—Original Article—

Urgent and early EUS-guided biliary drainage in patients with acute cholangitis

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ABSTRACT

Background and Objectives: EUS-guided biliary drainage (EUS-BD) has been reported as an effective alternative drainage technique. However, clinical data on EUS-BD for patients with acute cholangitis (AC) are limited. The aim of this study was to analyze the clinical outcomes of EUS-BD in patients with AC. **Patients and Methods:** Nineteen patients with AC who underwent urgent or early drainage (within 96 h) by EUS-guided hepaticoenterostomy (EUS-HES) between January 2014 and November 2019 were retrospectively reviewed. Furthermore, the clinical outcomes of EUS-HES using a plastic stent in the AC group ($n = 15$) were compared to those in the non-AC group ($n = 88$). **Results:** In the 19 AC cases, the technical and clinical success rate was 100% with 5.3% of moderate adverse events (biliary peritonitis [$n = 1$]). Regarding the comparison between the AC group and the non-AC group, the clinical success rate was 100% in both groups and the adverse event rate was not statistically significantly different ($P = 0.88$). Although the recurrent biliary obstruction (RBO) rate was not statistically significantly different ($P = 0.43$), the early RBO rate was statistically significantly higher in the AC group (26.7% *vs.* 3.4%, $P < 0.001$). Kaplan–Meier curves showed that AC was associated with a shorter time to RBO ($P = 0.046$). The presence of AC was found to be an independent risk factor of early RBO (odds ratio = 10.3; $P = 0.005$). **Conclusions:** Urgent or early biliary drainage (within 96 h) by EUS-BD can be a feasible and safe alternative procedure for patients with AC, although there is a tendency of early RBO.

Key words: acute cholangitis, endoscopic biliary drainage, EUS-guided, EUS-guided biliary drainage, hepaticoenterostomy, plastic stent

INTRODUCTION

Urgent or early biliary drainage (BD) is required for patients with acute cholangitis (AC), particularly for those with moderate or severe AC according to the updated Tokyo Guidelines of 2018 (TG18).[1] Endoscopic transpapillary BD (EBD) is recommended as the first-line drainage procedure.[2] However, EBD cannot be performed in patients with an inaccessible papilla owing to gastrointestinal tract obstruction or a surgically altered anatomy. Recently, EUS-BD was reported as a useful alternative drainage technique

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in such patients.[3,4] According to TG18, EUS-BD is recommended as an alternative drainage technique for AC, together with percutaneous transhepatic BD.[1] However, the majority of patients included in the reports of EUS-BD had obstructive jaundice without AC, and hence there is limited data regarding EUS-BD for AC. Herein, we retrospectively analyzed the clinical outcomes of EUS-BD in patients with AC, and compared them to the outcomes of patients without AC.

PATIENTS AND METHODS

Patients

This was a retrospective study conducted at Tokyo Medical University Hospital. EUS-BD was attempted in 198 patients for benign biliary diseases or malignant biliary obstruction, between January 2014 and November 2019. A flowchart of the EUS-BD procedures is shown in Figure 1. Among the 198 patients, 19 patients (9.6%) had a suspected or definite diagnosis of AC, which was diagnosed in accordance with the diagnostic criteria of TG18.[5] Briefly, a definite diagnosis of AC was made by the presence of systemic inflammation, cholestasis, and imaging findings, and AC was suspected upon the presence of systemic inflammation, and either the presence of cholestasis or imaging findings.

All 19 consecutive patients with AC (median age: 69 years) who underwent urgent (within 24 h after the onset of AC, n = 8) or early BD (within 24 h–96 h after the onset of AC, n = 11) by EUS-BD were retrospectively investigated in detail. Regarding the EUS-BD technique, EUS-guided hepaticoenterosotomy (EUS-HES; hepaticogastrostomy [HGS] or hepaticojejunostomy [HJS]) was performed in 17 patients and EUS-guided antegrade stenting combined with EUS-HGS (EUS-AGS with HGS) was performed in two patients. Clinical characteristics of the patients are shown in Table 1. Primary biliary diseases were benign biliary diseases in 6 patients and malignant biliary obstruction in 13 patients, in whom transpapillary drainage was not possible owing to duodenal stricture (n = 11) or balloon-enteroscopy-assisted endoscopic retrograde cholangiopancreatography (ERCP) failed due to surgically altered anatomy (n = 8). In 11 patients with duodenal stricture, duodenal stricture was managed by duodenal stent placement (n = 5), surgical gastrojejunostomy (n = 4), EUS-guided gastrojejunostomy (n = 1), and conservative management (n = 1). The severity of AC was evaluated in three grades (mild, moderate, and severe) in accordance with the severity assessment criteria of TG18.[5] Eighteen patients had mild or moderate cholangitis, and only one patient had severe cholangitis that was associated with hematological dysfunction, defined as a platelet count of <100,000/mm^3. None of the patients had cardiovascular dysfunction, respiratory dysfunction, and renal dysfunction.

Written informed consent was obtained from all the patients. This retrospective study was approved by our institutional review board (No. T2019-0231).

Endoscopic procedures

EUS-BD procedures were performed by one expert (T.I., with experience of more than 100 EUS-BD procedures) or three trainees (SM, TT, and RT). All patients received intravenous antibiotic treatment before

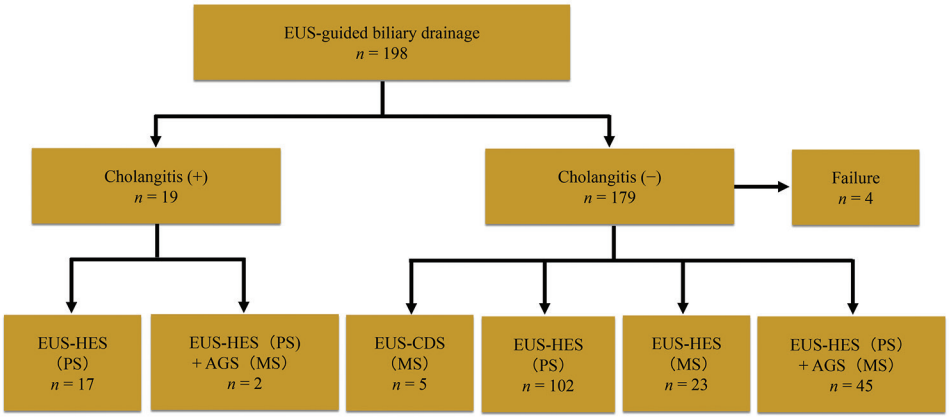

Figure 1. Flowchart of the EUS-BD procedures performed in this study. EUS-HES: EUS-guided hepaticoenterostomy; AGS: Antegrade stenting; EUS-CDS: EUS-guided choledochoduodenostomy; PS: Plastic stent; MS: Metal stent

Table 1. Clinical characteristics of patients with acute cholangitis

	Patients (*n*=19)
Median age, years (range)	69 (33-83)
Gender (male/female)	7/12
Primary biliary disease	
Benign (*n*=6)	
Common bile duct stones after gastrectomy by Roux-en-Y	2
Anastomotic stricture after hepaticojejunostomy by Roux-en-Y	2
Anastomotic stricture complicated by stones after hepaticojejunostomy by Roux-en-Y	2
Malignant (*n*=13)	
Pancreatic cancer	3
Bile duct cancer	2
Ampullary cancer	4
Gastric cancer	1
Gallbladder cancer	2
Cervical cancer	1
Causes of ERCP failure	
Duodenal stricture	11
Surgically altered anatomy	8
Timing of EUS-BD from the onset of cholangitis	
Urgent drainage <24 h	8
Early drainage	
24 h-48 h	5
48 h-72 h	3
72 h-96 h	3
Severity of acute cholangitis (mild/moderate/severe)	6/12/1
Cardiovascular dysfunction[§]	0
Respiratory dysfunction[§§]	0
Renal dysfunction[§§§]	0
Hematological dysfunction[§§§§] (%)	1 (5.3)
Fever, ºC, mean±SD	38.4±0.8
Laboratory data, mean±SD	
WBC (/μL)	10,732±3396
CRP (mg/L)	13.5±6.9
Total bilirubin (mg/dL)	4.6±3.1
AST (IU/L)	143±119
ALT (IU/L)	111±70
ALP (IU/L)	1523±739
γ-GTP (IU/L)	523±285

[§]Hypotension requiring dopamin ≥5 μg/kg per min, or any dose of norepinephrine, [§§]PaO_2/FiO_2 ratio <300, §§§Serum creatinine level >2.0 mg/dL, [§§§§]Platelet count <100,000/mm^3. WBC: White blood cell; CRP: C-reactive protein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; γ-GTP: γ-glutamyl transpeptidase; SD: Standard deviation

EUS-BD and intravenous hydrocortisone (300 mg) to prevent cholangiovenous reflux. We tried to finish the procedures in as short a time as possible to prevent leakage of infected bile juice into the abdominal cavity.

A standard 19G or 22G needle was advanced into the bile duct under echoendoscope visualization. A small amount of contrast medium was injected into the bile duct without increasing the pressure of the bile duct, to prevent cholangiovenous reflux causing bacteremia. After an insulated stiff guidewire (0.025-inch VisiGlide; Olympus Medical Systems, Tokyo, Japan for a 19G needle or 0.018-inch NovaGold; Boston Scientific, Natick, MA for a 22G needle) was advanced, and the needle tract was dilated using an ultra-tapered mechanical dilator (7-Fr diameter, ES dilator DC7R180S; Zeon Medical Co., Ltd., Tokyo, Japan), the tip of which was tapered to a 2.5-Fr diameter. When it failed due to the rigid wall of the bile duct, a cautery dilator or a dilating balloon was used for tract dilation. When a 0.018-inch guidewire was used, it was exchanged for a 0.025-inch guidewire after catheter advancement. After tract dilation, a single-pigtail plastic stent dedicated for EUS-HES (7-Fr or 8-Fr in diameter; Gadelius Medical Co., Ltd., Tokyo, Japan) was placed. If the guidewire could be easily advanced through the stricture to the duodenum in patients with malignant biliary obstruction, EUS-AGS with HES was performed

using an uncovered self-expandable metal stent for antegrade stenting and a dedicated plastic stent for EUS-HES, as described in our previous report.[6]

Outcome measures

The technical and clinical success rate, procedure-associated adverse event rate, 7-day mortality, and clinical outcomes including recurrent biliary obstruction (RBO) rate, early RBO rate, time to RBO (TRBO), and period of follow-up were calculated. Technical success was defined as successful stent placement in the hepatoenteric tract. Clinical success was determined by whether symptoms of AC and inflammatory findings, obstructive jaundice, liver dysfunction from laboratory data were improved at 7 days after BD. Procedure-associated adverse events were graded in accordance with the severity grading system.[7] This study was divided into two periods, the early period, from January 2014 to December 2016, and the late period, from January 2017 to November 2019 because of technical advancement. RBO was defined as recurrence of cholangitis or obstructive jaundice. Early RBO was defined as RBO occurrence within 4 weeks after EUS-BD. TRBO was defined as the duration from stent placement to the occurrence of RBO. Period of follow-up was set in the duration from stent placement to the occurrence of RBO, planned additional procedures via hepaticoenterostomy for benign biliary diseases, or patient death.

Comparison between EUS-BD with acute cholangitis and without acute cholangitis

To further analyze the feasibility and safety of EUS-BD for AC, the clinical outcomes of EUS-HES using a dedicated plastic stent in patients with AC were compared to those without AC. To compare the clinical outcomes accurately, cases of EUS-AGS with HES and cases of early death, in which patients had died within 30 days owing to the progression of malignant disease, were excluded. Thus, the clinical outcomes of 15 cases in the AC group (9 malignant and 6 benign cases) were retrospectively compared to those of 88 cases in the non-AC group (53 malignant and 35 benign cases). Clinical outcomes including the clinical success rate, procedure-associated adverse event rate, RBO rate, TRBO, and early RBO rate were compared.

Statistical analysis

Continuous variables were presented as means ± standard deviation or median with range and were compared using the Student's *t*-test or the Wilcoxon rank-sum test as appropriate. Categorical variables were compared using the Chi-squared or Fisher's exact test. Statistical analyses were performed using Statistical Package for the Social Sciences software version 26 (IBM, Chicago, IL, USA). Comparison of TRBO was performed using the Kaplan–Meier product-limit method. Kaplan–Meier curves were compared using the log–rank test and patients who were lost to follow-up or underwent planned additional antegrade intervention for benign diseases before RBO and died without RBO were dealt as censored cases. Predictive factors for the onset of early RBO were analyzed by logistic regression analysis to adjust for age and gender. $P < 0.05$ was considered to indicate a statistically significant difference.

RESULTS

The details and outcomes of EUS-BD for the 19 patients with AC are shown in Table 2. Puncturing of the intrahepatic bile duct, of which the median size was 4.5 mm, was successful in all patients. The needle tract was dilated using an ultra-tapered mechanical dilator in 17 patients. In two patients in the early period, a cautery dilator or a 4-mm balloon catheter was used because an ultra-tapered mechanical dilator was not available. Dedicated plastic stent placement was successful in all patients (19/19, 100%), with a median procedure time of 9 min (range: 6–17 min). In two patients, AGS across the malignant biliary stricture was performed using an uncovered metal stent because guidewire manipulation was performed easily and successfully. Symptoms and inflammation for AC immediately improved within 7 days, and clinical success was achieved in all patients (19/19, 100%). Regarding procedure-associated adverse events, moderate biliary peritonitis with symptoms of fever and abdominal pain was observed in one patient (1/19, 5.3%), which was managed conservatively by only antibiotic therapy. In this patient, a 4-mm balloon catheter was used for tract dilation, causing overdilation of the tract, and leakage of infected bile juice. RBO occurred in five patients (26.3%), and median TRBO was 22 days. Early RBO occurred in four patients (21.1%), of which three patients had malignant biliary obstruction with duodenal stricture and one patient had benign anastomotic stricture at the HJS site. In five patients, RBO was managed by nasobiliary catheter placement beside the placed plastic stent via the hepaticoenteric fistula.

A comparison between the clinical outcomes of EUS-HES using the dedicated plastic stent in patients with AC and

Table 2. Details of the EUS-guided biliary drainage procedures performed for acute cholangitis

	Patients (*n*=19)
EUS-BD technique	
EUS-HGS	16
EUS-HJS	1
EUS-AGS with HGS	2
Operator (expert/trainee)	11/8
Period (early/late)	9/10
Size of punctured IHBD (mm), median (range)	4.5 (2.7-7.0)
Puncture needle size (19G/22G)	14/5
Accessed biliary branch duct (B2/B3), *n*	9/10
Tract dilation device, *n*	
Ultra-tapered mechanical dilator	17
Cautery dilator	1
4-mm balloon catheter	1
Diameter of placed plastic stent (7-Fr/8-Fr), *n*	1/18
Placed stent for EUS-AGS	
Uncovered metal stent (10 mm in diameter)	2
Procedure time, median, min (range)	9 (6-17)
Technical success of stent placement, *n* (%)	19/19 (100)
Clinical success, *n* (%)	19/19 (100)
Procedure-associated adverse event, *n* (%)	1/19 (5.3)
Moderate, biliary peritonitis	1
7-day mortality for acute cholangitis, *n* (%)	0/19 (0)
Period of follow-up (days), median (range)	48 (12-125)
RBO, *n* (%)	5 (26.3)
Recurrence of cholangitis	4
Recurrence of obstructive jaundice	1
TRBO (days), median (range)	22 (12-49)
Early RBO (<4 weeks), *n* (%)	4 (21.1)

EUS-BD: EUS-guided biliary drainage; EUS-HGS: EUS-guided hepaticogastrostomy; EUS-HJS: EUS-guided hepaticojejunostomy; EUS-AGS: EUS-guided antegrade stenting; IHBD: Intrahepatic bile duct; RBO: Recurrent biliary obstruction; TRBO: Time to recurrent biliary obstruction

without AC is shown in Table 3. Patient characteristics and details of the procedures were similar in the two groups. The clinical success rate was 100% in both groups and the rate of procedure-associated adverse events was not statistically significantly different (6.7% *vs.* 5.7%, $P = 0.88$). Although the RBO rate was not statistically significantly different (33.3% *vs.* 23.9%, $P = 0.43$), the early RBO rate was statistically significantly higher in the AC group than in the non-AC group (26.7% [4/15] *vs.* 3.4% [3/88], $P < 0.001$). Kaplan–Meier curves showed that AC was associated with shorter TRBO compared with non-AC ($P = 0.046$) [Figure 2]. Median TRBO was 22 days in the AC group and 50 days in the non-AC group. Furthermore, predictive factors for early RBO were analyzed by logistic regression analysis [Table 4]. After adjusting for age and gender, the presence of AC was found to be an independent risk factor of early RBO (odds ratio: 10.3; 95% confidence interval [CI] 2.03–52.2; $P = 0.005$).

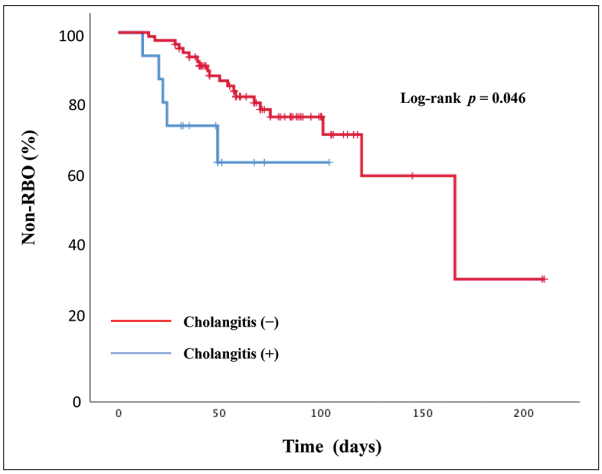

Figure 2. Kaplan–Meier curves of time to recurrent biliary obstruction of the acute cholangitis group and the nonacute cholangitis group. RBO: Recurrent biliary obstruction

DISCUSSION

To the best of our knowledge, this is the first retrospective cohort study focusing on urgent and early BD within 96 h after the onset of AC by EUS-BD. Since the first report of EUS-BD,[8] several reports have been published showing the efficacy of EUS-BD as a useful alternative drainage technique.[9-11] Wang *et al.* conducted a systematic review, including 42 studies with 1192 patients, showing a high cumulative technical success rate (94.7%) and functional clinical success rate (91.7%), with a 23.3% adverse events rate.[12] Although there is no mention of the presence of AC in these reports, the majority of patients are thought to have obstructive jaundice without AC. In the present study, only 9.6% of the EUS-BD patients had suspected or a definite diagnosis of AC although our institution is a tertiary referral center where patients with AC are often introduced for urgent or early BD.

AC may cause a rapid deterioration in a patient's condition owing to sepsis induced by bacteremia. The biliary stricture or blockage caused by stones increases the pressure within the biliary system and flushes microorganisms or endotoxins from the infected bile juice into the systemic circulation, inducing a systemic inflammatory response. Severe AC can lead to organ failure or coagulopathy owing to sepsis, leading to the need for respiratory and circulatory management. Therefore, the endoscopic drainage procedure may lead to an increase in adverse events over the non-AC patients, particularly in older patients.[13] EUS-BD may have a higher risk owing to the leakage of infected dirty bile juice. However, the clinical outcomes of this

Table 3. Comparison of outcomes between EUS-guided biliary drainage performed on patients with cholangitis and without cholangitis

	Cholangitis (+) (*n*=15)	Cholangitis (−) (*n*=88)	*P*
Median age, years (range)	69 (33-83)	69 (23-90)	0.92
Gender (male/female)	6/9	52/36	0.17
Primary biliary disease (malignant/benign)	9/6	53/35	0.99
Surgically altered anatomy	8 (53.3)	42 (47.7)	0.69
Period (early/late)	7/8	35/53	0.62
Operator (expert/trainee)	8/7	42/46	0.69
Technique of EUS-BD (EUS-HGS/EUS-HJS)	14/1	84/4	0.72
Puncture needle size (19G/22G)	11/4	68/20	0.74
Tract dilation device, *n*			
Ultra-tapered mechanical dilator	13	52	0.07
Cautery dilator	1	32	
4-mm balloon catheter	1	4	
Diameter of placed plastic stent (7-Fr/8-Fr), *n*	1/14	14/74	0.35
Clinical success, *n* (%)	15/15 (100)	88/88 (100)	N/A
Procedure-associated adverse events, *n* (%)	1/15 (6.7)	5/88 (5.7)	0.88
Moderate, biliary peritonitis	1	5	
Period of follow-up (days), median (range)	48 (12-104)	67 (15-210)	0.003
RBO, *n* (%)	5 (33.3)	21 (23.9)	
Recurrence of cholangitis	4	16	0.43
Recurrence of obstructive jaundice	1	5	
Early RBO (<4 weeks), *n* (%)	4 (26.7)	3 (3.4)	<0.001
TRBO (days), median (range)	22 (12-49)	50 (15-166)	0.046

EUS-BD: EUS-guided biliary drainage; EUS-HGS: EUS-guided hepaticogastrostomy; EUS-HJS: EUS-guided hepaticojejunostomy; RBO: Recurrent biliary obstruction; TRBO: Time to recurrent biliary obstruction; N/A: Not available

present study were comparable to previously reported clinical outcomes for non-AC patients, although the majority was mild or moderate cholangitis. The present study demonstrated that urgent or early EUS-HES using a dedicated plastic stent with a short procedure time can be a feasible and safe drainage procedure for AC.

We believe that there are three important points to safely accomplish EUS-BD in AC patients. The first point is the reduction of the bile juice leak into the abdominal cavity. In AC patients, infected and turbid bile juice leak has a higher risk of causing biliary peritonitis and abdominal abscesses than in non-AC patients. EUS-HES, which is performed via the liver parenchyma, may be associated with less bile leakage than EUS-choledochoduodenostomy and EUS-HES may hence be preferable for AC patients. In addition, mechanical dilation is preferable for minimizing fistula dilation. Electrical cautery dilation can result in adequate fistula dilation, but thermal ablation can cause the fistula to widen and lead to delayed bile leakage after a few days, particularly if a plastic stent is in place.[14] In this regard, the ultra-tapered mechanical dilator is a useful device for AC cases, as it can firmly dilate the fistula even in the rigid wall of the bile duct.[15] In fact, the ultra-tapered mechanical dilator was able to dilate the fistula without biliary peritonitis in all the 17 patients.

The second point is that the procedure from puncture to stenting should be accomplished as quickly as possible. In general, the longer the procedure, the greater the leakage of bile juice. In addition, patients with AC are more likely to have unstable respiratory and cardiovascular conditions and are at higher risk of organ damage and thromboembolism associated with low blood pressure. Therefore, it is important to ensure that the procedure is accomplished within a short time and to minimize physical stress.[16] It is hence necessary to simplify the procedure. In this regard, the dedicated plastic stent is considered useful because it is simple to place and does not require delicate position adjustment as for metal stent.[17] In fact, we have been able to perform stenting within an average of 10 min. In recent years, EUS-AGS combined with HES has been reported to prolong the duration of stent patency.[18,19] In AC cases, EUS-HES alone may be safer than EUS-AGS with HES. However, if the guidewire easily passes through the stenosis, sequential AGS may be considered. In two cases, we were able to accomplish EUS-AGS with HES within 12 and 15 min, without any adverse events.

Table 4. Predictive factors of early recurrent biliary obstruction

	Early-RBO (+), *n* (%)	Age-gender-adjusted OR (95% CI)	*P*
Age at EUS-BD			
<70 years (*n*=53)	4 (7.5)	1.28 (0.27-6.02)	0.53
≥70 years (*n*=50)	3 (6.0)	Referent	
Gender			
Male (*n*=58)	4 (6.9)	1.04 (0.22-4.89)	0.64
Female (*n*=45)	3 (6.7)	Referent	
Primary biliary disease			
Malignant (*n*=62)	5 (8.1)	1.71 (0.32-9.27)	0.42
Benign (*n*=41)	2 (4.9)	Referent	
Surgically altered anatomy			
Present (*n*=50)	3 (6.0)	0.78 (0.17-3.68)	0.53
Absent (*n*=53)	4 (7.5)	Referent	
Period (early/late)			
Early (*n*=42)	2 (4.8)	0.56 (0.10-3.03)	0.40
Late (*n*=61)	5 (8.2)	Referent	
Operator (expert/trainee)			
Expert (*n*=50)	2 (4.0)	0.40 (0.07-2.16)	0.24
Trainee (*n*=53)	5 (9.4)	Referent	
Technique of EUS-BD			
EUS-HGS (*n*=98)	7 (7.1)	N/A	0.54
EUS-HJS (*n*=5)	0 (0)		
Puncture needle size	6/1		
19G (*n*=79)	6 (7.6)	1.89 (0.21-16.5)	0.48
22G (*n*=24)	1 (4.2)	Referent	
Tract dilation device, *n*			
Ultra-tapered mechanical dilator (*n*=65)	5 (7.7)	1.50 (0.28-8.14)	0.49
Others (*n*=38)	2 (5.3)	Referent	
Diameter of placed plastic stent			
7-Fr (*n*=15)	0 (0)	N/A	0.32
8-Fr (*n*=88)	7 (8.0)		
Acute cholangitis			
Present (*n*=15)	4 (26.7)	10.3 (2.03-52.2)	0.005
Absent (*n*=88)	3 (3.4)	Referent	

RBO: Recurrent biliary obstruction; EUS-BD: EUS-guided biliary obstruction; OR: Odds ratio; EUS-HGS: EUS-guided hepaticogastrostomy; EUS-HJS: EUS-guided hepaticojejunostomy

The third point is the prevention of peripheral cholangitis and liver abscess formation associated with obstruction of bile duct branches. Covered metal stents have become more widely used for EUS-HES because of their more efficient drainage.[20] However, when a metal stent is used for AC, peripheral bile duct branch obstruction may cause insufficient drainage of infected bile juice in the bile duct branches, or the disruption of the bile duct branches, resulting in liver abscess formation. In this regard, the use of a plastic stent is less likely to occlude the bile duct branches.

This study demonstrates that a narrow-lumen plastic stent can provide adequate drainage and improve AC despite turbid and highly viscous infected bile juice. In all patients, AC improved within a week. However, plastic stents are more readily occluded by debris or bacterial biofilm formation after the improvement of AC than metal stents. A comparison between the AC group and the non-AC group showed that AC was a significant risk factor for early RBO. The present study showed that there are still some problems with our strategy that need to be solved. Therefore, early additional intervention after the improvement of AC may be necessary to prevent stent occlusion. We often perform additional antegrade intervention for benign biliary diseases about 4–8 weeks after maturation of the fistula.[21] However, in AC cases, it should be performed earlier. In malignant cases, additional AGS or initial stent replacement within 4 weeks may prevent early stent occlusion. Two patients in this study who underwent sequential additional AGS maintained good stent patency without occlusion for 83 and 125 days, until they died. Sequential additional AGS may hence provide good stent patency with or without AC.

The indication of EUS-BD for malignant biliary obstruction with duodenal stricture is mainly obstructive jaundice without cholangitis. However, the indication of EUS-BD for benign biliary diseases, especially the hepaticojejunal anastomotic stricture, is often cholangitis. Pizzicannella *et al.*[22] described that the indication of EUS-BD in the management of benign biliary stricture was cholangitis in all 12 cases although the timing of EUS-BD or the details about cholangitis were not described. Similarly, the indication of EUS-BD in our cases with benign biliary strictures was mainly recurrent cholangitis.[21] In this study, we focused on urgent or early EUS-BD (within 96 h). Therefore, when cholangitis had been already improved by conservative management, such cases were classified into the non-AC group. In most cases of mild AC, AC can be improved by the initial treatment including antibiotics without BD, but the longer duration of hospitalization may be required.[23] Urgent or early transpapillary BD within 48 h was recommended for moderate and severe AC because mortality was significantly lower in previous studies.[24] Although the recommended timing of EUS-BD for AC is unclear, according to the outcomes of this study, early or urgent EUS-BD for AC can be performed effectively and safely as with transpapillary BD.

There are several limitations to this study. First, there may be some biases, as technical biases could not be completely avoided because of the retrospective single-center study. To confirm the results, a prospective evaluation or randomized controlled study is required. Second, as we only used the dedicated plastic stent for EUS-HES, clinical data using a metal stent for AC patients and a comparative study are required to verify our strategies. Third, there was no patient who had severe respiratory or cardiovascular dysfunction owing to severe AC. It hence also remains unknown whether EUS-BD is safe for such patients.

CONCLUSIONS

If standard ERCP is unsuccessful or is not possible, urgent or early BD by EUS-BD can be a feasible and safe alternative procedure in patients with AC. However, the fact that the duration of stent patency in AC patients is shorter than that in non-AC patients if a plastic stent is placed is an issue to be solved in the future. In particular, early RBO tends to occur. Further prospective studies of EUS-BD in patients with AC are warranted.

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Conflicts of interest
There are no conflicts of interest.

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