Thieme

Comparison of stent patency between EUS-guided hepaticogastrostomy with bridging and endoscopic transpapillary biliary drainage for hilar obstruction

Authors

Kotaro Takeshita[1], Susumu Hijioka[1], Yoshikuni Nagashio[1], Yuta Maruki[1], Akihiro Ohba[1], Yuki Kawasaki[1], Tetsuro Takasaki[1], Shin Yagi[1], Daiki Agarie[1], Hidenobu Hara[1], Yuya Hagiwara[1], Daiki Yamashige[1], Kohei Okamoto[1], Soma Fukuda[1], Masaru Kuwada[1], Mark Chatto[1], Shunsuke Kondo[1], Chigusa Morizane[1], Hideki Ueno[1], Yutaka Saito[2], Takuji Okusaka[1]

Institutions

1 Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital, Tokyo, Japan
2 Endoscopy Division, National Cancer Center Hospital, Tokyo, Japan

Keywords

Pancreatobiliary (ERCP/PTCD), Strictures, Endoscopic ultrasonography, Biliary tract, Intervention EUS

received 20.2.2024
accepted after revision 12.4.2024

Bibliography

Endosc Int Open 2024; 12: E875–E886
DOI 10.1055/a-2333-7898
ISSN 2364-3722

Georg Thieme Verlag KG, Rüdigerstraße 14,
70469 Stuttgart, Germany

Corresponding author

Dr. Susumu Hijioka, MD.,PhD, National Cancer Center Japan, Department of Hepatobiliary and Pancreatic Oncology, 5-1-1 Tsukiji, Chuo-ku, Tokyo, 104-0045, Japan
shijioka@ncc.go.jp
rizasusu@gmail.com

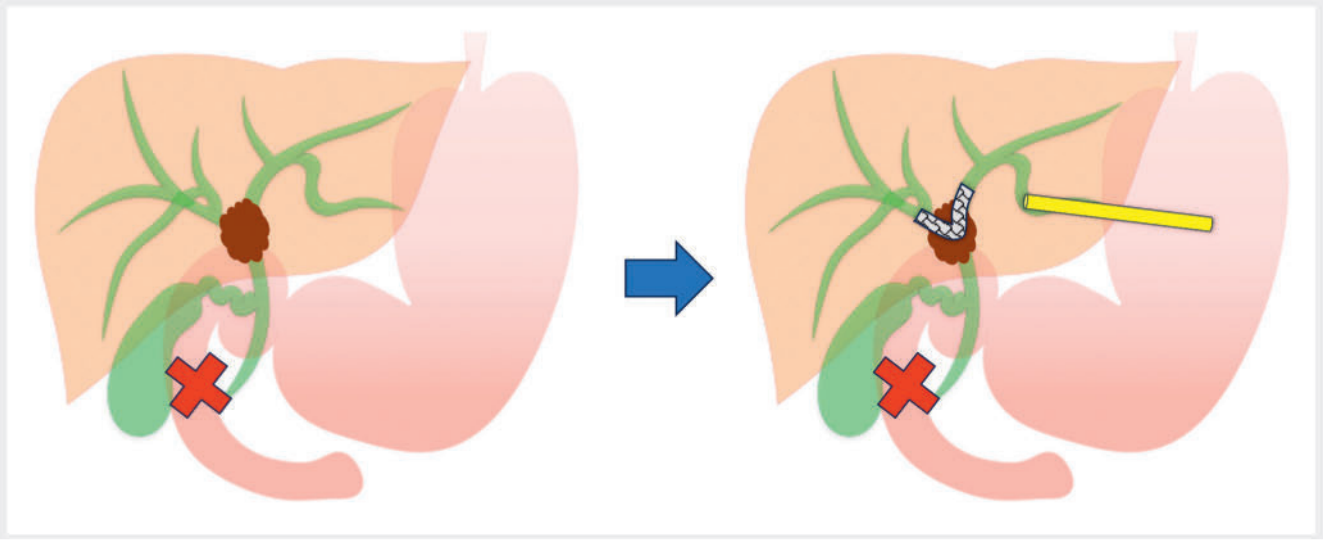
ABSTRACT

Background and study aims Endoscopic ultrasound-guided hepaticogastrostomy with bridging between the left and right bile ducts is an alternative to endoscopic transpapillary drainage for malignant hilar biliary obstruction. We aimed to analyze the long-term stent patency of endoscopic ultrasound-guided hepaticogastrostomy with bridging.

Patients and methods Patients who underwent endoscopic ultrasound-guided hepaticogastrostomy with bridging between April 2018 and July 2023 were retrospectively analyzed. We retrospectively compared the stent patency of these patients with that of the individuals who underwent endoscopic transpapillary drainage-multi-stenting using unmatched (entire) and propensity score-matched cohorts.

Results Endoscopic ultrasound-guided hepaticogastrostomy with bridging had a technical success rate of 90% (18/20). Adverse events were minimal. The number of clinical success cases was 17 and 82 for endoscopic ultrasound-guided hepaticogastrostomy with bridging using metallic stent and endoscopic transpapillary drainage-multi-stenting, respectively. The recurrent biliary obstruction rate was 17.6% and 58.5% for endoscopic ultrasound-guided hepaticogastrostomy with bridging and endoscopic transpapillary drainage-multi-stenting, respectively; the median time to recurrent biliary obstruction (days) was significantly longer for endoscopic ultrasound-guided hepaticogastrostomy with bridging in the entire (not reached vs. 104, $P=0.03$) and propensity score-matched (183 vs. 79, $P=0.05$) cohorts. The non-recurrent biliary obstruction rate for endoscopic ultrasound-guided hepaticogastrostomy with bridging was 91.6% at 3 and 6 months and 57% at 12 months. Multivariate analyses revealed that endoscopic ultrasound-guided hepaticogastrostomy with bridging contributed to a lower recurrent biliary obstruction incidence (hazard ratio, 0.31, $P=0.05$) without significant difference.

Conclusions Stent patency was significantly better for endoscopic ultrasound-guided hepaticogastrostomy with bridging. However, future prospective studies are needed.



▶ **Fig. 1** Endoscopic ultrasound-guided hepaticogastrostomy (EUS-HGS) with bridging method, in which stenting is performed between the right and left bile duct via the EUS-HGS route, allows bilateral drainage without percutaneous transhepatic biliary drainage in cases inaccessible to retrograde drainage.

Introduction

Biliary drainage is necessary for unresectable malignant hilar biliary obstruction (MHBO) caused by obstructive jaundice or cholangitis. In addition, endoscopic transpapillary biliary drainage (ETBD) is the first-choice drainage method for MHBO. However, complex intrahepatic bile duct stenosis in unresectable MHBO renders the appropriate drainage method selection difficult because factors such as bile duct anatomy, presence of hepatic atrophy, prognosis, and Bismuth classification must be considered [1].

Although various drainage methods for MHBO have been reported, the time to recurrent biliary obstruction (TRBO) varies among reports, and the optimal stenting method has not yet been established [1, 2, 3, 4, 5, 6, 7]. Recent reports suggest that self-expandable metallic stents (SEMSs) demonstrate superiority over plastic stents (PSs) in terms of stent patency duration despite the controversy regarding stent type selection in MHBO [1, 2, 3, 4]. Furthermore, the feasibility of side-by-side (SBS), partial stent-in-stent (PSIS), and hybrid (SBS and PSIS combined) methods for transpapillary SEMSs placement in MHBO, particularly in Bismuth type ≥II complex cases, has been reported [5, 6]. A prospective randomized study revealed that the median TRBO was similar for SBS and PSIS (262 and 253 days, respectively) [5]. In addition, a meta-analysis comparing SBS and PSIS showed that overall median TRBO in three analyzed publications was 155 to 262 and 104 to 253 days for SBS and PSIS, respectively [7]. Although these values were comparable, forest plot results of a fixed-effects model indicated a significantly longer median TRBO for PSIS than for SBS ($P = 0.006$) [7]. Furthermore, a study about the hybrid method reported a median TRBO of 189 days [6].

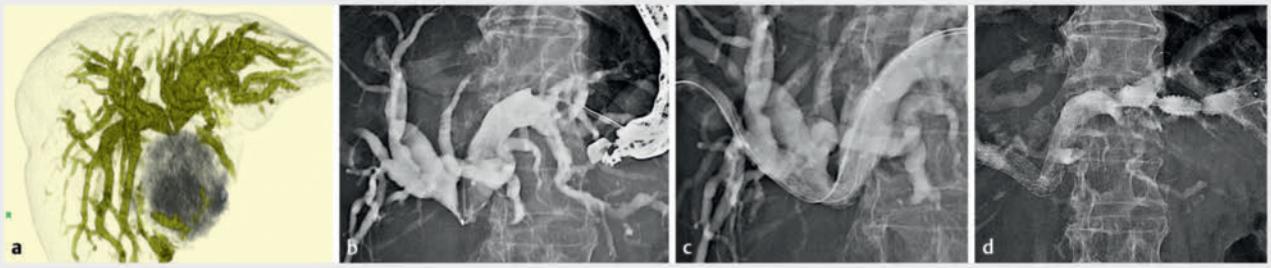
Endoscopic ultrasound-guided biliary drainage (EUS-BD) is widely used for cases in which ETBD is difficult for various reasons. The primary target of EUS-BD, particularly EUS-guided hepaticogastrostomy (EUS-HGS), conventionally focuses on addressing distal biliary obstruction. However, the EUS-HGS with bridging (EUS-HGSB) method, in which stenting is performed between the left and right bile ducts via the EUS-HGS route, has recently been developed for MHBO, allowing for bilateral drainage without ETBD or percutaneous transhepatic biliary drainage (▶ **Fig. 1**) [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19]. Currently, only three reports about the EUS-HGSB method, excluding case reports, are available, indicating technical and clinical success rates of 50% to 100% [10, 11, 12]. However, the previous reports primarily focused on technical and clinical success rates of EUS-HGSB as an alternative to ETBD, and no reports have addressed long-term outcomes after stent placement (for example, rate and causes of RBO and TRBO).

Therefore, this study aimed to retrospectively evaluate clinical outcomes and stent patency of EUS-HGSB for bilateral drainage in unresectable MHBO. We conducted a comparative study to better evaluate the long-term outcome and prove the non-inferiority of EUS-HGSB in MHBO cases. Specifically, we compared stent patency in patients with MHBO who had an inaccessible papilla and received EUS-HGSB with that in those who had an accessible papilla and underwent ETBD-MS.

Patients and methods

Patients

This study included patients referred for EUS-HGSB or ETBD-MS between April 2018 and July 2023. Patients who received PSs or only one metallic stent, those without malignant stenosis, those with missing data, or those who had no post-procedure follow-up were excluded. We retrospectively analyzed patients in whom EUS-HGSB was attempted due to unapproachable papilla. In addition, we compared stent patency outcomes between EUS-HGSB using SEMS and ETBD-MS among those who



▶ **Fig. 2** Endoscopic ultrasound-guided hepaticogastrostomy (EUS-HGS) with bridging. **a** A computed tomography scan before drainage shows a malignant hilar biliary obstruction (Bismuth type II). **b** The bile duct is punctured by a 19-gauge fine needle aspiration needle, followed by the insertion of a catheter into the hilar portion and contrast injection. **c** The guidewire is inserted into the right biliary duct, and an uncovered metallic stent is deployed. **d** Finally, a fully-covered metallic stent is deployed via the EUS-HGS route.

achieved clinical success in the entire and propensity score matched (PSM cohort) cohorts and determined factors contributing to RBO using univariate and multivariate analysis.

This study protocol was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the National Cancer Center Institutional Review Board (approval number: 2018–149). The requirement for informed consent was met by providing a summary of the study on the institution's website and allowing individuals to opt out.

Techniques

The indication for EUS-HGSB in our institution was unresectable MHBO with Bismuth types II-IV biliary obstruction, for which a transpapillary approach was difficult. In patients who did not undergo EUS-HGS, we punctured with a 19-G fine needle aspiration needle (EZ Shot3 Plus; Olympus, Tokyo, Japan), placed a guidewire (M Through; Medicos Hirata, Tokyo, Japan), and dilated the anastomosis with an instrumented dilator (ES dilator; ZEON Medical, Tokyo, Japan). A guidewire was negotiated via the EUS-HGS route to the right bile duct and an uncovered SEMS (ZEO stent, ZEON Medical, Tokyo, Japan; or YABUSAME, KANEKA, Tokyo, Japan) was placed from the right to the left biliary duct as a bridging stent (▶ **Fig. 2**). In cases of patients with Bismuth type IIIa or IV obstructions requiring stenting in the anterior and posterior segment branches, placement of two uncovered SEMS, similar to PSIS, was occasionally attempted in these branches [14]. Specifically, guidewires were placed in the anterior and posterior branches, and a SEMS was initially placed in the branch with the steepest angle. Subsequently, a guidewire was placed through the mesh gap in that stent to the remaining branches and a second SEMS was placed.

When the guidewire could not be negotiated into the right bile duct via the EUS-HGS route, we performed balloon occlusion [20] (occlusion of the common bile duct to insert the guidewire into the right hepatic duct) (▶ **Fig. 3a**). In contrast, two guidewires were placed in the right bile duct (double guidewire technique [21]) when a device could not be inserted into the right bile duct through the guidewire (▶ **Fig. 3b** and ▶ **Fig. 3c**). However, if stent delivery insertion remained difficult under the double guidewire technique, the hilar stenosis was dilated with a balloon catheter, and stent delivery insertion was reattempted (▶ **Fig. 3d**).

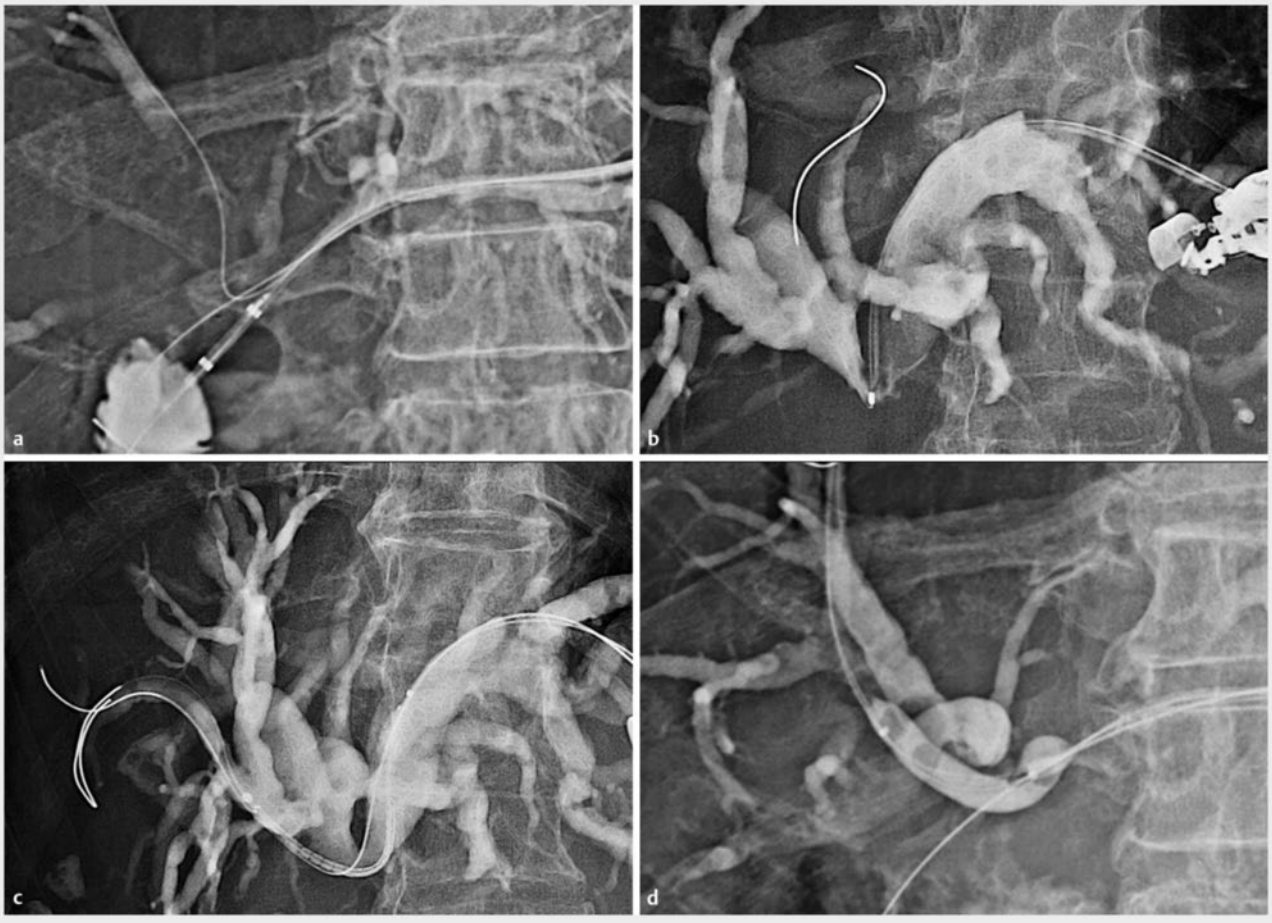
Outcomes and definitions

The study endpoints included technical and clinical success rates, incidence of RBO, TRBO, overall survival (OS), and other adverse events (AEs). The Tokyo Criteria 2014 were used to define RBO, TRBO, technical success, and clinical success [22]. In addition, the aim of the drainage strategy for MHBO was to drain at least 50% of the liver volume. Technical success was defined as achievement of stent placement as planned. Furthermore, if EUS-HGSB required two sessions due to initial procedure difficulties, to mitigate the risk of longer procedure times causing AEs, a stenting procedure spanning two sessions was deemed technically successful, provided no additional invasive interventions occurred between sessions. Clinical success was defined as a 50% decrease in or normalization of the bilirubin level within 14 days of stent placement. RBO was defined as a composite endpoint of occlusion or migration, and time to recurrent biliary obstruction referred to the time from SEMS placement to biliary obstruction recurrence. AEs other than RBO were classified according to the American Society for Gastrointestinal Endoscopy guidelines for AEs during the procedure, early AEs within 30 days from stent placement, and late AEs subsequently [23].

Statistical analysis

Continuous variables are expressed as medians and ranges and were evaluated using the Mann-Whitney U test. $\chi 2$ test or Fisher's exact test was used to evaluate the nominal variables and TRBO was evaluated with the log-rank test using the Kaplan-Meier method. Multivariate analysis using the Cox proportional hazards model was also performed to identify factors contributing to RBO.

Technical and clinical success rates and incidence of AEs other than RBO were determined in patients indicated for EUS-HGSB as a single-arm analysis. For the RBO rate, TRBO, and OS, the EUS-HGSB and ETBD-MS groups were compared between the entire and the PSM cohorts. PSM was performed to reduce the effects of selection bias. Logistic regression was used to estimate the propensity score based on age (>65 years or ≤65



▶ **Fig. 3** Troubleshooting in endoscopic ultrasound-guided hepaticogastrostomy with bridging. **a** Balloon occlusion method. For occlusion of a distal side biliary duct, the use of a multi-lumen balloon catheter renders negotiation into the right biliary duct easier. **b,c** Double guidewire method. Two guidewires are placed into the right bile duct; this obturates the hilar sharp angle and allows stent delivery insertion into the right bile duct. **d** Balloon dilation method. Balloon dilation of the hilar stenosis allows stent delivery insertion into the right bile duct, even in cases in which stent delivery insertion under the double guidewire method is difficult.

years), sex, primary disease (biliary or non-biliary tract cancer), stenosis type (Bismuth type II/III(a + b)/IV), distant metastasis, liver metastasis, portal vein stenosis, and ascites, using a 1:1 nearest-neighbor matching protocol without replacement and a caliper width of 0.2. The clinical characteristics before and after PSM were evaluated using the standardized mean difference (SMD) in addition to the *P* value.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, New York, United States), and statistical significance was set at $P < 0.05$.

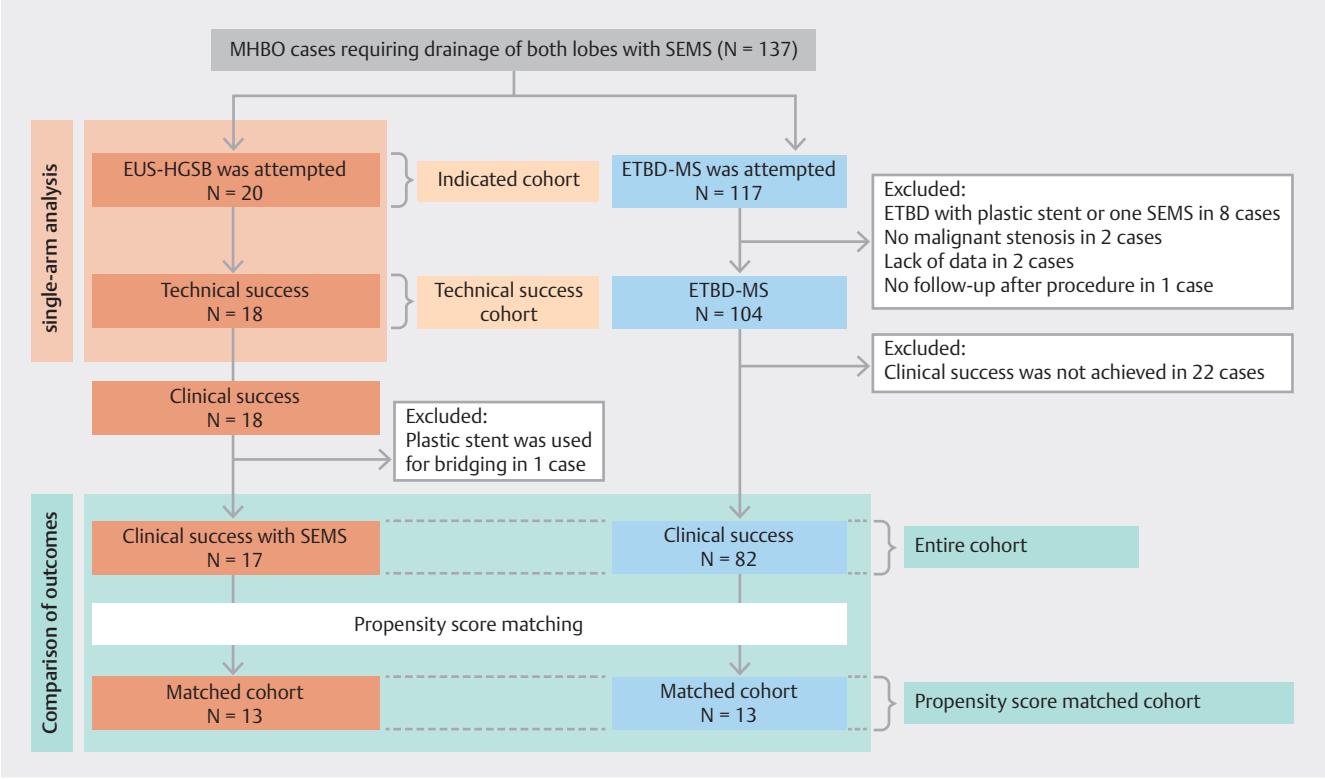
Results

Characteristics of patients referred for EUS-HGSB

A total of 137 patients with MHBO were referred for EUS-HGSB or ETBD-MS. EUS-HGSB and ETBD-MS were attempted in 20 patients (14.6%) (median age 71.5 years, range 47–85 years; 40% male) and 117 patients (85.4%), respectively (▶ **Fig. 4**). Overall, 18 patients (90%) and 82 patients (78.8%) achieved clinical success with EUS-HGSB and ETBD-MS, respectively. The difficulty in accessing the papilla, necessitating EUS-HGSB, was attributed to gastric outlet obstruction and digestive tract reconstruction in 55% and 45% of patients, respectively. ▶ **Table 1** presents the primary disease and stenosis type. Furthermore, simultaneous EUS-HGSB was planned in 13 (65%) patients.

Procedure details in patients referred for EUS-HGSB

▶ **Table 2** presents procedure outcomes for the indicated (n = 20) and technical success (n = 18) cohorts. In the technical success cohort, bridging initially failed in two patients but was successful upon retry. Fifteen and three patients received one and two stents, respectively, using the PSIS method. In all patients in the technical success cohort except one, an 8-mm uncovered SEMS was placed. Techniques such as balloon occlusion, double guidewire, balloon dilatation of hilar stenosis, and use of 8-mm fully-covered SEMS and 7F PSs via EUS-HGS were similarly applied in both cohorts.



▶ **Fig. 4** Study population flowchart. MHBO, malignant hilar biliary obstruction; EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; ETBD-MS, endoscopic transpapillary biliary drainage with multi-stenting; SEMS, self-expandable metallic stent.

Clinical outcomes in patients referred for EUS-HGSB

The technical success rate for the indicated cohort was 90% (18 of 20) (▶ **Table 3**). One failure involved the challenge of inserting the device despite successful guidewire navigation into the right bile duct and the other was due to difficulties in both contrast and guidewire manipulation into the right bile duct. Clinical success rates were 90% and 100% for the indicated and technical success cohorts, respectively.

The median observation period for assessing stent patency in EUS-HGSB was 60 days (range 9 to 465), and the RBO rate was 16.7% (3 of 18). One patient had bridging stent dysfunction and two experienced hepaticogastrostomy (HGS) stent dysfunction. The non-RBO rate was 91.6% at 3 and 6 months and 57% at 12 months.

For early AEs, one patient had moderate cholangitis, while no AEs during procedure or late AEs were observed.

Comparison with ETBD-MS

In the 18 technically successful EUS-HGSB cases, stent patency was examined in 17, excluding one case in which a PS was used for bridging. Of the 117 attempts at ETBD-MS, 104 were technically successful, with 82 of these also achieving clinical success, forming the control group (▶ **Table 4**). The EUS-HGSB group had significantly higher instances of duodenal strictures (47.1% vs. 3.7%, P <0.01) and intestinal tract reconstructions (52.9% vs. 8.5%, P <0.01) than the ETBD-MS group. PSM was applied to all characteristics except duodenal stenosis and intes-

▶ **Table 1** Characteristics of patients indicated for EUS-HGSB.

Characteristics, n = 20	Indicated, n = 20
Age, years	71.5 (47–85)
Sex, male	8 (40)
Primary disease	
▪ Biliary tract cancer	12 (60)
▪ Pancreatic cancer	5 (25)
▪ Other cancers	3 (15)
Reason for ETBD difficulty	
▪ Gastric outlet obstruction	11 (55)
▪ Reconstruction of the digestive tract	9 (45)
Stenosis type (Bismuth type II/IIIa/IIIb/IV)	9/9/0/2
Timing of EUS-HGS	
▪ EUS-HGS already performed	7 (35)
▪ EUS-HGS performed at the time of bridging	13 (65)

▶ **Table 2** Procedural outcomes of patients who underwent EUS-HGSB in indicated and technical success cohorts.

Procedure details	Indicated, n = 20	Technical success, n = 18
Median procedure time, min	93.5 (30–155)	93.5 (30–155)
Target biliary duct of EUS-HGS		
▪ B2	5 (25)	4 (22.2)
▪ B3	15 (75)	14 (77.8)
Puncture route of EUS-HGS		
▪ Stomach	18 (90)	17 (94.4)
▪ Jejunum	2 (10)	1 (5.6)
Dilation of EUS-HGS anastomosis		
▪ Mechanical dilator	20 (100)	18 (100)
Balloon occlusion method	5 (25)	4 (22.2)
Double guidewire method	11 (55)	11 (61.1)
Balloon dilation of hilar stenosis	9 (45)	8 (44.4)
Number of sessions required for bridging		
▪ One	NA	16 (88.8)
▪ Two	NA	2 (11.2)
Number of bridging stents		
▪ One	NA	15 (83.3)
▪ Two	NA	3 (16.7)
Type of bridging stent		
▪ Uncovered SEMS	NA	17 (94.4)
▪ Plastic stent	NA	1 (5.6)
Type of EUS-HGS route stent		
▪ Fully-covered SEMS	16 (80)	14 (77.8)
▪ Plastic stent	4 (20)	4 (22.2)

Data are presented as number (%) or median (range).
EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; ETBD, endoscopic transpapillary biliary drainage; SEMS, self-expandable metallic stent; NA, not applicable.

tinal reconstruction. ▶ **Table 5** presents procedure details and clinical outcomes in each group. Procedure time was significantly longer in the EUS-HGSB group than in the ETBD-MS group in both the entire and PSM cohorts. In addition, the RBO rate was significantly lower in the EUS-HGSB group than in the ETBD-MS group in the entire cohort (17.6% vs. 58.5%, $P<0.01$) and tended to be lower in the EUS-HGSB group than in the ETBD-MS group in the PSM cohort (23.1% vs. 61.5%, $P=0.11$). Patients who underwent EUS-HGSB fared better than those who underwent ETBD-MS, with a significantly longer median TRBO in the entire cohort (not reached [NR] [95% confidence interval (CI) 182-NR] vs. 104 [95% CI 80–133], $P=0.03$) and PSM cohort (183 [95% CI 48-NR] vs. 79 [22-NR], $P=0.05$) (▶ **Fig. 5a**). No statistical difference was found in OS between the EUS-HGSB and ETBD-MS groups in the entire and PSM cohorts (▶ **Fig. 5b**). Over-assessment may have occurred in the analysis using the Kaplan-Meier method and log-rank test because death without RBO was a competing risk. Therefore, we confirmed the trend using Gray's test and the Fine-Gray hazard model (▶ **Fig. 5c**). Cumulative incidence of RBO was significantly lower in the EUS-HGSB group than in the ETBD-MS group in the entire cohort (sub-distribution hazard ratio [HR], 0.21 [95% CI 0.07–0.67], stratified by Gray's test, $P=0.005$) and PSM cohort (sub-distribution HR, 0.23 [95% CI: 0.07–0.80], stratified by Gray's test, $P=0.02$). Technical and clinical success rates for endoscopic reintervention tended to be slightly lower in the EUS-HGSB group than in the ETBD-MS group in the entire and PSM cohorts, although the differences did not reach statistical significance.

▶ **Table 3** Clinical outcomes of EUS-HGSB in indicated and technical success cohorts.

Clinical outcomes, n = 20	Indicated, n = 20	Technical success, n = 18
Technical success*	18 (90)	*NA*
Clinical success†	18 (90)	18 (100)
Observation period of stent patency, days	*NA*	60 (9–465)
Recurrent biliary obstruction	*NA*	3 (16.7)
3-month non-RBO rate, %		91.6
6-month non-RBO rate, %		91.6
12-month non-RBO rate, %		57.0
Adverse events§	1 (5)	1 (5.6)
▪ During procedure	0	0
▪ Early adverse event	1 (5)	1 (5.6)
– Cholangitis (moderate)	1 (5)	1 (5.6)
▪ Late adverse event	0	0

Data are presented as number (%) or median (range).
*Technical success was defined as successful placement of a bridging stent at the right hepatic duct from the EUS-HGS route via the hilar stenosis.
†Clinical success was defined as a 50% decrease in or normalization of the bilirubin level within 14 days of stent placement.
§Early and late adverse events were defined as adverse events other than recurrent biliary obstruction within 30 and ≥ 31 days after the procedure, respectively.
EUS-HGS, endoscopic ultrasound-guided hepaticogastrostomy; EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; NA, not applicable; RBO, recurrent biliary obstruction.

▶ **Table 4** Characteristics of EUS-HGSB and ETBD-MS in the entire and PSM cohorts.

Patient characteristics	Entire cohort				PSM cohort			
	EUS-HGSB (n = 17)	ETBD-MS (n = 82)	*P* value	SMD	EUS-HGSB (n = 13)	ETBD-MS (n = 13)	*P* value	SMD
Age, ≥ 65 years	11 (64.7)	55 (69.6)	0.78	0.10	7 (53.8)	9 (69.2)	0.69	0.32
Sex, male	7 (41.2)	45 (54.9)	0.42	0.28	5 (38.5)	6 (46.2)	1	0.16
Primary disease			0.80	0.08			0.70	0.31
▪ Biliary tract cancer	10 (58.8)	45 (54.9)			7 (53.8)	5 (38.5)		
▪ Non-biliary tract cancer	7 (41.2)	37 (44.4)			6 (46.2)	8 (61.5)		
Stenosis type (Bismuth type II/IIIa/IIIb/IV)	8/8/0/1	26/39/2/15	0.54	0.65	5/7/0/1	9/2/1/1	0.11	0.96
Distant metastasis	13 (76.5)	63 (76.8)	1	0.01	10 (76.9)	8 (61.5)	0.67	0.34
Liver metastasis	5 (29.4)	32 (39.0)	0.59	0.20	3 (23.1)	3 (23.1)	1	< 0.01
Stenosis of portal vein	8 (47.1)	33 (40.2)	0.60	0.14	5 (38.5)	6 (46.2)	1	0.16
Ascites	10 (58.8)	28 (34.1)	0.10	0.51	6 (46.2)	7 (53.8)	1	0.15
Duodenal stenosis	8 (47.1)	3 (3.7)	<0.01	1.15	6 (46.2)	1 (7.7)	0.07	0.96
Reconstruction of the digestive tract	9 (52.9)	7 (8.5)	<0.01	1.10	7 (53.8)	3 (23.1)	0.23	0.67

Data are presented as n (%) or median (range).
PSM, propensity score-matched; EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; ETBD-MS, endoscopic transpapillary biliary drainage multi-stenting; SMD, standardized mean difference.

▶ **Table 5** Procedure details and clinical outcomes of EUS-HGSB and ETBD-MS in the entire and PSM cohorts.

	Entire cohort			PSM cohort		
	EUS-HGSB (n = 17)	ETBD-MS (n = 82)	*P* value	EUS-HGSB (n = 13)	ETBD-MS (n = 13)	*P* value
Procedural details						
Procedure time, min	97 (30–155)	66 (21–142)	0.01	98 (45–155)	60 (32–92)	0.01
Number of stents for hilar obstruction			NA			NA
▪ One	14 (82.4)	NA		10 (76.9)	NA	
▪ Two	3 (17.6)	46 (56.1)		3 (23.1)	10 (76.9)	
▪ Three or more	0	36 (41.5)		0	3 (23.1)	
Drainage method			NA			NA
▪ PSIS	NA	37 (45.1)		NA	5 (38.5)	
▪ SBS	NA	24 (29.3)		NA	7 (53.8)	
▪ Hybrid with PSIS and SBS	NA	21 (25.6)		NA	1 (7.7)	
Clinical outcomes						
Observation period of stent patency, days	64 (9–465)	74 (7–468)	0.74	64 (16–465)	59 (11–220)	0.56
Recurrent biliary obstruction	3 (17.6)	48 (58.5)	<0.01	3 (23.1)	8 (61.5)	0.11
Median time to recurrent biliary obstruction, days†	NR (182–NR)	104 (80–133)	0.03	183 (48–NR)	79 (22–NR)	0.05
Technical success rate of endoscopic reintervention, % (n)	66.7% (2/3)	79.2% (38/48)	0.53	66.7% (2/3)	80% (8/10)	1.0
Clinical success rate of endoscopic reintervention, % (n)	66.7% (2/3)	70.8% (34/48)	1.0	66.7% (2/3)	80% (8/10)	1.0

Data are presented as n (%) or median (range).
†The median time to recurrent biliary obstruction (95% confidence interval) is presented as the median time using the Kaplan-Meier method.
PSM, propensity score matched; EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; ETBD-MS, endoscopic transpapillary biliary drainage multi-stenting; PSIS, partial stent-in-stent; SBS, side-by-side; NA, not applicable; NR, not reached.

Factors predictive of RBO

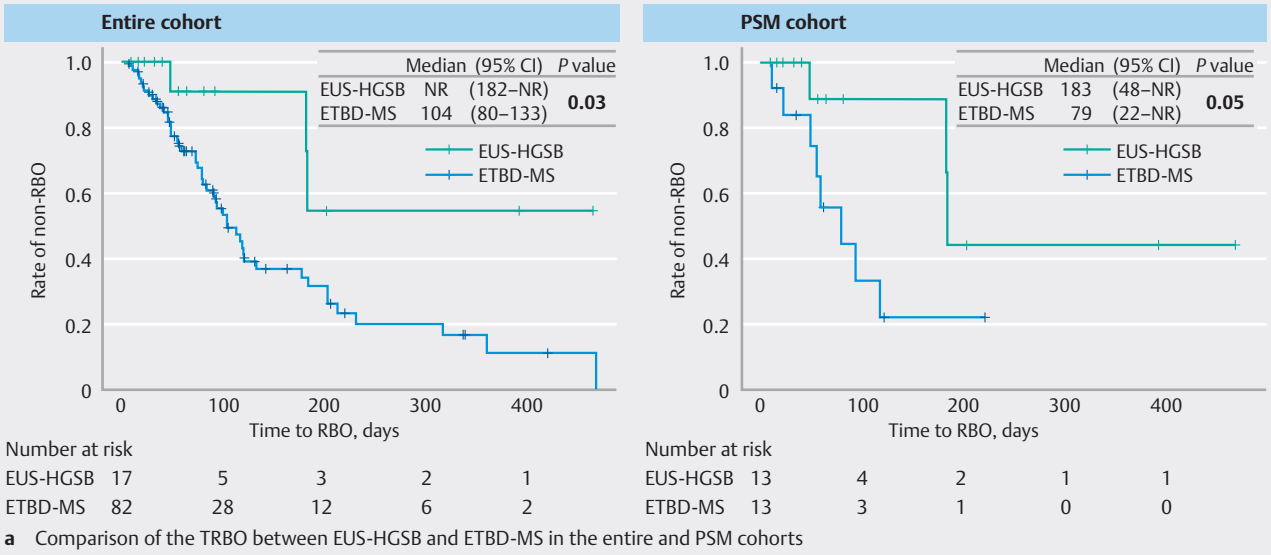
Biliary tract cancer (HR, 0.54 [95% CI 0.30–0.96], *P* = 0.03) and EUS-HGSB (HR, 0.29 [95% CI 0.09–0.95], *P* = 0.04) were predictive of a lower RBO rate on univariate analysis. However, no factors were predictive of RBO on multivariate analysis. Although EUS-HGSB tended to contribute to lower RBO, statistical significance was NR on multivariate analysis (HR, 0.31 [95% CI 0.10–1.00], *P* = 0.05) (▶ **Table 6**).

Discussion

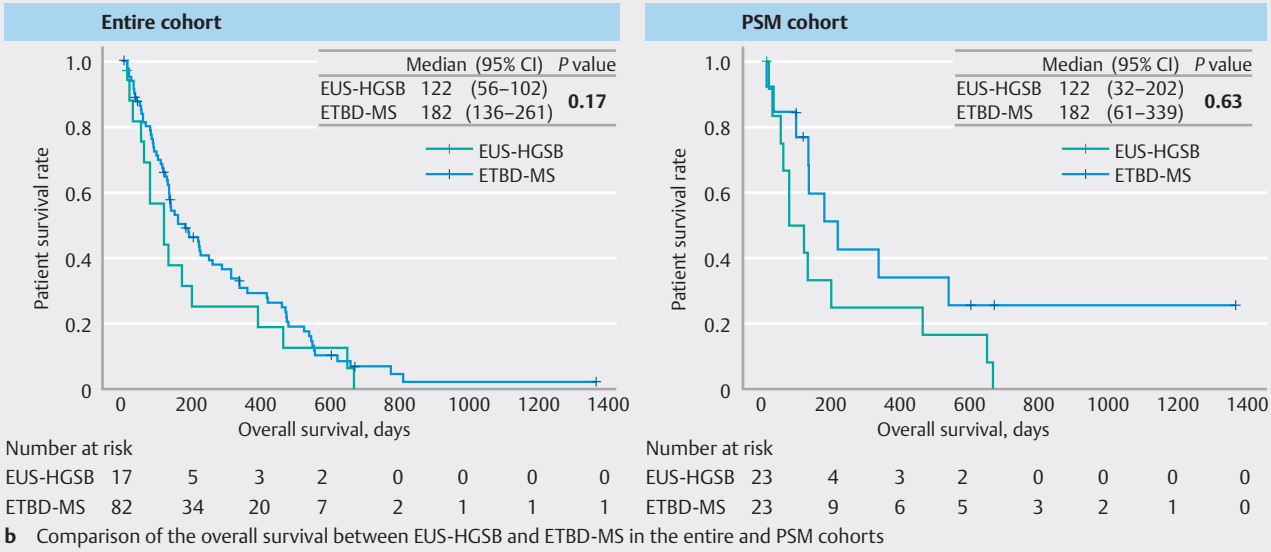
EUS-HGSB is a useful alternative drainage treatment for MHBOs that are difficult to approach using ETBD, particularly in patients who require bilateral drainage [8, 9, 10, 11, 12, 14]. However, to our knowledge, no clinical data have assessed long-term outcomes after EUS-HGSB. Therefore, in addition to analyzing long-term outcome of EUS-HGSB, we performed a comparative study using PSM and multivariate analysis to confirm non-inferiority of EUS-HGSB to a control group (not requiring EUS-HGSB) that could have undergone ETBD-MS. Our findings showed better TRBO with EUS-HGSB than with ETBD-MS. Furthermore, no significant difference was found in OS between the two groups. Therefore, these results indicate that EUS-HGSB may not be inferior to ETBD-MS in long-term outcomes.

In this study, EUS-HGSB had better stent patency than ETBD-MS. We hypothesize that a unique feature of EUS-HGSB is that the drainage route can be integrated into a single HGS route compared with ETBD-MS, which consequently may have contributed to better stent patency.

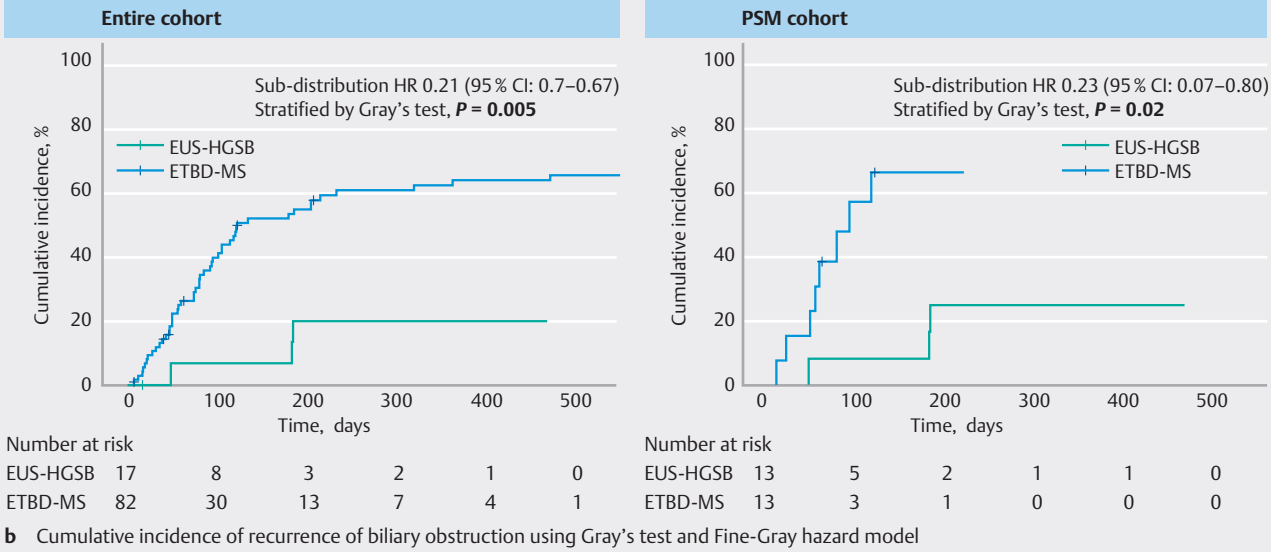
EUS-HGSB was not a significant independent factor contributing to RBO on multivariate analysis in this study. This may be due to the small number of patients and RBO events in the EUS-HGSB group. However, biliary tract cancer was an independent factor contributing to TRBO prolongation compared with other cancer types on univariate analysis. Vienne et al. similarly found that primary biliary tumors contributed to drainage effectiveness in MHBO on univariate analysis [24]. Certain oncological characteristics may contribute to this finding, although the mechanism remains unclear. Therefore, further research



a Comparison of the TRBO between EUS-HGSB and ETBD-MS in the entire and PSM cohorts



b Comparison of the overall survival between EUS-HGSB and ETBD-MS in the entire and PSM cohorts



b Cumulative incidence of recurrence of biliary obstruction using Gray's test and Fine-Gray hazard model

▶ **Fig. 5** **a** Comparison in the TRBO between EUS-HGSB and ETBD-MS in the entire and PSM cohorts. EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; ETBD-MS, endoscopic transpapillary biliary drainage with multi-stenting; PSM, propensity score-matched; RBO, recurrence of biliary obstruction; TRBO, time to RBO; CI, confidence interval; NR, not reached. **b** Comparison of the overall survival between EUS-HGSB and ETBD-MS in the entire and PSM cohorts. EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; ETBD-MS, endoscopic transpapillary biliary drainage with multi-stenting; PSM, propensity score-matched; CI, confidence interval. **c** Cumulative incidence of recurrence of biliary obstruction using Gray's test and Fine- Gray hazard model. EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; ETBD-MS, endoscopic transpapillary biliary drainage with multi-stenting; PSM, propensity score-matched; CI, confidence interval; HR, hazard ratio.

▶ **Table 6** Predictive factors associated with RBO after stenting for malignant hilar biliary obstruction in all clinically successful cases (univariate log-rank trend test and Cox proportional hazard regression).

Predictive factors	N	TRBO (95% CI)	Univariate analysis		Multivariate analysis	
			HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age					–	–
▪ ≥65 years	68	120 (91–183)	1.05 (0.57–1.92)	0.88		
▪ <65 years	31	113 (55–NR)	1 (reference)			
Sex					–	–
▪ Male	52	120 (80–203)	1.28 (0.72–2.28)	0.40		
▪ Female	47	117 (93–NR)	1 (reference)			
Primary cancer						
▪ Biliary tract cancer	55	182 (93–231)	0.53 (0.30–0.95)	0.03	0.62 (0.33–1.16)	0.14
▪ Other than biliary tract cancer	44	104 (73–119)	1 (reference)			
Distant metastasis					–	–
▪ Yes	76	119 (94–183)	0.94 (0.50–1.75)	0.84		
▪ No	23	104 (59–231)	1 (reference)			
Liver metastasis					–	–
▪ Yes	37	119 (75–NR)	0.78 (0.41–1.49)	0.45		
▪ No	62	117 (84–183)	1 (reference)			
Bismuth type						
▪ Type III-IV	67	121 (104–184)	0.65 (0.35–1.18)	0.15	0.74 (0.39–1.41)	0.36
▪ Type II	32	80 (46-NR)	1 (reference)			
Procedure						
▪ EUS-HGSB	17	NR (182–NR)	0.29 (0.09–0.95)	0.04	0.31 (0.10–1.00)	0.05
▪ ETBD-MS	82	104 (80–133)	1 (reference)			
Post-procedure chemotherapy					–	–
▪ Yes	56	104 (80–178)	1.56 (0.79–3.06)	0.20		
▪ No	43	183 (100–NR)	1 (reference)			

HR, hazard ratio; CI, confidence interval; NR, not reached; EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; ETBD-MS, endoscopic transpapillary biliary drainage multi-stenting; RBO, recurrent biliary obstruction; TRBO, time to recurrent biliary obstruction.

with an accumulation of cases is needed to elucidate the mechanism. Chemotherapy following stenting is anticipated to enhance prognostic factors in patients with perihilar carcinoma [25]. However, initiation of chemotherapy did not result in TRBO improvement in this study. The relationship between initiation of chemotherapy and RBO in perihilar carcinoma warrants further exploration. In contrast, the rate of chemotherapy resumption was significantly higher in the ETBD-MS group than in the EUS-HGSB group (61.0% vs. 35.3%, $P = 0.06$). This higher rate of chemotherapy resumption might be a contributing fac-

▶ **Table 7** Review of the literature on EUS-HGSB.

Author, year	Number of cases	Technical success	Clinical success (Intention to treat)	Adverse events
Ogura et al., 2014 [8]	1	100%	100%	0%
Prachayakul et al., 2015 [9]	1	100%	100%	0%
Maehara et al., 2020 [14]	1	100%	100%	0%
Ogura et al., 2015 [10]	7	100%	100%	0%
Moryousse et al., 2017 [11]	6	50%	50%	NA
Caillol et al., 2019 [12]	12	100%	83%	33%
Present study	**20**	**90%**	**90%**	**5%**

EUS-HGSB, endoscopic ultrasound-guided hepaticogastrostomy with bridging; NA, not applicable.

tor to the longer survival observed in the ETBD-MS group than in the EUS-HGSB group.

Both technical and clinical success rates in this study were relatively high (90%) and were comparable to those in previous reports, although EUS-HGSB was technically difficult (▶ **Table 7**). Inserting the guidewire into the right bile duct or bringing the device to the right bile duct through the hilar stenosis is usually difficult, particularly in cases in which the angle between the left and right bile duct is steep or the stenosis is severe. The balloon occlusion method, double guidewire method, and balloon dilation of the stenosis are useful as rescue techniques in such difficult cases (▶ **Fig. 3**). In this study, EUS-HGSB was unsuccessful in the primary session in two cases but was successful with a retrial-session procedure due to a change in the target bile duct from B8 to B5, use of the double guidewire technique, or a change in physicians. Therefore, two-session EUS-HGSB may be a novel troubleshooting strategy. When performing EUS-HGSB in two sessions, the EUS-HGS route is less likely to leak bile into the peritoneal cavity because the fistula is complete, and peritonitis is less likely to occur with a prolonged procedure. However, appropriate timing should be selected on a case-by-case basis because biliary drainage is delayed when two-session bridging is performed. In this study, two-session bridging was not pre-planned in any of the cases.

This study had some limitations as follows: a small number of cases of EUS-HGSB, selection bias due to the retrospective study design, short observation period for stent patency, non-standardized stent selection, and low reproducibility because technical success depended on practitioner skill. According to the selection bias, PSM was performed in the analysis of the TRBO to minimize confounding factors. However, background factors, such as duodenal stenosis and reconstructed bowel, favoring selection of EUS-HGSB were rarely observed in the ETBD-MS group, and consequently, could not be matched. In addition, EUS-HGSB did not reach statistical significance as an independent factor for improved TRBO on multivariate analysis. Although cumulative incidence of RBO with death as a competing risk showed a significantly lower RBO rate for EUS-HGSB than for ETBD-MS, the observation period for TRBO was shorter because survival time after stenting was shorter due to the high number of EUS-HGSB cases with malignant advanced stages and ETBD-MS cases with poor prognosis. Furthermore, the median survival time was 60 days shorter in the EUS-HGSB group than in the ETBD-MS group. This could have contributed to the finding of longer stent patency with EUS-HGSB than with ETBD-MS. Because duration of patency for EUS-HGS and ETBD-MS with SEMS in distal obstruction has been reported to be approximately 1 year [26, 27] and 6 months [5, 6], respectively, the observation period in this study appears inadequate. In addition, the stents placed via the EUS-HGS route were not standardized in this study. We excluded one EUS-HGSB case in which a PS was used as a bridging stent. In this case, the RBO did not occur within a 42-day survival period. The optimal stents for EUS-HGSB are also an issue for future studies. Therefore, concluding that EUS-HGSB is superior to ETBD-MS in terms of TRBO is difficult based on findings from this study. However, this result could suggest the inferiority of EUS-HGSB to ETBD-MS in long-term outcomes.

Conclusions

In conclusion, the EUS-HGSB technique is extremely useful in MHBO when transpapillary drainage is difficult. Our study suggests the inferiority of EUS-HGSB in stent patency. EUS-HGSB has potential as primary drainage in MHBO; however, given various limitations of this study, such as differences in patient background characteristics and short observation period, randomized controlled trials examining its potential as a primary drainage method should be conducted in the future.

Acknowledgement

We would like to thank the members of the National Cancer Center Hospital Japan for their support of this work.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding Information

The National Cancer Center Research and Development Fund 2022-A-16

References

[1] Qumseya BJ, Jamil LH, Elmunzer BJ et al. ASGE guideline on the role of endoscopy in the management of malignant hilar obstruction. Gastrointest Endosc 2021; 94: 222–234.e222

[2] Mukai T, Yasuda I, Nakashima M et al. Metallic stents are more efficacious than plastic stents in unresectable malignant hilar biliary strictures: a randomized controlled trial. J Hepatobiliary Pancreat Sci 2013; 20: 214–222

[3] Sawas T, Al Halabi S, Parsi MA et al. Self-expandable metal stents versus plastic stents for malignant biliary obstruction: a meta-analysis. Gastrointest Endosc 2015; 82: 256–267.e257

[4] Sangchan A, Kongkasame W, Pugkhem A et al. Efficacy of metal and plastic stents in unresectable complex hilar cholangiocarcinoma: a randomized controlled trial. Gastrointest Endosc 2012; 76: 93–99 doi:10.1016/j.gie.2012.02.048

[5] Lee TH, Moon JH, Choi JH et al. Prospective comparison of endoscopic bilateral stent-in-stent versus stent-by-stent deployment for inoperable advanced malignant hilar biliary stricture. Gastrointest Endosc 2019; 90: 222–230 doi:10.1016/j.gie.2019.03.011

[6] Maruki Y, Hijioka S, Wu SYS et al. Novel endoscopic technique for trisegment drainage in patients with unresectable hilar malignant biliary strictures (with video). Gastrointest Endosc 2020; 92: 763–769

[7] de Souza GMV, Ribeiro IB, Funari MP et al. Endoscopic retrograde cholangiopancreatography drainage for palliation of malignant hilar biliary obstruction - stent-in-stent or side-by-side? A systematic review and meta-analysis World J Hepatol 2021; 13: 595–610 doi:10.4254/wjh.v13.i5.595

[8] Ogura T, Masuda D, Imoto A et al. EUS-guided hepaticogastrostomy for hepatic hilar obstruction. Endoscopy 2014; 46: E32–E33 doi:10.1055/s-0033-1359133

[9] Prachayakul V, Aswakul P. Endoscopic ultrasound-guided biliary drainage: Bilateral systems drainage via left duct approach. World J Gastroenterol 2015; 21: 10045–10048 doi:10.3748/wjg.v21.i34.10045

[10] Ogura T, Sano T, Onda S et al. Endoscopic ultrasound-guided biliary drainage for right hepatic bile duct obstruction: novel technical tips. Endoscopy 2015; 47: 72–75 doi:10.1055/s-0034-1378111

[11] Moryoussef F, Sportes A, Leblanc S et al. Is EUS-guided drainage a suitable alternative technique in case of proximal biliary obstruction? Therap Adv Gastroenterol 2017; 10: 537–544 doi:10.1177/1756283X17702614

[12] Caillol F, Bosshardt C, Reimao S et al. Drainage of the right liver under EUS guidance: a bridge technique allowing drainage of the right liver through the left liver into the stomach or jejunum. Endosc Ultrasound 2019; 8: 199–203 doi:10.4103/eus.eus_64_18

[13] Nakai Y, Kogure H, Isayama H et al. Endoscopic ultrasound-guided biliary drainage for unresectable hilar malignant biliary obstruction. Clin Endosc 2019; 52: 220–225 doi:10.5946/ce.2018.094

[14] Maehara K, Hijioka S, Nagashio Y et al. Simultaneous endoscopic ultrasound-guided hepaticogastrostomy and bridging stenting with partial stent-in-stent method. Endoscopy 2020; 52: E381–E382

[15] Winkler J, Caillol F, Ratone JP et al. Feasibility of EUS-guided hepaticogastrostomy for inoperable malignant hilar biliary strictures. Endosc Ultrasound 2021; 10: 51–56 doi:10.4103/eus.eus_68_20

[16] Sundaram S, Dhir V. EUS-guided biliary drainage for malignant hilar biliary obstruction: A concise review. Endosc Ultrasound 2021; 10: 154–160 doi:10.4103/EUS-D-21-00004

[17] Kato H, Matsumoto K, Okada H. Recent advances regarding endoscopic biliary drainage for unresectable malignant hilar biliary obstruction. DEN Open 2022; 2: e33 doi:10.1002/deo2.33

[18] Dhar J, Gupta P, Samanta J. The role of endoscopy in malignant hilar obstruction. Ann Gastroenterol 2023; 36: 347–359 doi:10.20524/aog.2023.0810

[19] Pal P, Lakhtakia S. Endoscopic ultrasound-guided intervention for inaccessible papilla in advanced malignant hilar biliary obstruction. Clin Endosc 2023; 56: 143–154 doi:10.5946/ce.2022.198

[20] Nakahara K, Morita R, Itoh F. Endoscopic ultrasound-guided bilateral biliary drainage through the mesh of the metal stents using a balloon occlusion method. Dig Endosc 2020; 32: e104–e105 doi:10.1111/den.13701

[21] Nakai Y, Oyama H, Kanai S et al. Double guidewire technique using an uneven double lumen catheter for endoscopic ultrasound-guided interventions. Dig Dis Sci 2021; 66: 1540–1547 doi:10.1007/s10620-020-06345-9

[22] Isayama H, Hamada T, Yasuda I et al. TOKYO criteria 2014 for transpapillary biliary stenting. Dig Endosc 2015; 27: 259–264 doi:10.1111/den.12379

[23] Sherman S, Lehman GA. ERCP- and endoscopic sphincterotomy-induced pancreatitis. Pancreas 1991; 6: 350–367 doi:10.1097/00006676-199105000-00013

[24] Vienne A, Hobeika E, Gouya H et al. Prediction of drainage effectiveness during endoscopic stenting of malignant hilar strictures: the role of liver volume assessment. Gastrointest Endosc 2010; 72: 728–735

[25] Schoch A, Lisotti A, Walter T et al. Efficacy of EUS-guided hepaticogastrostomy in prolonging survival of patients with perihilar cholangiocarcinoma. Endosc Ultrasound 2022; 11: 487–494

[26] Minaga K, Ogura T, Shiomi H et al. Comparison of the efficacy and safety of endoscopic ultrasound-guided choledochoduodenostomy and hepaticogastrostomy for malignant distal biliary obstruction: Multicenter, randomized, clinical trial. Dig Endosc 2019; 31: 575–582 doi:10.1111/den.13406

[27] Shibuki T, Okumura K, Sekine M et al. Covered self-expandable metallic stents versus plastic stents for endoscopic ultrasound-guided hepaticogastrostomy in patients with malignant biliary obstruction. Clin Endosc 2023; 56: 802–811