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ORIGINAL ARTICLE

Uncovered Self-Expandable Metallic Stent with an Ultra-Thin Delivery Sheath in Unresectable Malignant Hilar Biliary Obstruction: A Multicenter Prospective Observational Study

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Abstract

Background Although various self-expandable metallic stents (SEMSs) for malignant hilar biliary obstruction (MHBO) have been introduced, the optimal SEMS for MHBO has not yet been established.

Purpose This study aimed to evaluate outcomes of the transpapillary placement of an uncovered laser-cut SEMS with an ultra-thin delivery sheath (YABUSAME) for MHBO.

Methods This multicenter, prospective study was conducted in 11 hospitals for 10 months (from March 2022 to December 2022). The primary outcome was the stent patency rate at 6 months. Key secondary outcomes were the technical success rate, clinical success rate, time to recurrent biliary obstruction (RBO), overall survival (OS), and adverse events.

Results Of 45 enrolled patients, 43 patients underwent biliary drainage, including 42 patients who underwent YABUSAME placement; 66.7% of patients received chemotherapy, and 60% had previously undergone biliary drainage. Drainage methods were partial stent-in-stent, side-by-side, and unilateral in 65.1%, 7.0%, and 27.9% of patients, respectively. Technical and clinical success rates were 93.2% (41/45) and 79.1% (34/45), respectively. The incidence rate of early postprocedural adverse events was 2.2%. The stent patency rate at 6 months was 55.3%. The median time to RBO was 231 days. The median OS was 125 days.

Conclusion This study showed that the primary outcome, the 6-month stent patency rate, exceeded the expected rate of 55%, which indicates the efficacy of YABUSAME placement for MHBO.

Keywords Metallic stent · Endoscopic retrograde cholangiopancreatography · Hilar biliary obstruction · Malignancy · Drainage

Introduction

Endoscopic drainage is the preferred treatment option for managing inoperable malignant hilar biliary obstruction (MHBO). Ensuring that the drainage area covers more than 50% of the liver parenchyma can improve the prognosis and reduce the risk of cholangitis recurrence [1–4]. Recent reports have indicated that the drainage of more than 80% of the liver parenchyma enhances the prognosis [5]. Therefore, the aim is to drain as much liver parenchyma as possible, using 50% as a benchmark. Stent options for MHBO include plastic stents (PS) and self-expandable metallic stents (SEMSs). Although SEMS are typically more expensive, they are associated with longer patency periods. Therefore, stent selection should consider both cost and patency.

When multiple uncovered SEMSs (UCSEMSs) are placed endoscopically via the papillary route, the primary methods are the partial stent-in-stent (PSIS) method, where the first stent is placed and subsequent stents are inserted through the mesh of the initial stent (Fig. 1A); the side-by-side (SBS) method, whereby stents are placed in parallel (Fig. 1B); and a hybrid method that combines the two (Fig. 1C). In prospective trials involving

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UCSEMSs, the median times to recurrent biliary obstruction (TRBO) were 253 and 262 days for the PSIS and SBS methods, respectively (p = 0.865) [6]. Meta-analyses have reported that the median TRBOs are 104–253 days for the PSIS method and 155–262 days for the SBS method [7]. Although some reports have suggested that the median TRBO may be longer with the PSIS method, they are considered equivalent. The median TRBO for the hybrid method has been reported as 189 days [8]. However, there is no clear superiority among these methods for placing multiple UCSEMSs.

UCSEMSs play a pivotal role in the placement of multiple SEMSs in MHBOs. Recently, a 5.4-French ultra-thin sheath, laser-cut UCSEMS was introduced. The ultra-thin delivery sheath and its tapered tip create almost no gap between the sheath and the 0.025-inch guidewire, making it easier to penetrate strictures or the mesh of the initial stent (Fig. 1D, E).

This study aimed to evaluate the clinical performance of a novel UCSEMS with an ultra-thin delivery sheath for unresectable MHBO.

Methods

Ethics Statements

This study was conducted in accordance with the guidelines of the Declaration of Helsinki (as revised in 2013). The protocol was developed before the initiation of the trial and was approved by the National Cancer Center Institutional Review Board (2021–224). This study was registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) (UMIN ID: 000046702). Written informed consent was obtained from all participants before their inclusion in the study.

Study Design

This multicenter prospective observational study was conducted at 11 facilities in Japan from March 2022 to December 2022.

Selection Criteria

The eligibility criteria included patients (1) with clinically and radiographically diagnosed inoperable MHBO, (2) who required biliary drainage with UCSEMS placement, (3) were ≥ 18 years of age, and (3) who provided written

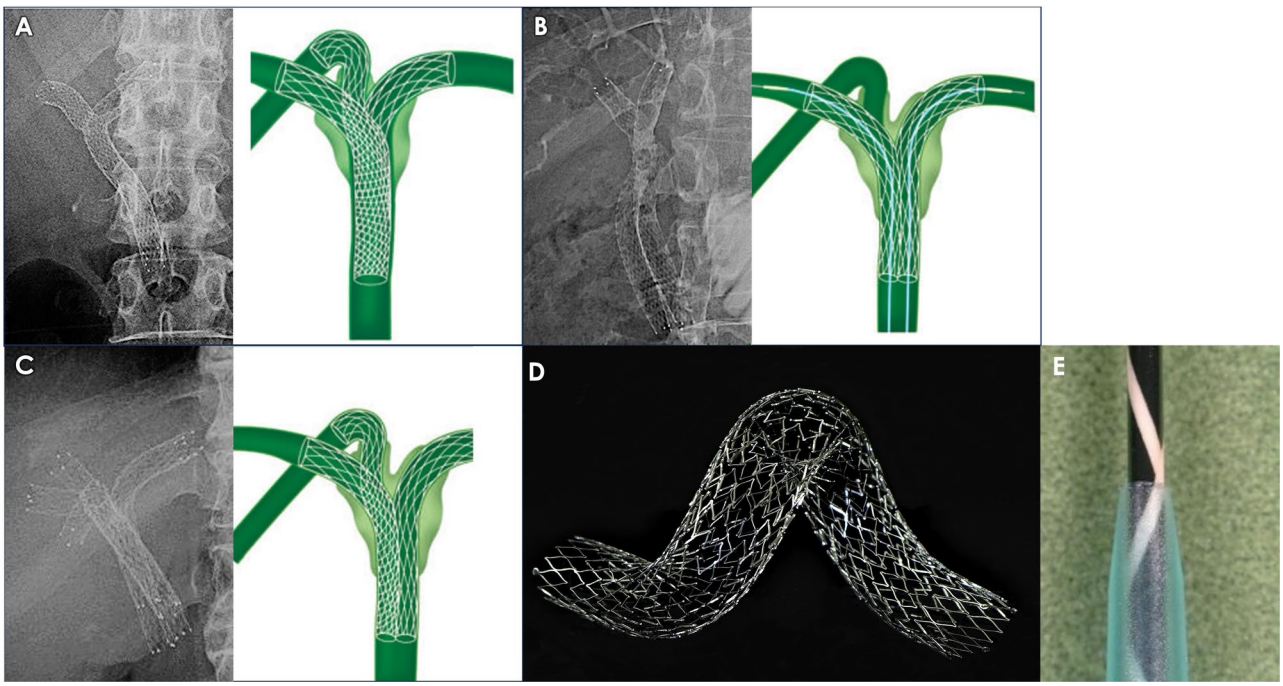

Fig. 1 **A** The partial stent-in-stent method. **B** The side-by-side method. **C** The hybrid method. **D** The uncovered self-expandable metallic stent used in this study (YABUSAME; Kaneka Medix, Osaka, Japan). **E** The gap between the 0.025-inch guidewire and the tapered tip of the delivery sheath is small

informed consent. The Bismuth classification was not considered for eligibility, and type 1 was eligible. The intended drainage area, unilateral or bilateral drainage method, and number of UCSEMS placements were not specified. Patients with in-place removable stents, including PS and fully covered SEMSs, who were planning to switch to UCSEMSs were also eligible.

Exclusion Criteria

Patients intended for UCSEMS placement via endoscopic ultrasound (EUS)-interventional anastomosis or a percutaneous route were excluded, as were those with nonremovable stents already inserted in the hepatic hilum.

Procedure

There were no specific requirements for operators in this study. For stent placement in the hepatic hilum, a novel, laser-cut UCSEMS with a 5.4-French ultra-thin sheath (YABUSAME; Kaneka Medix, Osaka, Japan) was used. Stent diameters of 8 or 10 mm were selected on the basis of the case, and the method of placement (including PSIS, SBS, hybrid, and unilateral drainage) was at the discretion of the operator. Balloon dilatation of the stricture, if performed, was conducted at the operator's discretion.

Study Outcomes

The primary outcome was the stent patency rate at 6 months. The secondary outcomes included the success rate of the procedure, clinical success rate, stent patency rates at 3- and 12 months, TRBO, survival time, and non-RBO-related adverse events.

Definitions

RBO was defined as a biliary obstruction due to stent occlusion or displacement according to the Tokyo Criteria 2014 [9]. The stent patency rate was defined as the proportion of cases that did not experience RBO. The TRBO and survival time were evaluated using the Kaplan–Meier method. Incidents that did not require reintervention or resulted in patient death were treated as censored events. The survival time was defined as the time from the date of stent placement to the date of death; patients still alive at the end of the observation period were censored. Technical success was confirmed when the YABUSAME stent was placed as intended during endoscopic retrograde cholangiopancreatography (ERCP). The clinical success was defined as a 50% reduction in total bilirubin levels within 14 days or a reduction to < 1.5 mg/dL if initially elevated due to hilar or existing stent obstruction and aspartate aminotransferase (AST) and alanine transaminase (ALT) levels decreasing to < 100 IU/L within 14 days, if elevated. Success was considered as no worsening of the total bilirubin or AST/ALT levels compared to the preoperative levels within 14 days, excluding immediate postoperative increases. Adverse events and reactions were assessed according to the Tokyo Criteria 2014 and the American Society of Gastrointestinal Endoscopy lexicon classification [9, 10]. Non-RBO-related adverse events were classified as intraoperative, early (within 30 days), or late (after 31 days) adverse events.

Statistical Analysis

On the basis of previous reports, the 6-month stent patency rates were 31.4% for SBS and 47.1% for PSIS [6]. Therefore, the threshold was set at 35% and the expected rate at 55%, with a one-sided significance level of 5% and a power of 80%, yielding a minimum required sample size of 41. A target sample size of 45 was set to account for a dropout rate of approximately 10%. The 6-month stent patency rate and TRBO were calculated using the Kaplan–Meier method. Under-assessment may have occurred because death without RBO was a competing risk in the Kaplan–Meier analysis. Therefore, we also calculated the cumulative incident rate of RBO while treating death as a competing risk in the competing risk analysis of the stent patency. The comparison of stent patency between patients with and without previous biliary drainage was evaluated using the log-rank test. Univariate and multivariate analyses of the 6-month stent patency rate and TRBO were performed using the χ^2 or Fisher exact test, log-rank test, logistic regression analysis, and Cox proportional hazard model, respectively. Registration began in March 2022 and was closed when the 45th patient was registered in December 2022. A 1-year observation period was followed for the final patient. The intention-to-treat (ITT) analysis defined the success rates on the basis of all registered patients, whereas the full analysis set (FAS) only included patients who underwent ERCP. All statistical analyses were performed using SPSS Statistics for Windows (version 29.0; IBM Corp., Armonk, N.Y., USA), and statistical significance was set at $p < 0.05$.

Results

Patient Characteristics

Forty-five patients were enrolled in the study; one patient was excluded because he was unable to undergo endoscopy due to deteriorating conditions, and in another patient the duodenal papilla could not be reached (Fig. 2). Therefore,

ERCP was performed in 43 patients. YABUSAME was placed in 42 patients and not placed in one patient due to an issue with the development of YABUSAME. As such, 45 patients were included in the ITT analysis, 43 in the FAS, and 42 in the per-protocol set analysis.

The background characteristics of the 45 patients are presented in Table 1. The primary disease was biliary tract cancer in 71.1% (32/45) of the patients (cholangiocarcinoma in the hilar region, $n = 13$; gallbladder cancer, $n = 8$; intrahepatic cholangiocarcinoma, $n = 9$; and distal bile duct cancer, $n = 2$). Of the patients, 66.7% were undergoing chemotherapy, and 7 (15.6%) underwent postoperative bowel reconstruction. Twenty-seven (60%) patients had a history of biliary drainage.

Procedural Outcomes

The median procedural time was 54 min, and YABUSAME was used in 42 patients (97.7%). Thirty-seven patients (86.0%) received only YABUSAME for SEMS implantation in the porta hepatis, and five patients received a combination of YABUSAME and another SEMS (Table 2). One YABUSAME was used in 15 patients (35.7%), two in 24 patients (57.1%), and three in three patients (7.1%). The YABUSAME diameters were 8 mm in 24 patients (57.1%) and 10 mm in 18 patients (42.9%). The final type of stent placement was PSIS with 2 SEMSs in 26 (60.5%), PSIS with 3 SEMSs in 2 (4.7%), SBS in 3 (7.0%), and unilateral drainage in 12 (27.9%) patients. Stenting of the distal bile duct was required in seven patients (16.3%).

Clinical Outcomes

The technical success rate of YABUSAME was 93.2% (41/45) in the ITT analysis (Table 3). As described in the patient characteristics section, ERCP was performed via the transpapillary approach in 43 cases. Among these, YABUSAME stent deployment was unsuccessful in one patient, resulting in successful placement in 42 patients. Additionally, in one patient, only two stents were placed despite an initial plan for three stents. Consequently, intended YABUSAME stent placement was successfully achieved in 41 patients. This means that the technical success rates, including the planned stent placement form and the form different from the planned form, were 95.6% (43/45) in the ITT analysis and 100% (43/43) in the FAS. The clinical success rate (ITT analysis) was 79.1% (34/45), and one clinically unsuccessful case required additional procedures. No adverse events occurred during the procedure. One patient experienced an early adverse event of moderate nonobstructive cholangitis. No late adverse events other than RBO were observed.

Long-term outcomes revealed that the stent patency rate at 6 months was 55.3% (95% confidence interval [CI], 29.5–75.0) (Fig. 3). The median TRBO using the Kaplan–Meier curve was 231 days (95% CI, 121–not reached [NR]), and the median overall survival was 125 days

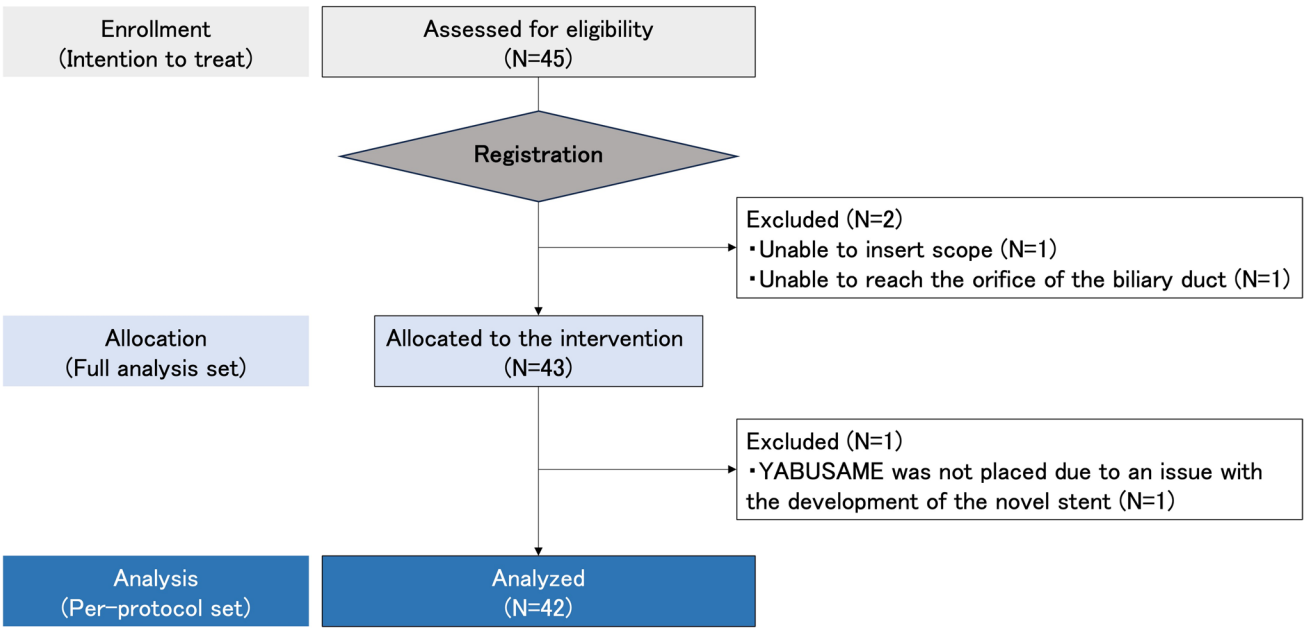

Fig. 2 CONSORT diagram. Forty-five patients were registered (intention-to-treat cohort). Forty-three patients underwent endoscopic therapy for malignant hilar biliary obstruction (full analysis set cohort). Forty-two patients underwent stent placement of YABUSAME in hilar obstruction (per-protocol set cohort). *CONSORT* Consolidated Standards of Reporting Trials

Table 1 Patient characteristics

Variable	ITT cohort ($N=45$), % (n)
Median age, years (IQR)	69 (63–77)
Sex, male	60.0 (27)
ECOG PS (0/1/2)	44.4 (20)/40 (18)/15.6 (7)
Primary disease	
Carcinoma of perihilar bile duct	28.9 (13)
Carcinoma of gallbladder	17.8 (8)
Intrahepatic cholangiocarcinoma	20.0 (9)
Pancreatic carcinoma	13.3 (6)
Carcinoma of distal bile duct	4.4 (2)
Others	15.6 (7)
Pathology of primary disease	
Adenocarcinoma	86.7 (39)
Adenosquamous carcinoma	2.2 (1)
Squamous cell carcinoma	2.2 (1)
Neuroendocrine tumor	4.4 (2)
Others	4.4 (2)
Previous chemotherapy	66.7 (30)
No. of chemotherapy lines, n (IQR)	1 (1–3)
PPI or PCAB	60.0 (27)
MRCP	64.4 (29)
Digestive tract reconstruction	15.6 (7)
Child's reconstruction	4.4 (2)
Roux-en-Y reconstruction	2.2 (1)
Billroth-II reconstruction	2.2 (1)
Billroth-I reconstruction	2.2 (1)
Others	4.4 (2)
Bismuth classification	
1	13.3 (6)
2	13.3 (6)
3a	24.4 (11)
3b	11.1 (5)
4	35.6 (16)
Not applicable	2.2 (1)
Previous biliary drainage	60.0 (27)
Plastic stent	40 (18)
Nasal drainage tube	11.1 (5)
Metallic stent	4.4 (2)
Percutaneous drainage tube	4.4 (2)
Duodenal stenting	0
Median laboratory data, (IQR)	
γ-Glutamyl transpeptidase, IU/L	427 (180–703.3)
Aspartate aminotransferase, IU/L	65 (32–109)
Alanine aminotransferase, IU/L	65 (30–92)
Total bilirubin, mg/dL	1.9 (1.1–8.0)
White blood cell count, /μL	6810 (5300–8760)

ITT intention-to-treat, *IQR* interquartile, *ECOG PS* Eastern Cooperative Oncology Group Performance Status, *no.* number, *PPI* proton pump inhibitor, *PCAB* potassium-competitive acid blocker, *MRCP* magnetic resonance cholangiopancreatography

Table 2 Procedural details

Variable	FAS cohort ($n=43$), % (n)
Procedural time, min (IQR)	54 (36.5–78)
Type of scope	
Duodenoscope	90.7 (39)
Double-balloon enteroscope	7.0 (3)
Forward-viewing endoscope	2.3 (1)
No. of guidewires, n (IQR)	2 (2–3)
Sphincterotomy	60.5 (26)
Balloon dilation for perihilar stenosis	20.9 (9)
Balloon diameter	
3 mm	11.1 (1)
4 mm	77.8 (7)
6 mm	11.1 (1)
YABUSAME placed in perihilar region	97.7 (42)
Combination with SEMS other than YABUSAME	11.6 (5)
Combination with PS	2.3 (1)
No. of YABUSAMEs	
One	35.7 (15/42)
Two	57.1. (24/42)
Three	7.1 (3/42)
Diameter of YABUSAME	
8 mm	57.1 (24)
10 mm	42.9 (18)
SEMS placement method	
PSIS using 2 SEMS	60.5 (26)
PSIS using 3 SEMS	4.7 (2)
SBS	7.0 (3)
Hybrid	0 (0)
Unilateral stenting	27.9 (12)
Additional stent placement for distal biliary tract	16.3 (7)

FAS full analysis set, *IQR* interquartile, *SEMS* self-expandable metallic stent, *PS* plastic stents, *no.* number, *PSIS* partial stent-in-stent method, *SBS* side-by-side method

(Fig. 4). In the competing risk analysis, the cumulative RBO incidence at 6 months was 24.9%, and the median time to cumulative RBO was not reached (95% CI, NR–NR) (Fig. 5). In the subgroup analysis, the TRBO of the patients who had not previously undergone biliary drainage was NR [79–NR], which was tended to be longer than that of patients who had undergone previously biliary drainage (231 [95–NR]) (Fig. 6). This difference was not statistically significant. The univariate and multivariate analyses identified no specific factors contributing to the 6-month RBO and TRBO (Tables 4 and 5).

Table 3 Clinical outcomes

Outcome	ITT cohort ($n=45$) % (n)
Technical success (YABUSAME placed as indicated)	93.2 (41/45)
Technical success (Including unindicated method)	95.6 (43/45)
Clinical success (ITT)	79.1 (34/45)
Clinical success (PPS)	73.3 (33/42)
Additional procedure when clinically unsuccessful	9.1 (1/11)
Adverse events during procedure	0 (0)
Early adverse events	2.2 (1/45)
Non-obstructive cholangitis (Moderate)	2.2 (1/45)
Late adverse events	0 (0)
Stent patency rate	73.8 (31/42)
Median TRBO, % (95% CI)	231 (121–NR)
3-month stent patency rate, % (95% CI)	85 (64.0–94.3)
6-month stent patency rate, % (95% CI)	55.3 (29.5–75.0)
12-month stent patency rate, % (95% CI)	29.5 (6.2–58.6)

ITT intention-to-treat, *PPS* per-protocol set, *TRBO* time to recurrent biliary obstruction, *CI* confidence interval, *NR* not reached

Discussion

We prospectively evaluated data on stent patency during drainage using a laser-cut UCSEMS with an ultra-thin sheath for MHBO. The results revealed that the 6-month stent patency rate and the median TRBO were comparable to those reported previously. The 6-month stent patency rate, which was the primary outcome of this study, was slightly higher than the expected value. When determining the sample size, we referenced Lee et al.'s study, which included only patients without any history of drainage [6]. Therefore, careful consideration is required when interpreting the present study's results. However, despite the tendency for patients with a history of biliary drainage to have shorter stent patency periods in Kaplan–Meier analysis, a median patency of 231 days has been achieved, which suggests that good outcomes are also attainable in patients with a history of biliary drainage.

Several studies have reported on the duration of stent patency for endoscopic drainage of MHBO [11]. Reports comparing PS and UCSEMS showed median TRBOs of 35–250 days for PS and 103–361 days for UCSEMS, with most studies reporting longer TRBOs for UCSEMS [12–17]. However, recently, the feasibility of the suprapapillary placement of PS has been reported because of similar stent

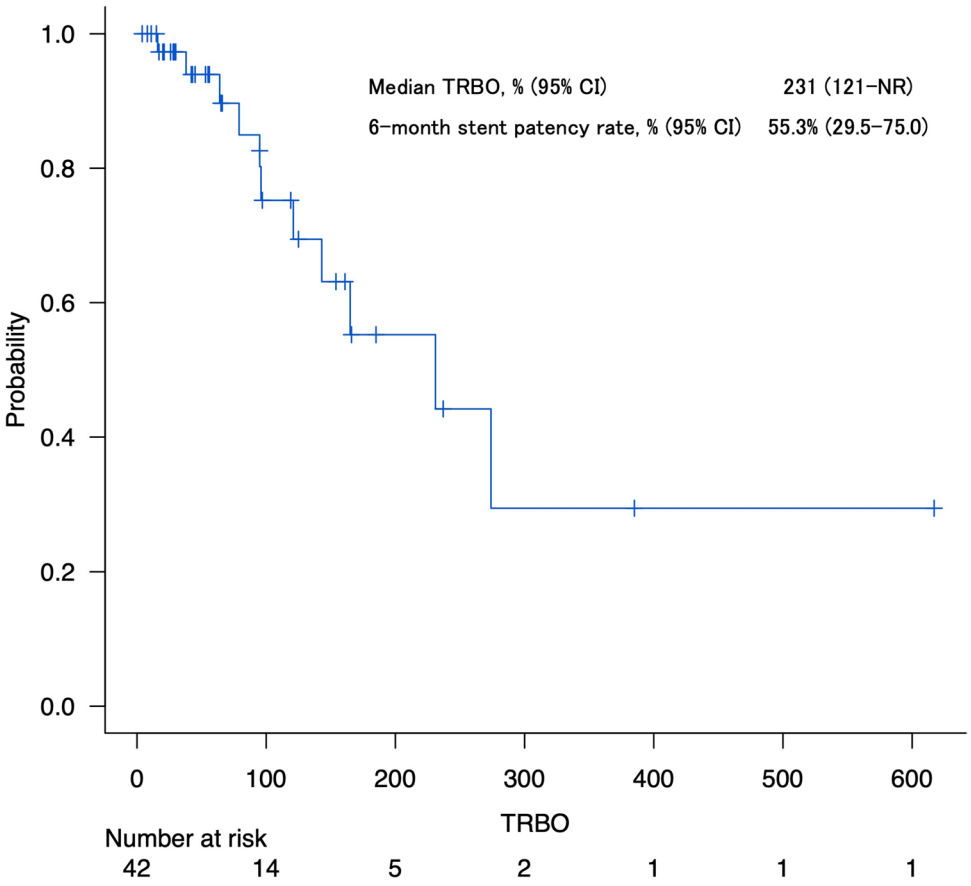

Fig. 3 Long-term clinical outcomes. The time to recurrence of biliary obstruction is described using the Kaplan–Meier curve. *TRBO* time to recurrent biliary obstruction, *CI* confidence interval, *3M* 3-month, *6M* 6-month, *12M* 12-month, *PPS* per-protocol set

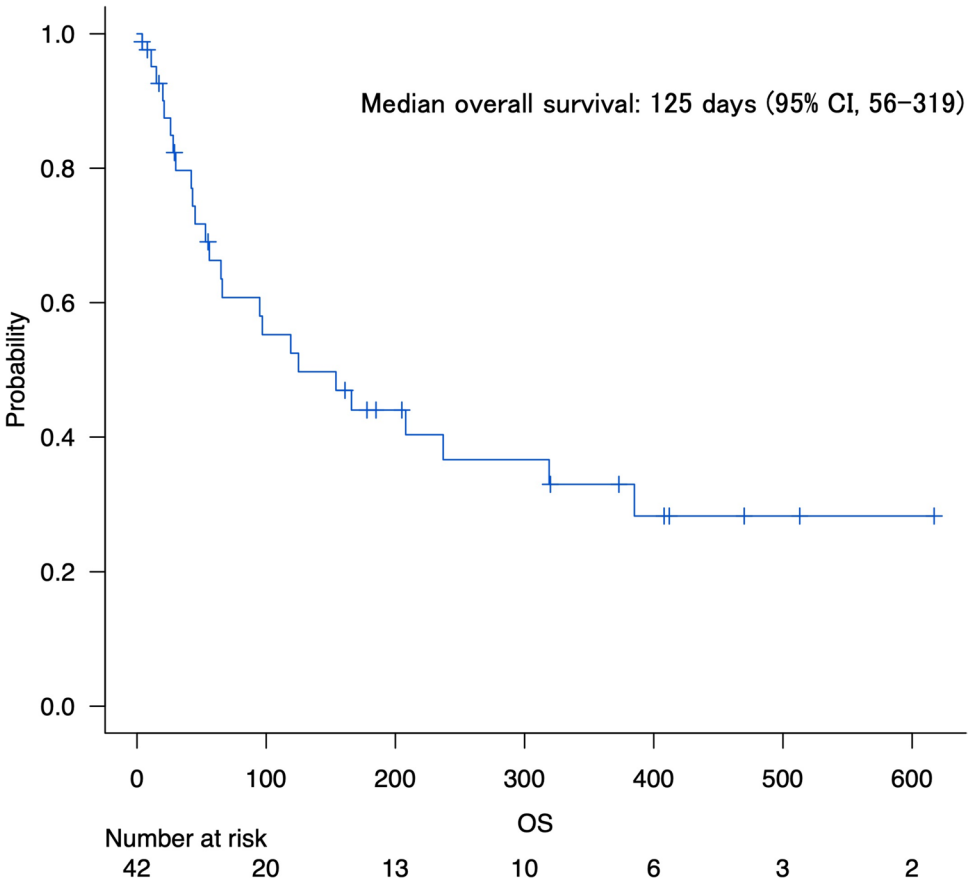

Fig. 4 OS period. The median OS is described using the Kaplan–Meier curve. *OS* overall survival, *CI* confidence interval

patency with UCSEMS [17]. Considering the lower cost of PS, ease of reintervention, and longer prognosis of biliary tract cancer associated with recent developments in chemotherapy, the periodic exchange of suprapapillary PS in the early stages and UCSEMS placement in patients with a short prognosis or in whom reintervention is not recommended could be one of the strategies for unresectable MHBO. In fact, the European Society of Gastrointestinal Endoscopy and American Society for Gastrointestinal Endoscopy guidelines recommend UCSEMS placement in the palliative stage [18, 19].

The drainage history could affect the stent patency of UCSEMS in MHBO; however, a previous report investigated the stent patency of UCSEMS in MHBO only at the initial drainage stage. In our study, 60% of the patients had a history of biliary drainage. The subgroup analysis results suggest that the stent patency period may differ depending on the presence or absence of a history of biliary drainage (Table 4, Fig. 6). However, there was no significant difference between the presence or absence of a history of biliary drainage. In the univariate and multivariate analyses, the drainage history was also a factor that did not significantly contribute to the stent patency. This indicates that YABUSAME could be a useful stent in the palliative stage even after periodic PS exchange.

Regarding the drainage area of the UCSEMS for MHBO, bilateral drainage is recommended when possible because of its associated benefits regarding better patency duration and prognosis [1, 2, 20–22]. Most studies were conducted in patients who were eligible for bilateral drainage. In practice, a case-specific strategy is important, and unilateral drainage could be more appropriate when a part of the liver lobe is atrophic or portal vein obstruction is present, the short prognosis does not indicate bilateral

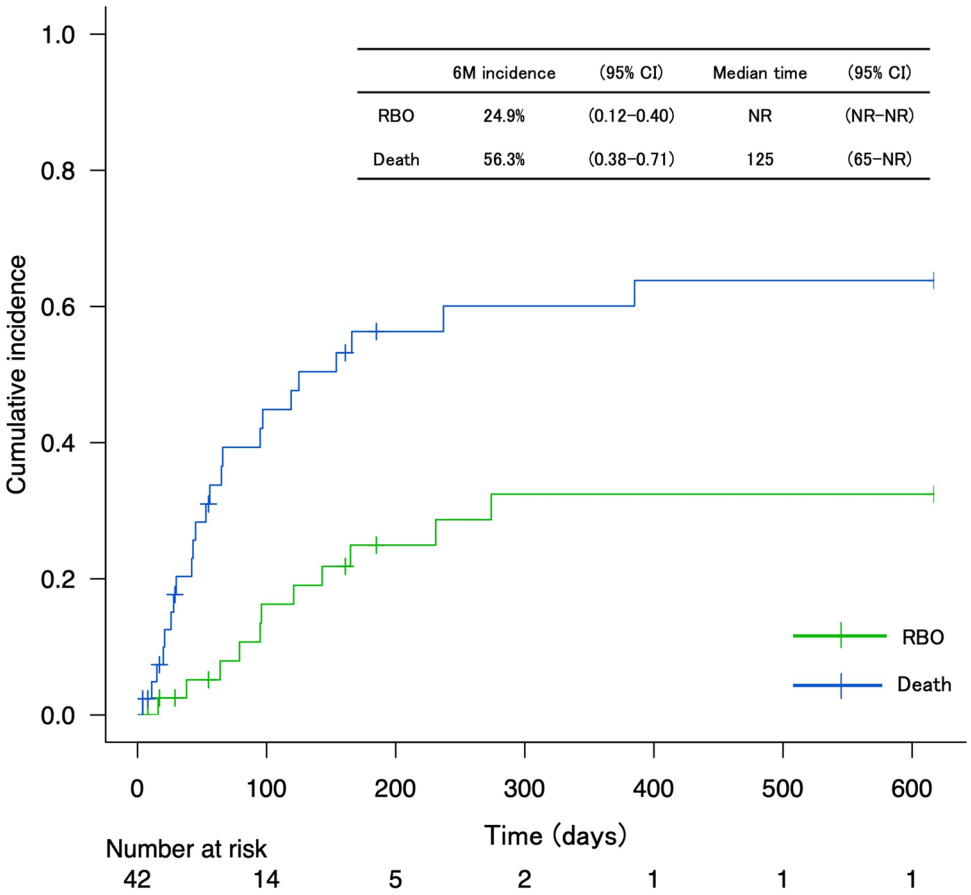

Fig. 5 Cumulative incidence rate. The cumulative incidence rate is analyzed using competing risk analysis, in which death is the competitive risk of RBO. *6M* 6-month, *CI* confidence interval, *RBO* recurrence of biliary obstruction, *NR* not reached

drainage, or there is a complicated obstruction pattern. Additionally, unilateral drainage may be a viable option if jaundice can be improved using this method, because subsequent reintervention is easier. Of note, 27% of cases in our study involved unilateral drainage, which may be because we did not exclude cases in which unilateral drainage would be recommended. In fact, the median overall survival time was 125 days in this study, indicating that the patients included in this prospective study had limited prognoses. The stent patency rate at 6 months of over 55% and the median stent patency period of 231 days indicate that YABUSAME was acceptable as the final palliative stenting for MHBO.

YABUSAME, which was placed for MHBO in this study, has a thin sheath and tapered structure at the tip that contributed significantly to the success of the procedure. The technical success rate (including unindicated manners) in the FAS was 100%, whereas the technical success rate of UCSEMS placement in prospective studies was approximately 90%, suggesting that stent characteristics may have contributed to these results [6, 17]. The stent patency was not inferior to that in previous reports. Therefore, this stent may be useful in cases in which UCSEMS placement is intended.

The present study has some limitations such as not being a randomized controlled trial, having a small sample cohort, and including patients regardless of the Bismuth classification. Further, the stenting method and number of stents were not specified, the initial drainage and reintervention were mixed, a population with a short prognosis was also included, and bilateral drainage, which is the current standard treatment, was not indicated in all patients. Although

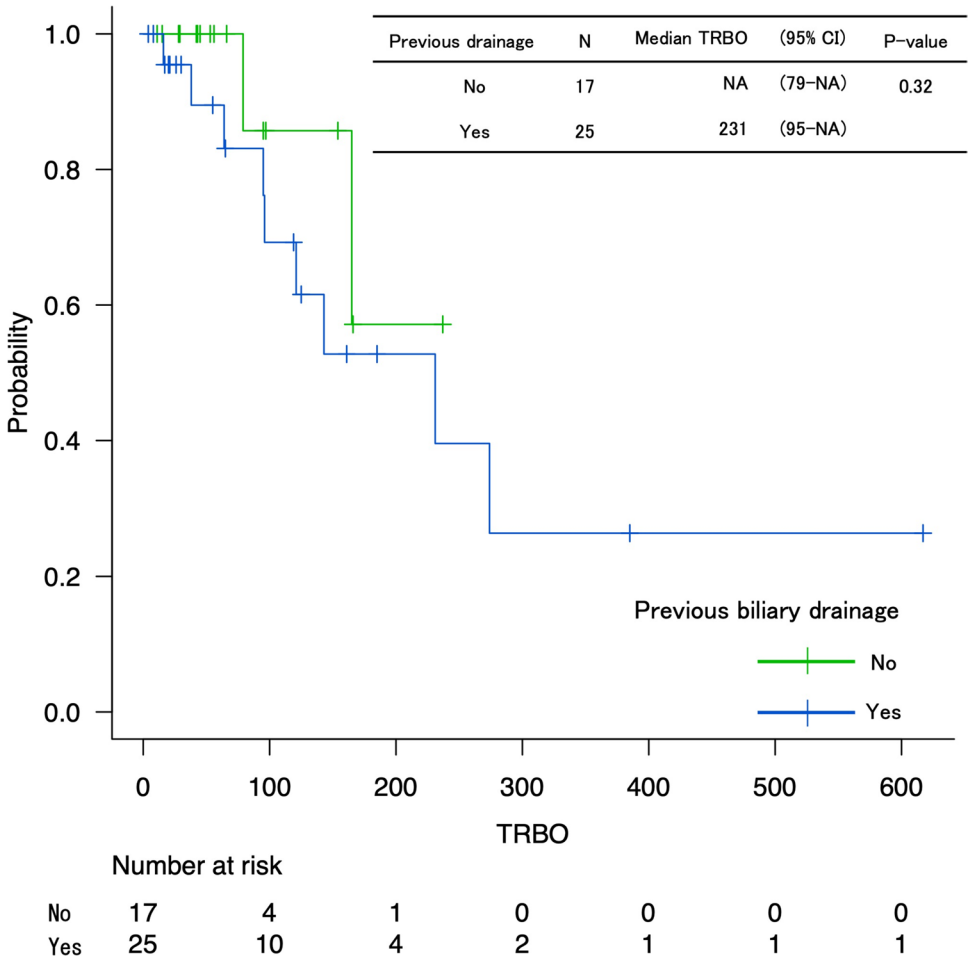

Fig. 6 Subgroup comparison of median TRBO in patients with or without previous biliary drainage using the log-rank test. *TRBO* time to recurrent biliary obstruction, *CI* confidence interval, *NA* not applicable

chemotherapy has the ability to prolong the stent patency, the continuation or initiation of chemotherapy after the procedure has not been recorded [23]. Thus, data from a future prospective study conducted at a Japanese multicenter institution, in which a single type of UCSEMS is used for MHBO following actual clinical practice, would be valuable.

In conclusion, we performed stent placement using a single type of UCSEMS according to the current treatment

Table 4 Results of univariate analysis of 6-month RBO

Factor	*N*	6-month RBO (95% CI)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age, years						
≥ 75	14	28.6 (8.4–58.1)	1.84 (0.41–8.33)			
< 75	28	17.9 (6.1–36.9)	1 (reference)			
Sex				0.28		
Male	26	26.9 (11.6–47.8)	2.58 (0.46–14.4)			
Female	16	12.5 (1.6–38.3)	1 (reference)			
Primary disease				0.27		
BTC	21	28.6 (11.3–52.2)	2.40 (0.51–11.30)			
Other than BTC	21	14.3. (3.0–36.3)	1 (reference)			
Chemotherapy				0.53		0.12
Yes	29	24.1 (10.3–43.5)	1.75 (0.31–9.87)		5.29 (0.64–43.7)	
No	13	15.4 (1.9–45.4)	1 (reference)		1 (reference)	
Concurrent PPI or PCAB				0.66		
Yes	26	19.2 (6.6–39.4)	0.71 (0.16–3.18)			
No	16	25 (7.3–52.4)	1 (reference)			
Bismuth classification				NA		
Type1 or 2	11	18.2 (2.3–51.8)	0.76 (0.13–4.38)		0.32 (0.04–2.58)	0.28
Other	31	22.6 (9.6–41.1)	1 (reference)		1 (reference)	
YABUSAME diameter				0.52		
8 mm	24	25 (9.8–46.7)	1.67 (0.36–7.82)			
10 mm	18	16.7 (3.6–41.4)	1 (reference)			
Sphincterotomy				0.30		
Yes	25	16 (4.5–36.1)	0.46 (0.10–2.04)			
No	17	29.4 (10.3–56.0)	1 (reference)			
Balloon dilation for perihilar				0.33		
Yes	9	33.3 (7.5–70.1)	2.25 (0.44–11.60)			
No	33	18.2 (7.0–35.5)	1 (reference)			
Drainage method				0.76		
Bilateral	31	22.6 (9.6–41.1)	1.31 (0.23–7.54)			
Unilateral	11	18.2 (2.3–51.8)	1 (reference)			
Stent for distal biliary tract				NA		
Yes	7	0 (0–0.41)	0.01 (0.00–NA)			
No	35	25.7 (12.5–43.3)	1 (reference)			
Previous biliary drainage				0.22		0.06
Yes	25	28 (12.1–49.4)	2.92 (0.53–16.20)		7.18 (0.91–56.9)	
No	17	11.8 (1.5–36.4)	1 (reference)		1 (reference)	
Total bilirubin				0.08		
≥ 2.0	21	9.5 (1.2–30.4)	0.21 (0.04–1.17)			
< 2.0	21	33.3 (14.6–57.0)	1 (reference)			

RBO recurrent biliary obstruction, *OR* odds ratio, *BTC* biliary tract cancer, *PPI* proton pump inhibitor, *PCAB* potassium-competitive acid blocker, *NA* not applicable, *CI* confidence interval

Table 5 Results of univariate analysis of TRBO

Factor	*N*	TRBO, days (95% CI)	Univariate analysis		Multivariate analysis	
			HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age				0.37		
≥ 75	14	NA (95–NA)	0.79 (0.48–1.32)			
< 75	28	231 (143–NA)	1 (reference)			
Sex				0.10		
Male	26	143 (95–231)	3.09 (0.81–11.78)			
Female	16	274 (79–NA)	1 (reference)			
Primary disease				0.59		
BTC	21	231 (96–NA)	0.71 (0.20–2.50)			
Other than BTC	21	165 (79–NA)	1 (reference)			
Chemotherapy				0.40		0.24
Yes	29	274 (95–NA)	1.79 (0.46–6.91)		2.32 (0.57–9.46)	
No	13	231 (121–NA)	1 (reference)		1 (reference)	
Taking PPI or PCAB				0.89		
Yes	26	231 (95–NA)	1.09 (0.33–3.65)			
No	16	274 (79–NA)	1 (reference)			
Bismuth classification				0.76		0.59
Type 1 or 2	11	274 (64–NA)	0.83 (0.24–2.87)		0.71 (0.20–2.52)	
Others	31	165 (95–NA)	1 (reference)		1 (reference)	
YABUSAME diameter				0.16		
8 mm	24	165 (79–NA)	2.74 (0.67–11.18)			
10 mm	18	274 (95–NA)	1 (reference)			
Sphincterotomy				0.69		
Yes	25	231 (121–NA)	1.28 (0.38–4.25)			
No	17	NA (79–NA)	1 (reference)			
Balloon dilation for perihilar				0.18		
Yes	9	121 (96–NA)	2.61 (0.64–10.58)			
No	33	274 (143–NA)	1 (reference)			
Drainage method				0.54		
Bilateral	31	NA (79–NA)	1.62 (0.35–7.53)			
Unilateral	11	231 (121–NA)	1 (reference)			
Stent for distal biliary tract				0.30		
Yes	7	274 (NA–NA)	0.34 (0.04–2.67)			
No	35	165 (96–NA)	1 (reference)			
Previous biliary drainage				0.33		0.23
Yes	25	231 (95–NA)	2.16 (0.45–10.25)		2.71 (0.54–13.6)	
No	17	NA (79–NA)	1 (reference)		1 (reference)	
Total bilirubin				0.43		
≥ 2.0	21	231 (143–NA)	0.58 (0.15–2.21)			
< 2.0	21	274 (79–NA)	1 (reference)			

TRBO time to recurrent biliary obstruction, *HR* hazard ratio, *NA* not applicable, *BTC* biliary tract cancer, *PPI* proton pump inhibitor, *PCAB* potassium-competitive acid blocker, *CI* confidence interval

strategy for MHBO. All patients in whom the duodenal papilla could be approached experienced technical successes, and the median duration of stent patency was 231 days, which was comparable to those of previous reports. Thus, this novel stent is useful as a palliative stent in terms of the high technical success rate and long stent patency regardless of the history of biliary drainage. It is especially recommended for patients whose expected prognosis is less than six months. Further research on the optimal strategy for drainage in unresectable MHBO and appropriate metal stents in the palliative stage is warranted.

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Data Availability No datasets were generated or analyzed during the current study.

Declarations

Competing interests Kotaro Takeshita, Susumu Hijioka, Kenji Ikezawa, Takeshi Ogura, Masaki Kuwatani, Nao Fujimori, Shinpei Doi, Masato Endo, Saburo Matsubara, Reiko Yamada, Hirosato Mashima, Mikinori Kataoka, Ryoji Takada, Atsushi Okuda, Akihisa Ohno, Nobuhiro Katsukura, Hirokiyo Suzuki, Takamitsu Tanaka, Masanari Sekine, Hidetoshi Kitamura, and Takuji Okusaka have no conflicts of interest to disclose.

Ethical approval The protocol was developed before the initiation of the trial and was approved by the National Cancer Center Institutional Review Board (2021-224).

Consent to participate Written informed consent was obtained from all participants before their inclusion in the study.

Consent to publish Not applicable.

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