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Comparison of the hybrid and partial stent-in-stent method for endoscopic three-segment drainage for unresectable malignant hilar biliary obstruction

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ABSTRACT

Background and study aims The clinical outcome of the new hybrid drainage method for unresectable malignant hilar biliary obstruction (UMHBO) has not yet been compared with that of the partial stent-in-stent (PSIS) method with three or more stents.

Patients and methods Patients with UMHBO underwent drainage of three segments using the hybrid or PSIS method. The clinical outcomes of both methods were compared retrospectively.

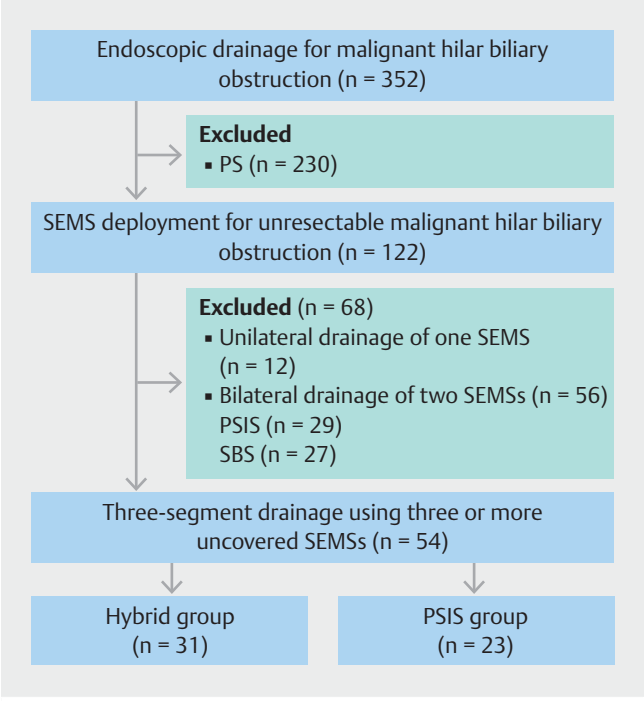
Results Overall, 54 patients underwent the hybrid (n = 31) or PSIS (n = 23) method of drainage with three or more stents for UMHBO. There were no significant differences in the technical success rate (hybrid vs. PSIS, 87.1% vs. 87%), clinical success rate according to per-protocol analysis (81.5% vs. 70%), early adverse events rate (14.8% vs. 10%), late adverse events rate (7.4% vs. 0%), and technical success rate of the endoscopic transpapillary reintervention (90.9% vs. 100%). Time to recurrent biliary obstruction (TRBO) of the hybrid and PSIS methods was 178 and 231 days, respectively, with no significant difference ($P = 0.354$).

Conclusions The choice between the two methods should be made at the physician's discretion.

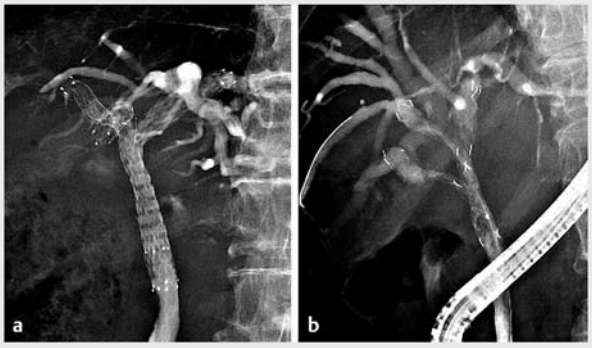
Introduction

Endoscopic multi-stenting with uncovered self-expandable metal stents (SEMSs) is a method of biliary drainage for unresectable malignant hilar biliary obstruction (UMHBO) [1–5]. For multi-stenting with SEMS, the partial stent-in-stent (PSIS) method, wherein stents are deployed one by one, is predominantly used [6–8]. PSIS has good technical success rates (80%–100%); however, previous studies assessed bilateral stenting using two stents [6, 7,9,10]. Recently, the bilateral side-by-side (SBS) method has been widely performed because delivery of thin stents (small diameter) can be used [5, 11, 12], and the technical success rate is good (73.3%–100%) [5, 11,12]. The SBS method simplifies the procedure because the stents are implanted parallelly [13, 14]. However, this method has the potential disadvantage of overexpanding the common bile duct (CBD) because of the risk of portal vein thrombosis with the parallel placement of multiple SEMSs [14].

To date, four studies [15–18] have compared the SBS and PSIS methods, of which those on two stents [16–18] showed comparable results in technical and clinical success rates, ad-



▶ **Fig. 1** Flow diagram of the study. PS, plastic stents; SEMS, self-expandable metal stents; PSIS, partial stent-in-stent; SBS, side-by-side; hybrid, side-by-side and partial stent-in-stent method.



▶ **Fig. 2** Fluoroscopic images of the hybrid and partial stent-in-stent methods .**a** SEMS deployment in the posterior branch, anterior branch, and left bile duct for malignant hilar biliary obstruction of Bismuth IV using the hybrid method. **b** SEMS deployment in the posterior branch, anterior branch, and left bile duct for malignant hilar biliary obstruction of Bismuth IV using the PSIS method. SEMS, self-expandable metal stents; hybrid, side-by-side and partial stent-in-stent method; PSIS, partial stent-in-stent.

verse events, and reintervention (RI) rates. However, these studies reported bilateral stenting using two SEMSs, not three.

Clinically, three-segment drainage (left hepatic duct, right anterior segment, and right posterior segment) with three or more SEMSs may be necessary for severe UMHBO of Bismuth III-IV [19]. For these situations, the PSIS method has been conventionally used [20, 21]. However, a new method combining the SBS and PSIS methods (the "hybrid method") has been developed recently [22–26]. Its technical success rate is 85 % to 100 %, and stent patency is 109 to 189 days. However, to date, no studies have compared the technical success rate, stent patency, adverse events, and RI rates of the hybrid and PSIS methods for three-segment drainage using three or more SEMSs. Therefore, we retrospectively compared the outcomes of these methods to assess their effectiveness as drainage treatments for complicated hilar biliary obstruction.

Patients and methods

Patients

We performed endoscopic drainage in 352 cases with UMHBO at the National Cancer Center Hospital, Japan, from October 2017 to September 2021. Overall, 298 cases with plastic stents (PS) and those in whom one or two SEMS were deployed were excluded. Finally, 54 patients (14.5 %) with UMHBO, who underwent drainage of three segments with three or more uncovered SEMSs using the hybrid or PSIS methods, were included (▶ **Fig. 1**). The diagnosis of UMHBO was made based on imaging examinations, and all cases were proven to be malignant with cytological or histological diagnosis. In terms of stent selection and strategy for UMHBO drainage, the basic policy was to place PS before initial drainage and chemotherapy. However, SEMS placement was performed from the initial drainage in cases where more than three PS were difficult to place due to severe hilar bile duct stenosis, and in cases where best supportive care was deemed desirable without chemotherapy. When exchanging PS for SEMSs, SEMSs were deployed in the same bile duct where PS drainage was performed (i. e., we replaced two PS for two SEMSs and three PS for three SEMSs). Endoscopic nasobiliary drainage was performed in cases with cholangitis, and SEMS implantation was performed after the cholangitis had healed. All patients provided informed consent for this treatment strategy. This study was approved by our hospital ethics committee (approval no. 2018–149).

Technique for the hybrid and PSIS methods

For ease of stenting, the hybrid method was the first choice for patients with an acceptable CBD diameter for the SBS method and with preserved portal blood flow in the hilar region, whereas the PSIS method was chosen for those with small CBDs or with tumor invasion into the portal vein, to avoid portal vein thrombosis. However, the final choice of stenting method was determined by the operator, considering not only the diameter of the CBD and the presence of portal vein invasion but also the form of bile duct confluence. We decided whether to use the hybrid or PSIS method before SEMS deployment. Laser cut-type uncovered SEMSs were used for the hybrid method, and braided-type uncovered SEMSs were mainly used for the PSIS method. Stents with an 8-mm diameter were used for the hilar bile duct in all cases of both methods. The hybrid method was performed using a combination of SBS and PSIS, based on our previously reported method (▶ **Fig. 2**) [25]. First, under radiologic guidance, two guidewires were passed via the papilla into the left hepatic duct and the posterior branch of the right

hepatic duct (p-RHD) in a SBS fashion, and two SEMSs were simultaneously introduced over these guide wires (SBS deployment). Next, a guide wire was introduced through the stent mesh placed within the p-RHD into the anterior branch of the right hepatic duct (a-RHD), where the stent delivery system was subsequently deployed (PSIS deployment). If the hilar biliary obstruction was long and there was extensive obstruction of the CBD, a 10-mm-diameter SEMS was placed in the CBD first, followed by the hybrid method. The PSIS method was performed by deploying the uncovered SEMS one by one, as previously reported (▶**Fig. 2**) [20, 21]. In the PSIS method, an 8-mm-diameter SEMS was placed in the CBD if obstruction was present. When the stent could not break through the stent mesh during the second or subsequent implantation, 8-mm-diameter balloon dilation (REN; Kaneka Medix, Tokyo, Japan) was performed.

Outcomes and definitions

The technical success rate, clinical success rate, procedure time, time to recurrent biliary obstruction (TRBO), adverse events (AEs), and RI rates were evaluated and each item was defined based on the 2014 Tokyo criteria [27]. Technical success was defined as the deployment of three or more uncovered SEMSs using the hybrid or PSIS method as planned. Clinical success was defined as a 50 % decrease in or normalization of the bilirubin level within 14 days of stent placement. In cases without hyperbilirubinemia before SEMS deployment, clinical success was defined as the absence of exacerbation after SEMS deployment compared to that after PS drainage. Clinical success was defined using both per-protocol analysis, wherein the denominator is the number of technically successful cases, and intention-to-treat analysis, in which the denominator is the total number of cases. Procedure time was defined as the time from cholangiography to stent placement. Recurrent biliary obstruction (RBO) was defined as obstruction of the hilar stent. TRBO was defined as the time from the deployment of the SEMS to RBO. Technical success in RI was defined as successful endoscopic transpapillary RI (ETP-RI) as planned. Portal vein invasion was classified into three categories as follows: mild (no stenosis due to tumor contact only), moderate (mild to moderate stenosis due to tumor invasion), and severe (severe stenosis due to tumor invasion). Cases classified as “moderate” or “severe” were considered positive for portal vein invasion. The CBD diameter was defined as the diameter of the CBD below the hilar biliary stricture.

Statistical analysis

Statistical comparisons were made using the chi-square or Fisher's exact test for categorical variables, the Mann-Whitney U test for continuous variables, and the *t*-test for a comparison of the means of two normally distributed populations. To yield more clinically relevant results, analysis of TRBO was limited to cases in which clinical success was achieved. TRBO was calculated using the Kaplan-Meier method, and curves were compared using the log-rank test. The associations between TRBO and other parameters were evaluated using univariate and multivariate Cox proportional hazard model analyses. All statistical analyses were performed using SPSS Statistics, version 23, for Windows (IBM Corp., Armonk, New York, United States).

Results

Patient characteristics

▶**Table 1** shows the background characteristics of 54 patients who underwent multi-stenting with three or more uncovered SEMSs. There were 31 patients in the hybrid group and 23 patients in the PSIS group. There were no significant differences between the groups in terms of the primary disease, Bismuth classification, presence of liver metastasis, portal vein invasion, total bilirubin levels before SEMS placement, previous biliary drainage, endoscopic sphincterotomy, chemotherapy, CBD diameter, and SEMS placement for CBD obstruction.

Clinical outcomes

▶**Table 2** presents the main outcomes of the study. The technical success rate was 87 % (47/54) overall, 87.1 % (27/31) in the hybrid group, and 87 % (20/23) in the PSIS group ($P = 1.00$). Among the patients who experienced technical failure in the hybrid group, three underwent two SBSs due to difficulty with PSIS and one underwent two PSISs due to stent dislodgement. All technical failure cases in the PSIS group had difficulty in inserting the third stent, resulting in two PSISs. In the hybrid and PSIS groups, pre-dilation of the stent mesh was required in five (16.1 %) and six (26.1 %) patients, respectively ($P = 0.50$). The median procedure time was 58 minutes (interquartile range [IQR]: 45–78) in the hybrid group and 70 minutes (IQR: 54–90) in the PSIS group ($P = 0.14$).

Laser cut-type stents were used in all patients in the hybrid method, braided-type stents in 20 patients, and laser cut-type stents in three patients in the PSIS method, showing a significant difference ($P < 0.01$). The stent diameter used for the hilar bile duct was 8 mm in all cases.

The clinical success rate according to the per-protocol analysis was 76.6 % (36/47) overall, 81.5 % (22/27) in the hybrid group, and 70 % (14/20) in the PSIS group ($P = 0.49$). The clinical success rate according to the intention-to-treat analysis was 79.6 % (43/54) overall, 83.9 % (26/31) in the hybrid group, and 73.9 % (17/23) in the PSIS group ($P = 0.50$).

Early AEs occurred in six (12.7 %) of the patients, including five (10.6 %) with moderate cholecystitis and one (2.1 %) with post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) (▶**Table 2**). These included four patients with cholecystitis (14.8 %) in the hybrid group and one patient each with cholecystitis (5 %) and PEP (5 %) in the PSIS group ($P = 0.25$). All patients improved with conservative treatment. Late AEs were observed in two patients in the hybrid group, including moderate cholecystitis in one patient (3.7 %) and moderate liver abscess in one patient (3.7 %). No late AEs were observed in the PSIS group ($P = 1.00$).

Recurrent biliary obstruction

▶**Table 3** shows the outcomes of RBO. RBO occurred in 45 % of patients (21/47) with technical success. The median (IQR) observation period in the hybrid and PSIS groups was 139 days

▶ **Table 1** Baseline characteristics of the hybrid and PSIS groups.

	Total	Hybrid	PSIS	*P* value
N	54	31	23	
Age, y, median (IQR)	69 (58–75)	69 (57–74)	68 (59–76)	0.72
Sex, M/F, n	28/26	14/17	14/9	0.28
Diagnosis, n (%)				0.48
▪ Biliary tract cancer	32 (59)	19 (61)	13 (57)	
▪ Pancreatic cancer	10 (19)	4 (13)	6 (26)	
▪ Others	12 (22)	8 (26)	4 (17)	
Bismuth classification, n (%)				0.57
▪ III a	29 (54)	18 (58)	11 (48)	
▪ III b	1 (2)	1 (3)	0	
▪ IV	24 (44)	12 (39)	12 (52)	
Liver metastasis, n (%)	24/54 (44)	12/31 (39)	12/23 (52)	0.41
Portal vein invasion, n (%)	12/54 (22)	4/31 (13)	8/23 (35)	0.10
Total bilirubin, mg/dL, median (range)	1.3 (0.3–22)	1.0 (0.4–21)	1.5 (0.3–22)	0.46
Previous biliary drainage, n (%)				0.59
▪ EBS of plastic stent	38 (70)	22 (71)	16 (70)	
▪ PTBD	2 (4)	2 (6)	0	
▪ None	14 (26)	7 (23)	7 (30)	
Endoscopic sphincterotomy				1.00
▪ No (post-EST)	38 (70)	22 (71)	16 (70)	
▪ Yes	16 (30)	9 (29)	7 (30)	
Chemotherapy, n (%)	27 (56)	15 (60)	12 (52)	0.77
▪ Palliative medicine, n (%)	21 (44)	10 (40)	11 (48)	
Common bile duct, mm, mean (range)	6.8 (3.5–11)	7.2 (4.5–10)	6.3 (3.5–11)	0.09
▪ Common bile duct < 6 mm, n (%)	19 (35)	8 (26)	11 (48)	0.15
SEMS placement for common bile duct obstruction, n (%)	13 (24)	7 (23)	6 (26)	1.00

Hybrid, side-by-side and partial stent-in-stent method; PSIS, partial stent-in-stent; PS, plastic stent; SEMS, self-expandable metal stent; EBS, endoscopic biliary stenting; PTBD, percutaneous transhepatic biliary drainage; EST, endoscopic sphincterotomy; IQR, interquartile range.

(85–250) and 178 days (98–403), and RBO was observed in 13 patients (48.1%) and eight patients (40%), respectively (P = 0.77). The main cause of obstruction was tumor ingrowth (76.9%) in the hybrid group and tumor ingrowth or sludge (37.5%) in the PSIS group (P = 0.23).

Median TRBO was 178 days (95% confidence interval [CI]: 82–274) in the hybrid group and 231 days (95% CI: 93–369) in the PSIS group (P = 0.354) (▶ **Fig. 3**). The non-obstruction rates in the hybrid and PSIS groups were 67% and 92.3% at 3 months, 40.2% and 52.4% at 6 months, and 20.1% and 17.5% at 12 months, respectively (P = 0.35).

Univariate and multivariate analyses of factors related to TRBO were extracted as a result of shorter TRBO in cases with total bilirubin levels ≥ 2.0 mg/dL (hazard ratio [HR]: 4.06, 95% CI: 1.25–13.2, P = 0.02) (▶ **Table 4**). No significant difference was noted in the factors related to TRBO between the hybrid and PSIS methods.

Reintervention

Supplementary Table S1 shows the outcomes of RI. Twenty-one patients with RBO underwent ETP-RI, RI with endoscopic ultrasound-guided biliary drainage (EUS-BD) or percutaneous transhepatic biliary drainage (PTBD). Overall, 17 patients underwent ETP-RI (11 patients in the hybrid group and 6 patients in the PSIS group, P = 0.10), and four patients underwent EUS-BD or PTBD (2 in the hybrid group and 2 in the PSIS group, P = 0.75). The technical success rate of ETP-RI in the hybrid and the

▶ **Table 2** Procedural outcomes and adverse events.

	Total	Hybrid	PSIS	*P* value
N	54	31	23	
Technical success, n (%)	47/54 (87.0)	27/31 (87.1)	20/23 (87.0)	1.00
Pre-dilation of stent mesh, n (%)	11 (20.3)	5 (16.1)	6 (26.1)	0.50
Procedure time, min, median (IQR)	64 (47–86)	58 (45–78)	70 (54–90)	0.14
Stent type, n				<0.01
Laser cut-type				
▪ ZEO stent V		23	0	
▪ BileRush selective		7	0	
▪ YABUSAME		1	3	
Braided-type				
▪ HILZO stents		0	3	
▪ Niti-S large cell SR slim delivery		0	14	
▪ BONASTENT M-Hilar		0	3	
No. SEMSs placed, n (%)				0.25
▪ Three	44 (93.6)	24 (88.9)	20 (100)	
▪ Four	3 (6.4)	3 (11.1)	0 (0.0)	
Clinical success (per-protocol analysis), n (%)	36/47 (76.6)	22/27 (81.5)	14/20 (70.0)	0.49
Clinical success (intention-to-treat analysis), n (%)	43/54 (79.6)	26/31 (83.9)	17/23 (73.9)	0.50
Early adverse event, n (%)	6/47 (12.7)	4/27 (14.8)	2/20 (10.0)	0.25
▪ Cholecystitis	5 (10.6)	4 (14.8)	1 (5.0)	
▪ PEP	1 (2.1)	0 (0.0)	1 (5.0)	
Late adverse event, n (%)	2/47 (4.3)	2/27 (7.4)	0 (0.0)	1.00
▪ Cholecystitis	1 (2.1)	1 (3.7)	0 (0.0)	
▪ Liver abscess	1 (2.1)	1 (3.7)	0 (0.0)	

Hybrid, side-by-side and partial stent-in-stent method; PSIS, partial stent-in-stent; IQR, interquartile range; SEMS, self-expandable metal stent; PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis.

PSIS groups was 90.9 % (10/11) and 100 % (6/6), respectively (P = 1.00).

In the hybrid group, one patient underwent PTBD due to duodenal obstruction and one patient had difficulty with ETP-RI and underwent EUS-BD. In the PSIS group, two patients underwent EUS-BD due to duodenal obstruction.

The clinical success rate according to the per-protocol analysis was 87.5 % (14/16) overall, 80.0 % (8/10) in the hybrid group, and 100 % (6/6) in the PSIS group, (P = 0.50). The clinical success rate according to the intention-to-treat analysis was 88.2 % (15/17) overall, 81.8 % (9/11) in the hybrid group, and 100 % (6/6) in the PSIS group (P = 0.51).

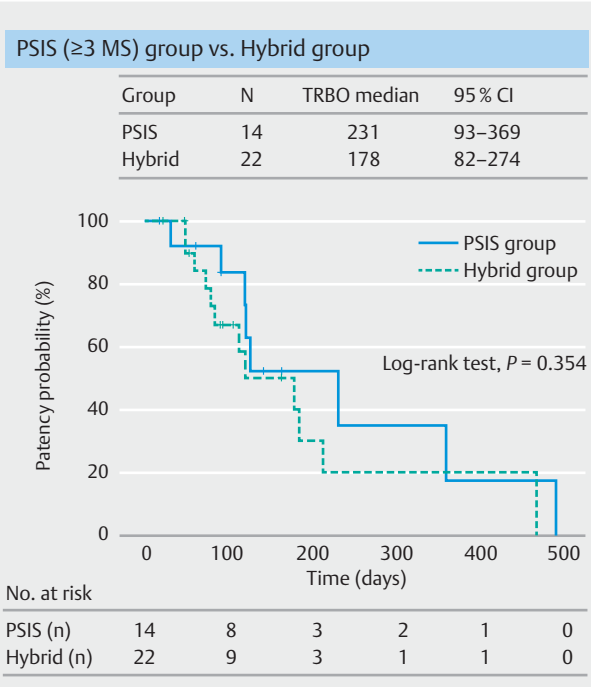
Discussion

The usefulness of the hybrid and PSIS methods for three-segment drainage of UMHBO has been reported, but the choice between the two methods remains controversial. In this study, both the hybrid and PSIS methods showed high technical success rates (87.1 % and 87.0 %, respectively). The hybrid procedure tended to be shorter than PSIS because it is an SBS-based stenting method, indicating that it is more convenient than the PSIS in terms of procedural simplicity. Inoue et al. [24] reported that the hybrid procedure was unsuccessful in 14.8 %, attributed to the high possibility of failure in cases with a CBD diameter of < 6 mm. However, in our study, eight patients in the hybrid group had a CBD diameter of < 6 mm, and the technical success rate in these patients was high, at 87.5 % (7/8). The reason for the high technical success rate was the devising of the order of stent placement.

▶ **Table 3** Recurrent biliary obstruction.

	Total	Hybrid	PSIS	*P* value
N	47	27	20	
RBO, n (%)	21 (45.0)	13 (48.1)	8 (40.0)	0.77
Causes of RBO, n (%)				0.23
▪ Tumor ingrowth	13 (61.9)	10 (76.9)	3 (37.5)	
▪ Sludge	5 (23.8)	2 (15.4)	3 (37.5)	
▪ Duodenal occlusion	3 (14.3)	1 (7.7)	2 (25.0)	
Non-obstruction rates, (%)				0.35
▪ 3 months		67.0	92.3	
▪ 6 months		40.2	52.4	
▪ 12 months		20.1	17.5	
Observation period, days, median (IQR)	153 (91–304)	139 (85–250)	178 (98–403)	0.34

Hybrid, side-by-side and partial stent-in-stent method; PSIS, partial stent-in-stent; RBO, recurrent biliary obstruction; IQR, interquartile range.



▶ **Fig. 3** Cumulative time to recurrent biliary obstruction according to the Kaplan-Meier analysis. The median TRBO is 178 days (95 % CI: 82–274) in the hybrid group and 231 days (95 % CI: 93–369) in the PSIS group (log-rank $P = 0.354$). CI, confidence interval; PSIS, partial stent-in-stent; hybrid, side-by-side and partial stent-in-stent method; MS, metallic stents; TRBO, time to recurrent biliary obstruction.

In this study, TRBO did not differ significantly between the hybrid and PSIS groups (178 vs. 231 days, $P = 0.354$). The previously reported TRBO for the hybrid and PSIS methods ranged as 109 to 189 days [22–26] and 150 to 176 days [21, 28], respectively. The TRBO of the hybrid method in this study was comparable to that reported in a previous study, and the TRBO of the PSIS method in this study was longer than that previously reported. This may be because the hybrid method is a newer and more recent technique, while the TRBO data for the PSIS method was likely older. With recent device improvements, the TRBO of the PSIS method has increased, compared with that previously reported; therefore, we believe that the PSIS method showed a trend toward longer TRBO in this study. In multivariate analysis, total bilirubin levels ≥ 2.0 mg/dL was the only factor associated with TRBO. Overall, there were 22 cases with bilirubin levels of 2 mg/dL or higher, and 15 of these cases were drained with PS. Three SEMS placements in patients with high jaundice, even after drainage with PS, resulted in a shorter TRBO. We hypothesized that these cases may have had hepatic parenchymal jaundice or severe bile duct stenosis, which would have increased the risk of stent failure. No significant difference was noted in the factors related to TRBO between the hybrid and PSIS methods.

Although not significant, the hybrid method was found to cause more cholecystitis (14.8 %) as an early AE, suggesting that comparatively it may contribute to the development of cholecystitis more often due to the larger dilatation of the CBD.

Although the hybrid method was originally devised considering the ease of RI, the technical success rate of ETP-RI in the PSIS method was high (100 %) due to device improvements, which may be the reason for no significant differences. In our study, ETP-RI was performed in 75 % of patients with RBO in the PSIS group. However, additional SEMS deployment in the posterior branch was difficult. In our PSIS method, the first SEMS was deployed in the posterior branch in many cases where insertion was expected to be difficult. We thought that ETP-RI in the posterior branch would be difficult to perform because it would require passing through two stent meshes. Before multi-stenting with the PSIS method, it is important to determine the sequence of stent insertion, knowing that ETP-RI in

▶ **Table 4** Risk factors for time to recurrent biliary obstruction according to the univariate and multivariate analyses.

		Univariate			Multivariate		
Factor	**N**	**HR**	**95 % CI**	***P* value**	**HR**	**95 % CI**	***P* value**
Age (≥ 70 years)	18	1.30	0.51–3.34	0.58			
Hybrid vs. PSIS (hybrid)	22	1.56	0.61–3.99	0.36	1.54	0.58–4.08	0.38
Diagnosis (other than cholangiocarcinoma)	12	1.88	0.67–5.24	0.23	1.30	0.43–3.89	0.64
Bismuth III vs. IV (III)	24	1.85	0.65–5.27	0.25	1.49	0.49–4.56	0.48
Liver metastasis (yes)	12	1.34	0.46–3.94	0.59			
Portal vein invasion (yes)	10	1.05	0.34–3.27	0.34			
Total bilirubin (≥ 2.0 mg/dL)	14	4.38	1.38–13.9	0.01	4.06	1.25–13.2	0.02
Previous biliary drainage (yes)	31	1.25	0.28–5.53	0.77			
SEMS for common bile duct obstruction (yes)	10	1.10	0.38–3.15	0.86			

HR, hazard ratio; CI, confidence interval; hybrid, side-by-side and partial stent-in-stent method; PSIS, partial stent-in-stent; SEMS, self-expandable metal stents.

the first stenting segment will be more difficult. By contrast, additional SEMS deployment in the posterior branch could be performed in 45 % of ETP-RI in the hybrid group; therefore, the hybrid method might be superior to the PSIS method in this respect. With both methods, it was considered necessary to perform RI by EUS-BD or PTBD when ETP-RI was difficult.

We found that these two methods were comparable, and the choice between the two should be made depending on the endoscopist's experience level.

Our study has some limitations. First, it is a retrospective comparative study that included a small number of cases, which reduces its statistical power. Second, we did not compare the same stents because uncovered SEMS (laser cut-type, 5.4F delivery) were considered suitable for the hybrid method, and the braided-type (mainly 6F delivery) was considered suitable for the PSIS method. To address these issues, prospective studies, studies with a large sample size, and those comparing the same stents are necessary.

Conclusions

In conclusion, to our knowledge, this is the first comparative study of the hybrid and PSIS methods using three or more stents for UMHBO. Although the hybrid method is a new procedure, the technical success rate, TRBO, and RI of both methods were comparable, and we believe that either method can be chosen at the physician's discretion. As for RI, we showed that a reasonably high success rate could be achieved by understanding the characteristics of each method. We hope that this study will be useful for physicians and facilitate further advances in the field.

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Competing interests

The authors declare that they have no conflict of interest.

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