Journal of Gastrointestinal Surgery (2019) 23:192–198
https://doi.org/10.1007/s11605-018-3914-7

MULTIMEDIA ARTICLE

EUS-Guided Antegrade Biliary Stenting Using a Novel Fully Covered Metal Stent (with Video)

Masanori Yamada[1] · Takeshi Ogura[1] · Rieko Kamiyama[1] · Akira Miyano[1] · Nobu Nishioka[1] · Tadahiro Yamada[1] · Kazuhide Higuchi[1]

Received: 18 May 2018 / Accepted: 1 August 2018 / Published online: 20 August 2018

Abstract

Background Recently, endoscopic ultrasound (EUS)-guided hepaticogastrostomy (HGS) combined with antegrade stenting (AS) has been reported to be associated with longer stent patency and reduced procedure-related adverse events. In EUS-AS, an uncovered metal stent is usually selected to prevent stent misplacement or dislocation. However, because patient survival has improved with advances in chemotherapy, longer stent patency may be required.

Aim The technical feasibility and safety of EUS-guided transhepatic biliary drainage combined with EUS-AS using a novel covered metal stent were evaluated.

Methods Patients with malignant biliary obstruction leading to obstructive jaundice, in whom standard ERCP had failed or was contraindicated, were enrolled in this study between July 2015 and October 2017. As the control group, patients undergoing EUS-AS using an uncovered metal stent were enrolled between October 2014 and June 2015.

Results A total of 39 patients were enrolled in this study. Among them, EUS-AS using a covered metal stent was performed in 17 patients and using an uncovered metal stent in the remaining 22 patients. Median stent patency including stent dysfunction and patient death was longer in the covered metal stent group (153 days) compared with that of the uncovered metal stent group (108 days) although there were no significant differences ($P = 0.06$). In only cases with stent dysfunction was median stent patency of the covered metal stent group significantly longer than that of the uncovered metal stent group (not available vs 150 days, $P = 0.02$).

Conclusions In conclusion, EUS-guided transluminal biliary drainage combined with EUS-AS using a covered metal stent may be feasible and safe, although the indications for this procedure should be carefully considered.

Keywords EUS · EUS-guided biliary drainage · EUS-guided antegrade stenting · ERCP

Introduction

Malignant biliary obstruction is usually treated by biliary drainage under endoscopic retrograde cholangiopancreatography (ERCP) guidance. However, if ERCP fails due to difficult cannulation, duodenal obstruction, or surgical-altered anatomy, percutaneous transhepatic biliary drainage (PTBD) is indicated as an alternative method. Although this procedure is well established, it is associated with several disadvantages, such as cosmetic problems and the need for external drainage.

Endoscopic ultrasound-guided biliary drainage (EUS-BD) has been developed as another alternative technique.[1–10] EUS-BD can be performed via two main approach routes. The first route is transhepatic, such as by EUS-guided hepaticogastrostomy (HGS) or hepaticojejunostomy (HJS). The second route is transduodenal, via EUS-guided choledochoduodenostomy or gallbladder drainage. Recently, EUS-HGS combined with antegrade stenting (AS) has been reported to be associated with longer stent patency and reduced procedure-related adverse events.[11–15] In EUS-AS, an uncovered metal stent is usually selected to prevent stent misplacement or dislocation. However, because patient survival has improved with advances in chemotherapy, longer stent patency may be required. Recently, a novel covered metal stent with a

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11605-018-3914-7) contains supplementary material, which is available to authorized users.

✉ Takeshi Ogura
oguratakeshi0411@yahoo.co.jp

[1] 2nd Department of Internal Medicine, Osaka Medical College, 2-7 Daigakuchou, Takatsukishi, Osaka 569-8686, Japan

fine gauge stent delivery system has become available in Japan. In this pilot study, the technical feasibility and safety of EUS-guided transhepatic biliary drainage combined with EUS-AS using this novel covered metal stent were evaluated.

Patients and Methods

Patients with malignant biliary obstruction leading to obstructive jaundice, in whom standard ERCP had failed or was contraindicated, such as due to duodenal obstruction or surgical-altered anatomy, were enrolled in this study between July 2015 and October 2017. As the control group, patients undergoing EUS-AS using an uncovered metal stent (Zilver635 biliary self-expanding stent, Cook Medical, Bloomington, IN, USA) were enrolled between October 2014 and June 2015. This pilot study was approved by the institutional review board of Osaka Medical College. Written, informed consent was obtained from all patients.

Characteristics of the Novel Metal Stent and Performance of EUS-BD

In this study, a novel covered metal stent (NIR) was used for EUS-AS. This covered metal stent consists of laser-cut metal membranes (Fig. 1a), which minimizes shortening of the stent. In addition, the size of the stent delivery system is only 7.5 Fr and it has a fine gauge tip, despite the stent being a covered metal stent (Fig. 1b). Therefore, insertion of this stent into the stricture site through the fistula may be easy compared to that of other covered metal stents.

EUS-BD was performed under conscious sedation using midazolam and pentazocine hydrochloride. An echoendoscope (UCT 260, Olympus Optical Co. Ltd., Tokyo, Japan) connected to an ultrasound device (SSD5500; Aloka Medical Ltd., Tokyo, Japan) was advanced into the intestine or stomach. Following visualization of the intrahepatic bile duct, it was punctured using a 19-G fine-needle aspiration (FNA) needle (SonoTip Pro Control; Medi-Globe GmbH, Rohrdorf, Germany). After bile juice was aspirated, the contrast medium was injected into the biliary tract through the FNA needle. Next, the 0.025-in. guidewire (VisiGlide 1; Olympus Medical Systems, Tokyo, Japan) was advanced into the common bile duct. To facilitate adequate cholangiography and to improve guidewire operation, an ERCP catheter (MTW Endoskopie Co., Dusseldorf, Germany) was inserted into the biliary tract. After the obstruction site was evaluated in the biliary tract (Fig. 2a), the guidewire was advanced into the intestine across this site (Fig. 2b). Next, the novel metal stent was inserted without fistula dilation, and advanced across the obstruction site (Fig. 2c). If stent insertion was difficult, additional fistula dilation was performed using a balloon catheter (REN biliary dilation catheter, KANEKA Co., Inc., Osaka, Japan). EUS-AS was carefully performed under fluoroscopic guidance (Fig. 2d). If obstruction was present in the lower common bile duct, transpapillary stent placement was performed. If the middle common bile duct was obstructed, stent placement was performed above the papilla. After this procedure, EUS-HGS or HJS was performed using a covered metal stent (Niti-S Biliary Covered Stent; TaeWoong Medical, Seoul, South Korea) or plastic stent (Type IT stent, Gadelius Medical Co, Ltd., Tokyo, Japan), as previously described (Fig. 2e).[5,6]

Definitions and Statistical Analysis

The obstruction site was evaluated by cholangiography under EUS-BD guidance. Overall survival (OS) was measured from the day of EUS-transhepatic biliary drainage combined with EUS-AS to the time of the patient's death. In addition, time to dysfunction was measured from the day of EUS-guided biliary drainage combined with EUS-AS to the time of stent dysfunction. Stent patency was also measured from the day of EUS-transhepatic biliary drainage combined with EUS-AS until stent dysfunction or patient death or the last follow-up. Stent dysfunction was defined by the presence of cholangitis or recurrence of obstructive jaundice. Technical success was defined as successful stent placement for both EUS-AS and EUS-HGS or EUS-HJS. If the fistula was dilated using a balloon catheter, it was considered as additional fistula dilation. Procedure time was measured from intrahepatic bile duct puncture to EUS-HGS or EUS-HJS stent placement. Clinical success was defined by a decrease in serum bilirubin to < 75% of the immediate preoperative values within 30 days after stent placement or a decrease in the diameter of the biliary tract. Adverse events were graded according to the American Society of Gastrointestinal Endoscopy lexicon's severity system.[16]

Fig. 1 The tip of the novel stent delivery system is extremely fine, and the diameter is only 7.5 Fr (**a**). This stent consists of laser-cut fully covered metal membranes (**b**)

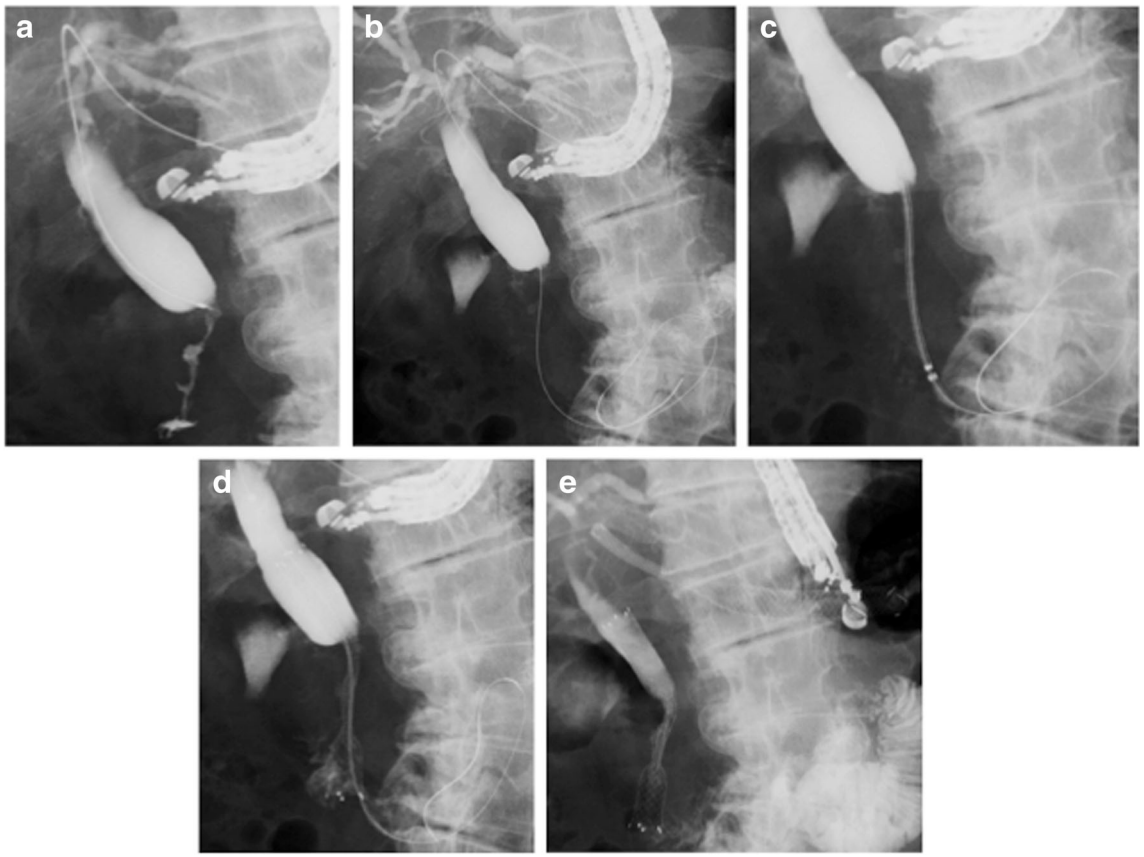

Fig. 2 **a** Endoscopic ultrasound-guided cholangiography demonstrated obstruction of the lower bile duct. **b** The guidewire was successfully advanced into the intestine across the site of bile duct obstruction. **c** The stent delivery system of the fully covered metal stent was inserted into the biliary tract. **d** Transpapillary stent deployment was performed. **e** Subsequently, endoscopic ultrasound-guided hepaticogastrostomy was successfully performed

In this study, continuous variables were expressed as median values. The proportion of patients who underwent EUS-AS using a covered metal stent and EUS-AS using an uncovered metal stent was compared using the χ^2 test, Mann-Whitney *U* test, and Kruskal-Wallis test, as appropriate. Survival curves for OS and stent patency were estimated using the Kaplan-Meier method. A *P* value of < 0.05 was considered significant. Finally, all statistical analyses were performed using SPSS version 13.0 (SPSS, Chicago, IL, USA).

Results

A total of 39 patients were enrolled in this study. Among them, EUS-AS using a covered metal stent was performed in 17 patients (median age, 79 years; 7 male) and using an uncovered metal stent in the remaining 22 patients (median age, 76 years; 12 male) (Table 1). The reasons for EUS-BD such as surgical anatomy, duodenal obstruction, or failed ERCP were not significantly different between both groups ($P = 0.59$). Also, the kinds of malignancies leading to obstruction were not significantly different between both groups ($P = 0.09$). During the EUS-BD procedure, both the middle and lower bile ducts were obstructed, and there were no significant differences between both groups ($P = 0.65$). In the covered metal stent group, the EUS-AS stent was placed above the papilla in three patients (17.6%, 3/17). On the other hand, in the uncovered metal stent group, the EUS-AS stent was placed above the papilla in three patients (36.4%, 8/22). The median procedure time was 21 min (range, 10–52 min) in the covered metal stent group and 19 min (range, 10–48) ($P = 0.48$) in the uncovered metal stent group. Fistula dilation prior to EUS-AS stent insertion was performed in two patients of the covered metal stent group and in three patients of the uncovered metal stent group ($P = 0.86$). In terms of the kind of transluminal stent used, most patients underwent EUS-HGS using a covered metal stent. A plastic stent was used in one patient of the covered metal stent group because this patient had previously undergone total gastrectomy with the Roux-en-Y procedure. Technical and clinical success were obtained in both groups. Adverse events related to the procedure were seen in three patients ($n = 1$ in the covered metal stent group, $n = 2$ in the uncovered metal stent group), and there were no significant differences in both groups ($P = 0.71$). All patients were successfully treated, conservatively.

Table 1 Patient characteristics

	Covered group	Uncovered group	*P* value
Total patients	17	22	
Median age (years, range)	79 (43–90)	76 (45–88)	0.15
Gender (male to female)	7:10	12:10	0.41
Reason for EUS-BD			
Surgical-altered anatomy	4	8	0.59
Duodenal obstruction	12	12	
Failed ERCP	1	2	
Disease			
Pancreatic cancer	11	18	0.09
Gastric cancer	4	0	
Bile duct cancer	1	3	
Bladder cancer	1	0	
Cancer of ampulla of Vater	0	1	
Site of obstruction			
Middle common bile duct	3	6	0.65
Lower common bile duct	11	11	
Both	3	5	
Location of antegrade stenting			
Transpapillary	14	14	0.20
Above the papilla	3	8	
Kind of transluminal stent			
Covered metal stent	16	22	0.25
Plastic stent	1	0	
Mean procedure time, min (range)	21 (10–52)	19 (10–48)	0.48
Additional fistula dilation (*n*)	2	3	0.86
Technical success, % (*n*)	100 (17/17)	100 (22/22)	–
Clinical success, % (*n*)	100 (17/17)	100 (22/22)	–
Adverse events (*n*)	Abdominal pain (1)	Acute pancreatitis ($n = 1$) Abdominal pain ($n = 1$)	0.71

Figure 3 shows a comparison of median OS in patients between the covered metal stent group and the uncovered metal stent group. Median OS in the covered metal stent group was 182 days [95% confidence interval (CI), 139.3 to 226.5], which was similar to that in the uncovered metal stent group (177 days; 95% CI, 120.3 to 234.5; $P = 0.84$). Figure 4 shows median stent patency including stent dysfunction and patient death. Stent dysfunction was seen in two patients in the covered metal stent group due to cholangitis. On the other hand, in the uncovered metal stent group, stent dysfunction was seen in seven patients due to cholangitis ($n = 2$) and obstructive jaundice ($n = 5$). Median stent patency was longer in the covered metal stent group (153 days; 95% CI, 123.8 to 182.3) compared with that of the uncovered metal stent group (108 days; 95% CI, 77.0 to 139.6) although there were no significant differences ($P = 0.06$). However, as shown in Fig. 5, in only cases with stent dysfunction was median stent patency of the covered metal stent group significantly longer than that of the uncovered metal stent group (not available vs 150 days; 95% CI, 44.5 to 237.2; $P = 0.02$).

Stent dysfunction was seen in two patients (cholangitis). Patients with cholangitis were treated conservatively.

Discussion

Recent advances in chemotherapy have improved the survival of cancer patients. Patients with advanced malignant tumors with associated obstructive jaundice must undergo biliary drainage using a metal stent before undergoing chemotherapy. Further, prolonged stent patency is highly desirable when undergoing continuous chemotherapy because chemotherapy cannot be performed in cases with stent dysfunction. To date, various biliary drainage techniques have been reported, including the EUS-guided approach. Among these procedures, EUS-guided transluminal biliary drainage combined with EUS-AS has been reported as a novel biliary drainage technique.[11–15]

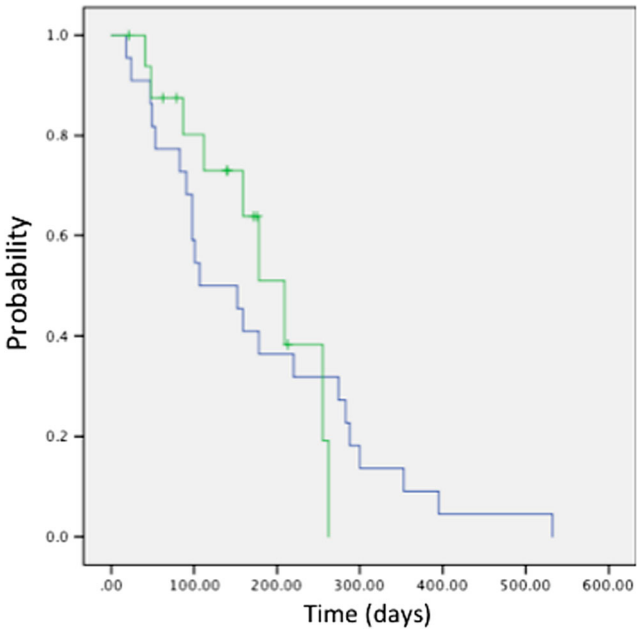

Fig. 3 Kaplan-Meier curves of overall survival of the covered and uncovered metal stent groups (green line: covered metal stent group, blue line: uncovered metal stent group). There was no significant difference between both the covered metal stent group (median, 182 days; 95% CI, 139.3 to 226.4) and uncovered metal stent group (median, 177 days; 95% CI, 120.3 to 234.5) ($P = 0.837$)

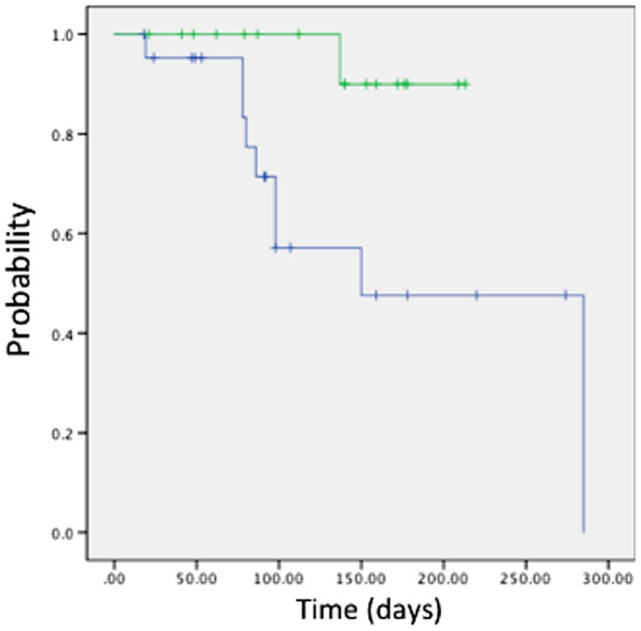

Fig. 5 Kaplan-Meier curves of stent dysfunction including stent dysfunction in the covered and uncovered metal stent groups (green line: covered metal stent group, blue line: uncovered metal stent group). Median stent patency is significantly longer in the covered metal stent group (not available) compared with that of the uncovered metal stent group (150 days; 95%, CI 44.5 to 237.2) ($P = 0.02$)

The technique of the EUS-AS procedure has been previously amply reported.[17–22] Godat et al. reported the efficacy and safety of EUS-AS in a monocentric study.[22] In their study, a total of 20 patients underwent EUS-AS using an uncovered metal stent. Two patients died of infectious adverse events resulting from incomplete biliary drainage. However, these adverse events were not directly related to EUS-AS. In addition, the patients who died had advanced malignant tumors, and therefore, they mentioned that these adverse events were acceptable. Due to the high clinical success rate and the fact that bilioma or bile leakage was not seen in any of the patients, they concluded that EUS-AS is a clinically effective and safe procedure. Iwashita et al. evaluated the feasibility and safety of EUS-AS for patients who had unresectable malignant biliary obstruction and surgically altered anatomy.[17] In their study, EUS-AS using an uncovered metal stent was attempted in 20 patients, of whom it was successfully performed in 19 patients (technical success rate, 95%). Clinical success was also achieved in 19 patients (95%). Recurrent biliary obstruction was seen in 3 patients (3/20, 15%), for whom re-intervention was performed using PTBD and repeat EUS-AS. Therefore, if only EUS-AS is performed, relatively invasive re-intervention may be required.

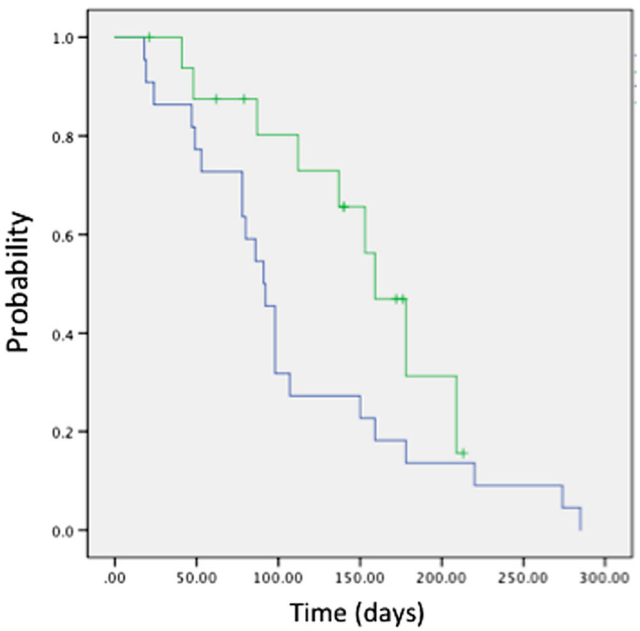

Fig. 4 Kaplan-Meier curves of stent patency including stent dysfunction and patient death in the covered and uncovered metal stent groups (green line: covered metal stent group, blue line: uncovered metal stent group). There was no significant difference between both the covered metal stent group (median, 153 days; 95% CI, 123.8 to 182.3) and uncovered metal stent group (median, 108 days; 95% CI, 77.0 to 139.6) ($P = 0.06$)

On the other hand, EUS-guided transluminal biliary drainage combined with EUS-AS has several advantages over EUS-AS alone. First, re-intervention can be easily attempted if required. In cases of only EUS-AS, if stent dysfunction occurs, re-intervention with PTBD or a repeat EUS-guided approach is needed. On the other hand, in cases of EUS-guided transluminal biliary drainage combined with EUS-AS, biliary access can be easily obtained through the

transluminal biliary stent. Second, compared with EUS-guided transluminal biliary drainage, such as EUS-HGS or EUS-HJS, the risk of bile leakage may be lower with EUS-AS. Third, longer stent patency may be obtained by the combined procedure. However, this procedure may be technically complex and involve a high cost due to the need for two metal stents.

In our study, we used a covered metal stent as the EUS-AS stent to obtain longer stent patency. In the present study, median stent patency including stent dysfunction and patient death was 153 days, and compared with that of the uncovered metal stent group, median stent patency was longer although there were no significant differences. In addition, stent patency in only stent dysfunction cases was significantly longer in the covered metal stent group compared with the uncovered metal stent group ($P = 0.02$). Our result is superior to that previously reported.[12] Imai et al. performed a retrospective comparative study of EUS-AS and EUS-HGS.[12] In their study, in which EUS-AS was performed using an uncovered metal stent, median stent patency of EUS-HGS combined with EUS-AS was 63 days, although median overall survival was extremely short. Therefore, although the patient population was different between our two studies, EUS-AS using a covered metal stent is likely to offer significant clinical benefit.

However, EUS-AS using a covered metal stent has several limitations. First, if transpapillary stent placement is performed, acute pancreatitis can occur due to obstruction of the orifice of the pancreatic duct. Moreover, use of a covered metal stent for EUS-AS is associated with a higher risk of acute pancreatitis compared to that with an uncovered metal stent although this adverse event was not seen in the covered metal stent group of our study. Therefore, the indications of EUS-AS itself seem to be limited to selected patients, such as those with pancreatic atrophy.[11,15] Second, stent dislocation or misplacement occurs easily with a covered versus an uncovered metal stent. To overcome this problem, we selected a laser-cut-type metal stent. Indeed, in the present study, stent dislocation and misplacement were not seen in any of the patients.

In the present study, there were several limitations. First, our study was a retrospective study. Second, our study also had a small sample size, despite having a control group. Therefore, a prospective, randomized controlled study between both groups is needed to confirm our results.

In conclusion, EUS-guided transluminal biliary drainage combined with EUS-AS using a covered metal stent may be feasible and safe, although the indications for this procedure should be carefully considered.

Author Contribution Masanori Yamada and Takeshi Ogura wrote the paper. Takeshi Ogura, Akira Miyano, Rieko Kamiyama, Nobu Nishioka, Tadahiro Yamada, and Kazuhide Higuchi interpreted the data for the work, revising it critically for important intellectual content, final approval of the version to be published, and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with Ethical Standards

This pilot study was approved by the institutional review board of Osaka Medical College. Written, informed consent was obtained from all patients.

Conflict of Interest The authors declare that they have no conflicts of interest.

References

1. Dhir V, Isayama H, Itoi T, et al. Endoscopic ultrasonography-guided biliary and pancreatic duct interventions. Dig Endosc 2017;29:472–485
2. Itoi T, Dhir V, Moon JH. EUS-guided biliary drainage: moving into a new era of biliary drainage. Gastrointest Endosc 2017;85:915–917
3. Sharaiha RZ, Khan MA, Kamal F, et al. Efficacy and safety of EUS-guided biliary drainage in comparison with percutaneous biliary drainage when ERCP fails: a systematic review and meta-analysis. Gastrointest Endosc 2017;85:904–914
4. Ogura T, Higuchi K. Technical tips of endoscopic ultrasound-guided choledochoduodenostomy. World J Gastroenterol 2015;21:820–828
5. Ogura T, Higuchi K. Technicap tips for endoscopic ultrasound-guided hepaticogastrostomy. World J Gastroenterol 2016;22:3945–3951
6. Hara K, Yamao K, Mizuno N, et al. Endoscopic ultrasonography-guided biliary drainage: who, when, which, and how? World J Gastroenterol 2016;22:1297–1303
7. Sharaiha RZ, Kumta NA, Desai AP, et al. Endoscopic ultrasound-guided biliary drainage versus percutaneous transhepatic biliary drainage: predictors of successful outcome in patients who failed endoscopic retrograde cholangiopancreatography. Surg Endosc 2016;30:5500–5505
8. Law R, Baron TH. Endoscopic ultrasound-guided biliary interventions: an update on recent developments. Curr Opin Gastroenterol 2016;32:232–237
9. Khashab MA, Valeshabad AK, Afghani E, et al. A comparative evaluation of EUS-guided biliary drainage and percutaneous drainage in patients with distal malignant biliary obstruction and failed ERCP. Dig Dis Sci 2015;60:557–565
10. Lee TH, Choi JH, Park do H, et al. Similar efficacies of endoscopic ultrasound-guided transmural and percutaneous drainage for malignant distal biliary obstruction. Clin Gastroenterol Hepatol 2016;14:1011–1019
11. Ogura T, Kitano M, Takenaka M, et al. Multicenter prospective evaluation study of endoscopic ultrasound-guided hepaticogastrostomy combined with antegrade stenting (with video). Dig Endosc 2018;30:252–259
12. Imai H, Takenaka M, Omoto S, et al. Utility of endoscopic ultrasound-guided hepaticogastrostomy with antegrade stenting for malignant biliary obstruction after failed endoscopic retrograde cholangiopancreatography. Oncology 2017;93:69–75
13. Kumbhari V, Tleu AH, Khashab MA. EUS-guided biliary drainage made safer by a combination of hepaticogastrostomy and antegrade transpapillary stenting. Gastrointest Endosc 2015;81:1015–1016
14. Ogura T, Edogawa S, Imoto A, et al. EUS-guided hepaticojejunostomy combined with antegrade stent placement. Gastrointest Endosc 2015;81:462–463
15. Ogura T, Masuda D, Imoto A, et al. EUS-guided hepaticogastrostomy combined with fine-gauge antegrade stenting: a pilot study. Endoscopy 2014;46:416–421

16. Cotton PB, Eisen GM, Abakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE work shop. Gastrointest Endosc 2010;71:446–454
17. Iwashita T, Yasuda I, Mukai T, et al. Endoscopic ultrasound-guided antegrade biliary stenting for unresectable malignant biliary obstruction in patients with surgically altered anatomy: single-center prospective pilot study. Dig Endosc 2017;29: 362–368
18. Almadi MA, Eltayeb M, Thaniash S. Endscopic ultrasound-guided antegrade stenting in an occluded biliary self-expandable metal stent. Saudi J Gastroenterol 2016;22:337–340
19. Iwashita T, Nakai Y, Hara K, et al. Endoscopic ultrasound-guided antegrade treatment of bile duct stone in patients with surgically altered anatomy: a multicenter retrospective cohort study. J Hepatobiliary Pancreat Sci 2016;23:227–233
20. Itoi T, Sofuni A, Tsuchiya T, et al. Endoscopic ultrasonography-guided transhepatic antegrade stone removal in patients with surgically altered anatomy: case series and technical review (with videos). J Hepatobiliary Pancreat Sci 2014;21:E86-E93
21. Weilert F, Binmoeller KF, Marson F, et al. Endoscopic ultrasound-guided anterograde treatment of biliary stones following gastric bypass. Endoscopy 2011;43:1105–1108
22. Godat S, Bories E, Caillol F, et al. Efficacy and safety in case of technical success of endoscopic ultrasound-guided transhepatic antegrade biliary drainage: a report of a monocentric study. Endosc Ultrasound 2017;6:181–186