayama H, Nakai Y, Takahara N, Mizuno S, et al. Feasibility of conversion of percutaneous cholecystostomy to internal transmural endoscopic ultrasound-guided gallbladder drainage. *Saudi J Gastroenterol*. 2017;23:318-22.
12. Ahmed O, Rogers AC, Bolger JC, Mastrosimone A, Lee MJ, Keeling AN, et al. Meta-analysis of outcomes of endoscopic ultrasound-guided gallbladder drainage versus percutaneous cholecystostomy for the management of acute cholecystitis. *Surg Endosc*. 2018;32:1627-35.
13. Jain D, Bhandari BS, Agrawal N, Singhal S. Endoscopic ultrasound-guided gallbladder drainage using a lumen-apposing metal stent for acute cholecystitis: a systematic review. *Clin Endosc*. 2018;51:450-62.
14. Manta R, Mutignani M, Galloro G, Conigliaro R, Zullo A. Endoscopic ultrasound-guided gallbladder drainage for acute cholecystitis with a lumen-apposing metal stent: a systematic review of case series. *Eur J Gastroenterol Hepatol*. 2018;30:695-8.

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