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Efficacy of multi-hole self-expandable metallic stents versus partially covered self-expandable metallic stents in patients with malignant distal biliary obstruction caused by unresectable pancreatic cancer: a retrospective comparative cohort study in Japan

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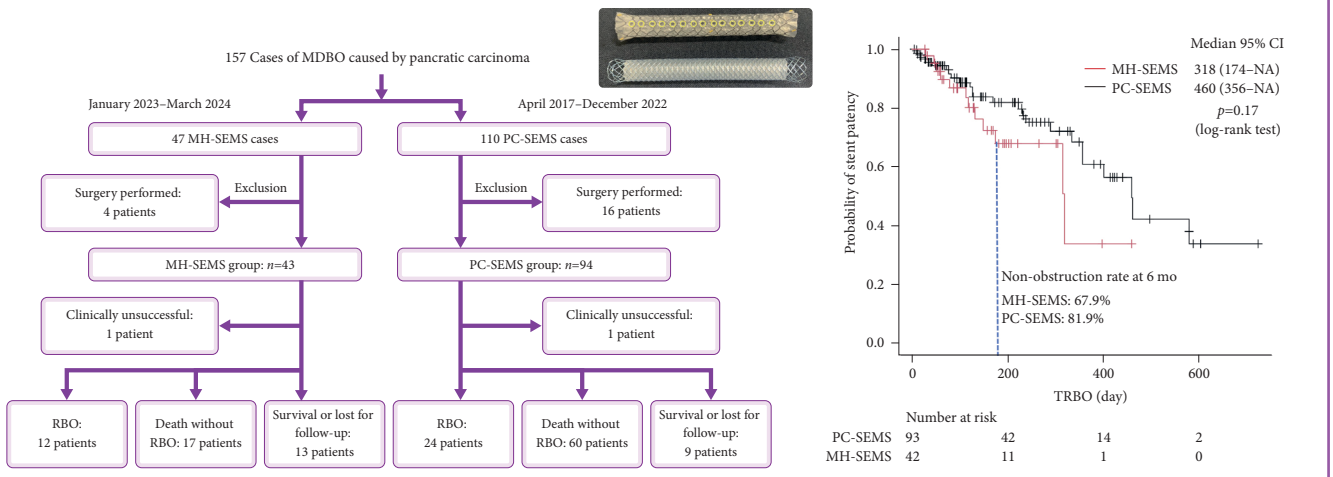

The clinical outcomes of MH-SEMS and PC-SEMS in patients with MDBO caused by pancreatic cancer were similar.

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Background/Aims: This study aimed to compare the stent patency between the novel multi-hole self-expandable metallic stent (MH-SEMS) and conventional partially covered SEMS (PC-SEMS) for malignant distal biliary obstruction (MDBO) in patients with pancreatic carcinoma.
Methods: This retrospective study compared stent patency between patients with MH-SEMS (n=43) and those with PC-SEMS (n=94). Secondary outcomes were overall survival (OS), incidence of recurrent biliary obstruction (RBO), causes of RBO, and adverse events (AEs).
Results: The median time to RBO did not differ significantly between the MH-SEMS and PC-SEMS groups (318 vs. 460 days, p=0.17). Furthermore, the two groups did not differ significantly in terms of OS and incidence rate of AEs, including RBO and cholecystitis. RBO caused by tumor ingrowth was slightly more common in the MH-SEMS group (p=0.089). The MH-SEMS group had a slightly lower 12-month non-obstruction rate than the PC-SEMS group (33.9% vs. 60.9%). In the MH-SEMS group, stent removal was successful in all seven patients in whom it was attempted.
Conclusions: The clinical outcomes of MH-SEMS and PC-SEMS were similar in patients with MDBO caused by pancreatic carcinoma were similar.

Keywords: Adverse effects; Endoscopic retrograde cholangiopancreatography; Obstructive jaundice; Pancreatic neoplasms; Self-expandable metallic stents

INTRODUCTION

Malignant distal biliary obstruction (MDBO) is a common complication of pancreatic carcinoma (PC). Biliary drainage using endoscopic retrograde cholangiopancreatography (ERCP) is widely performed to treat MDBO-induced obstructive jaundice.[1] With respect to long-term patency, various studies and guidelines recommend the use of self-expandable metallic stents (SEMSs) over plastic stents for biliary drainage in patients with MDBO. Furthermore, covered SEMSs (C-SEMSs) can prevent stent occlusion due to tumor ingrowth.[2-4] However, C-SEMSs can migrate if the tumor shrinks, specifically with strong chemotherapy; conversely, recurrent biliary obstruction (RBO) increases.[5]

Recent studies have reported the usefulness of a partially covered SEMS (PC-SEMS), in which both ends of the stent are bare, in preventing C-SEMS migration.[6,7] However, in terms of disadvantages, PC-SEMS is challenging to remove as the mucosa of the bile duct is embedded in the bare portion at both stent ends. Furthermore, the development of acute cholecystitis due to cystic duct obstruction in C-SEMS implantation is an important issue that cannot be neglected.[8-10] Several meta-analyses have attempted to compare the benefits of C-SEMSs with those of uncovered SEMS in patients with MDBO; however, these remain unidentified.[11,12] Thus, the best SEMS for drainage in patients with MDBO caused by PC remains debatable.

Conversely, previous studies reported that the novel multi-hole SEMS (MH-SEMS) is effective.[13,14] This stent has the longest patency with a lower risk of stent migration and tumor ingrowth.[14] Nonetheless, no studies have directly compared this novel MH-SEMS with PC-SEMS, and there are no reports on the efficacy of MH-SEMS in patients with unresectable PC. Therefore, a retrospective comparative study was conducted to determine the clinical efficacy of MH-SEMS and PC-SEMS in patients with MDBO caused by unresectable PC.

METHODS

Study design

This was a single-center, retrospective, comparative cohort study. Figure 1 shows a flowchart of this study. A total of 157 patients underwent initial SEMS placement for MDBO caused by PC between April 2017 and March 2024 at our institution, whereas 110 patients underwent PC-SEMS placement between April 2017 and December 2022. Sixteen patients who underwent surgery after stent placement were excluded. Moreover, 47 patients who underwent MH-SEMS placement between January 2023 and March 2024, and four patients who underwent surgery after stent placement were excluded from the analysis. Finally, 137 patients (MH-SEMS group, n=43; PC-SEMS group, n=94) were enrolled. MDBO was diagnosed based on pathological and/or radiological findings and/or clinical courses. Moreover, data on patient characteristics, PC status, chemotherapy regimens, and therapeutic effects were analyzed. Clinical stages of PC were evaluated using the Union for International Cancer Control TNM classification.[15] Patients unable to undergo surgical resection due to factors, such as advanced age or poor performance staus, were also included in the study, even if their

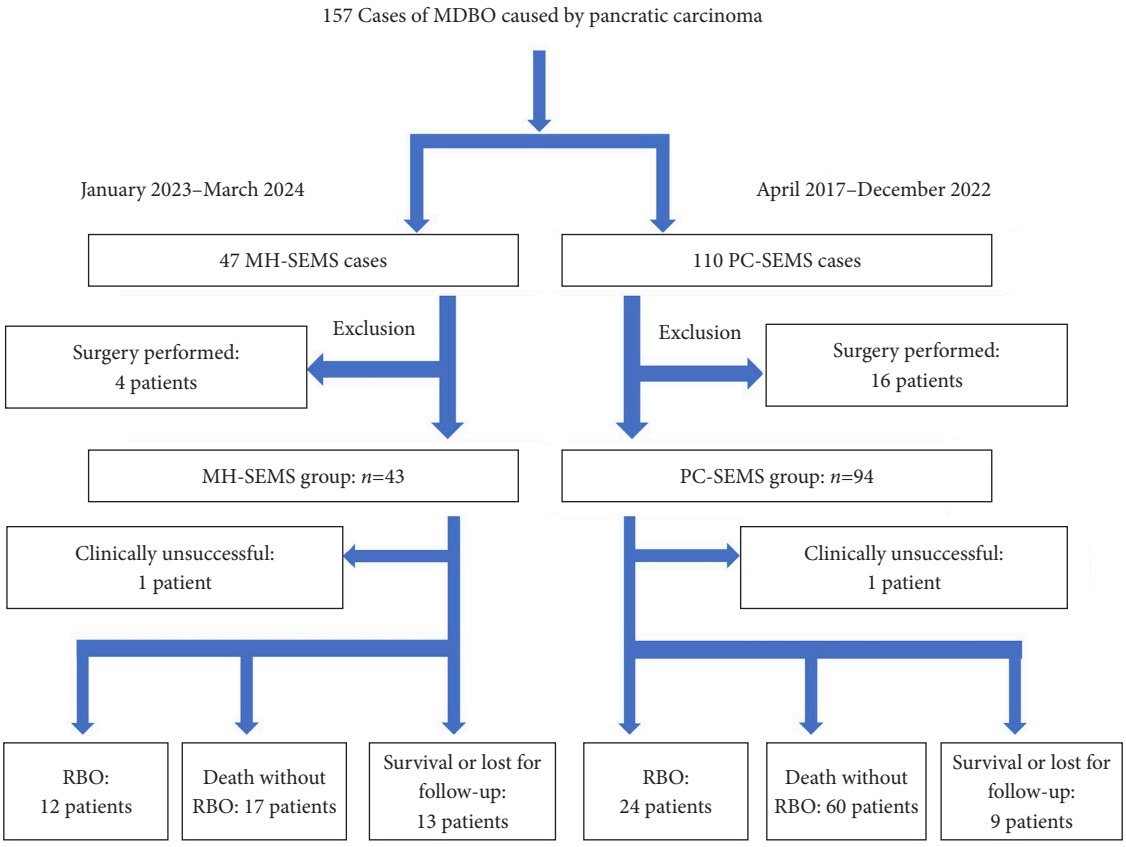

Fig. 1. Patient flowchart. MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent; MDBO, malignant distal biliary obstruction; RBO, recurrent biliary obstruction.

imaging findings corresponded to stage I–II. Therapeutic effects were determined using computed tomography (CT) 2 to 3 months after the SEMS placement. Patients who died within 2 months of stent placement were considered to have a progressive disease. Therapeutic efficacy was evaluated using the revised Response Evaluation Criteria in Solid Tumors guidelines.[16] After discharge, the patient was cautiously followed up via imaging, and blood tests were performed as needed until death. For patients whose hospital visits were interrupted early, the transferring medical institution was contacted via phone or writing to investigate the prognosis as much as possible.

The MH-SEMS and PC-SEMS manufactured by M.I. Tech (HANAROSTENT Biliary Multi-hole NEO) and Boston Scientific (WallFlex Biliary RX Partially Covered Stent System) were used in this study (Fig. 2). Both the C-SEMSs were structured using a similar woven nitinol wire with a silicone-covered membrane. However, the MH-SEMS was structured with a woven hook and cross-wire, whereas the PC-SEMS was structured with only a woven cross-wire.

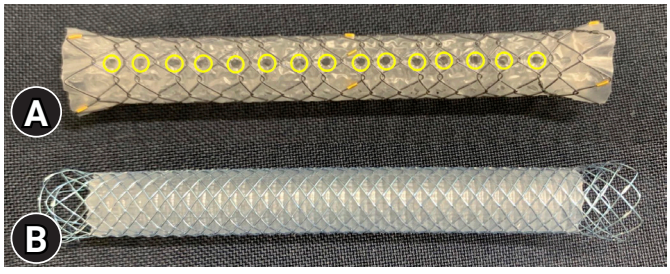

Fig. 2. (A) Multi-hole self-expandable metallic stent. Six rows of side holes were drilled on the membrane in line with the longitudinal direction of the stent (yellow circles). The diameters of each side hole was 1.8 mm. (B) Partially covered self-expandable metallic stent. The 5-mm portions at both ends of this stent were not covered by the membrane to prevent stent migration.

ERCP

All patients provided written informed consent before undergoing ERCP. A side-viewing endoscope (JF-260V, TJF-260V, or TJF-Q290V; Olympus Medical) was used. Alternatively, a balloon-assisted enteroscope (EI-580BT; Fujifilm Medical) was

used in patients with a surgically altered anatomy (except those undergoing Billroth I gastrectomy). Selective bile duct cannulation was performed using a standard ERCP catheter (MTW Endoskopie) with wire-guided cannulation and contrast medium injection. After selective bile duct cannulation, cholangiography was performed, and bile duct stricture length was measured. Thereafter, the SEMSs were placed in the biliary stricture during ERCP. The stent length was examined based on the length of the biliary stricture in the bile duct. The stent diameter was 10 mm in all patients. The distal end of the C-SEMS was positioned below the papilla in all patients. None of the patients received rectal indomethacin during the peri-procedural period.

Outcomes and definition

The primary outcome was median time to RBO (TRBO). Secondary outcomes were overall survival (OS), incidence rate of RBO, cause of RBO, and adverse events (AEs) for each type of C-SEMS.

Outcomes including technical success, clinical success, RBO, TRBO, and AEs were defined according to the Tokyo Criteria 2024.[17] The cause of RBO was determined based on CT, cholangiography during ERCP, and endoscopic images. Patients who died or did not require biliary stenting were excluded. AEs requiring SEMS removal were treated as RBOs according to Tokyo Criteria 2024. The severities of AEs and RBO were defined using the Tokyo Criteria 2024. OS was defined as the period between the initial metallic stent placement and mortality or the last follow-up. The stent removal rate was defined as the percentage of stents removed in all patients in each group. Cholangitis and cholecystitis were diagnosed according to the Tokyo Guidelines of 2018.[18,19]

Statistical analyses

Statistical analyses were performed using EZR ver. 1.68 (Saitama Medical Center, Jichi Medical University),[20] which is a graphical user interface for R ver. 4.3.1 (The R Foundation for Statistical Computing). The chi-squared test or Fisher's exact test was used to compare categorical variables. The *t*-test or Mann-Whitney *U*-test was used to analyze continuous data with skewed distributions. The non-obstruction rates at 3, 6, and 12 months, TRBO, and OS were estimated using the Kaplan–Meier method and compared using the log-rank test. Univariate logistic regression analyses were performed to assess the association between the possible risk factors and cholecystitis. Univariate and multivariate analyses for shorter TRBO were performed using the Cox proportional hazards model. Statistical significance was set at $p<0.05$.

Ethical statements

This study was approved by the Nara Medical University Ethics Committee (#3774) and was performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology Statement. The need for written informed consent was waived because of the retrospective design of the study. Hence, an opt-out approach was used.

RESULTS

Characteristics of the participants

Table 1 shows the clinical and demographic characteristics

Table 1. Characteristics of the participants

Characteristic	All participants (*n*=137)	MH-SEMS group (*n*=43)	PC-SEMS group (*n*=94)	*p*-value
Age (yr)	74 (67–79)	74 (67.5–78.5)	74 (67–80)	0.75
Sex				0.20
Male	69 (50.4)	18 (41.9)	51 (54.3)	
Female	68 (49.6)	25 (58.1)	43 (45.7)	
ECOG PS				0.72
0	52 (38.0)	18 (41.9)	34 (36.2)	
1	77 (56.2)	22 (51.2)	55 (58.5)	
2	8 (5.8)	3 (6.9)	5 (5.3)	
Surgically altered anatomy (except for Billroth I gastrectomy)	3 (2.2)	0 (0)	3 (3.2)[a]	0.55
Intact gallbladder	131 (95.6)	42 (97.7)	89 (94.7)	0.67

(Continued on the next page)

Table 1. Continued

Characteristic	All participants (*n*=137)	MH-SEMS group (*n*=43)	PC-SEMS group (*n*=94)	*p*-value
Clinical stage				0.38
IA+IB	7 (5.1)	2 (4.7)	5 (5.3)	
IIA+IIB	19 (13.9)	9 (20.9)	10 (10.6)	
III	37 (27.0)	9 (20.9)	28 (29.8)	
IV	74 (54.0)	23 (53.5)	51 (54.3)	
Resectability				0.16
Resectable	15 (10.9)	5 (11.6)	10 (10.6)	
Borderline resectable	12 (8.8)	7 (16.3)	5 (5.3)	
Unresectable local advanced	35 (25.6)	8 (18.6)	27 (28.7)	
Unresectable metastasis	75 (54.7)	23 (53.5)	52 (55.3)	
Duodenal invasion	64 (46.7)	24 (55.8)	40 (41.5)	0.14
Biliary stricture length (cm)	16.5 (11.5–25)	16 (14–20)	17 (11–27)	0.47
Maximum diameter of the common bile duct (mm)	12 (10–14.5)	13 (10–15)	12 (10–15)	0.85
Serum bilirubin before stenting (mg/dL)	2.4 (1.1–5.1)	2.9 (1.0–6.8)	2.1 (1.0–4.7)	0.24
Stent placement in acute cholangitis	27 (19.7)	12 (27.9)	15 (16.0)	0.11
Endoscopic sphincterotomy	1 (0.7)	0 (0)	1 (1.1)	1.00
Previous drainage history				
Yes	41 (29.9)	12 (27.9)	29 (30.9)	0.84
Endoscopic biliary stenting	35 (25.5)	11 (25.6)	24 (25.6)	
Endoscopic naso-biliary drainage	6 (4.4)	1 (2.3)	5 (5.3)	
Stent length (cm)				<0.01
5	1	1	0	
6	52	4	48	
7	21	21	0	
8	61	15	46	
10	2	2	0	
Stent diameter (mm)				
10	137 (100.0)	43 (100.0)	94 (100.0)	1.00
Chemotherapy				
Yes	84 (61.3)	27 (62.8)	57 (60.6)	0.85
Regimens				
GnP	60 (43.7)	22 (51.2)	38 (40.4)	0.26
mFFX	5 (3.6)	2 (4.7)	3 (3.2)	0.64
SOXIRI	32 (23.4)	11 (25.6)	21 (22.3)	0.67
5-FU+nal-IRI	16 (11.7)	3 (7.0)	13 (13.8)	0.39
Others	25 (18.2)	4 (9.3)	21 (22.3)	0.094
Therapeutic effects				0.40
Partial response	14 (16.7)	5 (18.5)	9 (15.8)	
Stable disease	60 (71.4)	17 (63.0)	43 (75.4)	
Progressive disease	10 (11.9)	5 (18.5)	5 (8.8)	
Treatment with radiotherapy	1 (0.74)	0 (0)	1 (1.1)	1.00
Follow-up period days	189 (95–297)	177 (94–237)	212 (102–330)	0.23

Values are presented as median (range) or number (%).
MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent; ECOG, Eastern Cooperative Oncology Group; PS, performance status; GnP, gemcitabine/nab-paclitaxel; mFFX, modified FOLFIRINOX (fluorouracil/irinotecan/oxaliplatin); SOXIRI, S-1/oxaliplatin/irinotecan; 5-FU, 5-fluorouracil; nal-IRI, nanoliposomal-irinotecan.
[a]Two cases of gastrojejunostomy bypass and one case of proximal gastrectomy.

of the patients are shown in Table 1. The MH-SEMS and PC-SEMS groups did not differ significantly in terms of demographic characteristics, including age, sex, performance status, PC status, duodenal invasion, biliary stricture length, total bilirubin level, or previous drainage history. As the length of the PC-SEMS was only 6 or 8 cm, there was a significant difference in terms of length between the two types of stents. There were no significant differences in chemotherapy regimens or therapeutic effects between the two types of stents.

Clinical outcomes

Table 2 presents the patients' clinical outcomes. Technical success was achieved in all patients in both groups. One patient in each group did not achieve clinical success because of insufficient stent expansion. In both cases, ERCP was performed again at a later date, and the stent was expanded using a 10-mm balloon catheter. Jaundice improved after the additional expansion. In the MH-SEMS group, stent removal was successful in all patients for whom it was attempted. However, in the PC-SEMS group, stent removal was successful in two of the four patients in whom it was attempted. The two groups did not differ in the total number of endoscopic procedures performed during the survival period.

RBO

Table 3 lists the RBO and its causes. The overall incidence rate of RBO did not differ significantly between the MH-SEMS and PC-SEMS groups (p=0.83). The 6-month non-occlusion rates were 67.9% and 81.9% in the MH-SEMS and PC-SEMS groups, respectively. Sludge obstruction was the most common cause of RBO in both groups. The MH-SEMS group was more likely to present with tumor ingrowth than the PC-SEMS group. There was no significant difference in the incidence of stent migration between the two groups. Figure 3 shows the Kaplan–Meier curves for TRBO. The median TRBOs was 318 days in the MH-SEMS group and 460 days in the MH-and PC-SEMS group, respectively (p=0.17). There was no significant difference in median TRBO between the MH-SEMS and PC-SEMS groups. The 6-month non-obstruction rates were 67.9% and 81.9% in the MH-SEMS and PC-SEMS groups, respectively. Figure 4 shows the OS duration of the patients. The OS did not significantly differ between the two groups (p=0.96). Figure 5 shows cumulative patient survival without stent dysfunction. The cumulative time to stent dysfunction or patient mortality did not differ significantly between the two groups (p=0.57).

Table 4 presents univariate and multivariate analyses for shorter TRBO using the Cox proportional hazards model. In the univariate analysis, poor performance status and duodenal invasion were significant risk factors. Multivariate analysis identified duodenal invasion (hazard ratio, 2.05; 95% confidence interval, 1.01–3.82; p=0.048) as an independent risk factor for shorter TRBO. Conversely, stent type was not a significant risk for shorter TRBO.

AEs

Table 5 shows the AEs. The incidence of AEs did not differ

Table 2. Clinical outcomes of the patients

Outcome	All patients (n=137)	MH-SEMS group (n=43)	PC-SEMS group (n=94)	p-value
Technical success	137 (100.0)	43 (100.0)	94 (100.0)	1.00
Clinical success	135 (98.5)	42 (97.7)	93 (98.9)	1.00
Cause of clinical failure				
Insufficient stent dilation	2 (1.5)	1 (2.3)	1 (1.1)	1.00
Successful stent removal in attempted cases	9/11 (81.8)	7/7 (100.0)	2/4 (50.0)	0.11
Days from stent placement to attempt stent removal	112 (12–357)	112 (28–337)	207.5 (12–357)	0.79
Cause of stent removal				
RBO of sludge	5 (3.6)	5 (11.6)	0	<0.01
RBO of ingrowth	1 (0.7)	1 (2.3)	0	0.31
RBO of migration (incomplete)	2 (1.5)	0	2 (2.1)	1.00
Cholecystitis	1 (0.7)	1 (2.3)	0	0.31
No. of endoscopic biliary drainage procedures during survival periods	1 (1–2)	1 (1–2)	1 (1–2)	0.87

Values are presented as number (%) or median (range).
MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent; RBO, recurrent biliary obstruction.

Table 3. Recurrent biliary obstruction

RBO	All patients (*n*=135)	MH-SEMS group (*n*=42)	PC-SEMS group (*n*=93)	*p*-value
Incidence rate of RBO (*n*, %)	36 (26.7)	12 (28.6)	24 (25.8)	0.83
Non-obstruction rate at 3 months (%)	89.7	86.7	90.1	
Non-obstruction rate at 6 months (%)	78.1	67.9	81.9	
Non-obstruction rate at 12 months (%)	55.8	33.9	60.9	
Time to RBO (95% CI)	460 (335–NA)	318 (174–NA)	460 (356–NA)	0.17
Overall survival without stent dysfunction (95% CI)	172 (128–222)	147 (112–202)	186 (126–238)	0.57
RBO grade, moderate/severe	16/20	4/8	12/12	0.48
Cause of RBO (*n*, %)				
Sludge	16 (11.9)	5 (11.9)	11 (11.8)	1.00
Food impaction	2 (1.5)	0 (0)	2 (2.2)	1.00
Ingrowth	4 (3.0)	3 (7.1)	1 (1.1)	0.089
Overgrowth	5 (3.7)	1 (2.4)	4 (4.3)	1.00
Stent migration	5 (3.7)	2 (4.8)	3 (3.2)	0.65
Cholecystitis (required stent removal)	1 (0.7)	1 (2.4)	0	0.31
Others	3 (2.2)	0 (0)	3 (3.2)	0.55

RBO, recurrent biliary obstruction; MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent; CI, confidence interval; NA, not applicable.

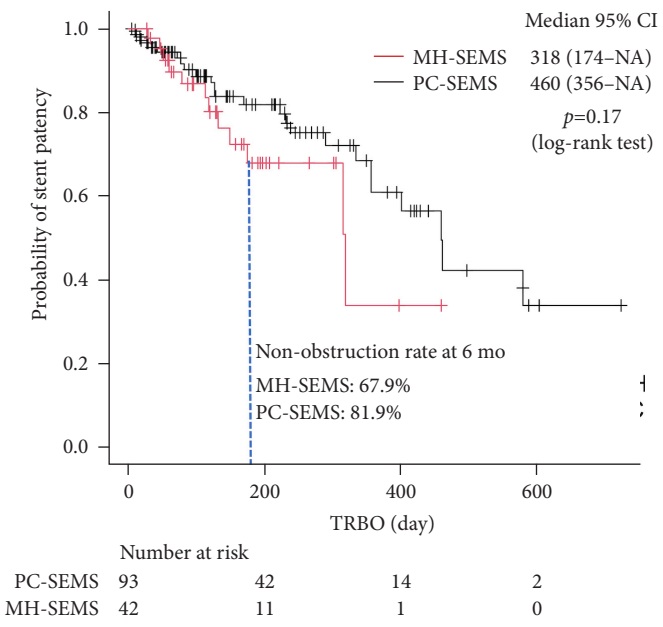

Fig. 3. Kaplan–Meier curve showing the time to recurrent biliary obstruction (TRBO). There was no significant difference in the median TRBO between the MH-SEMS and PC-SEMS groups. MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent; CI, confidence interval.

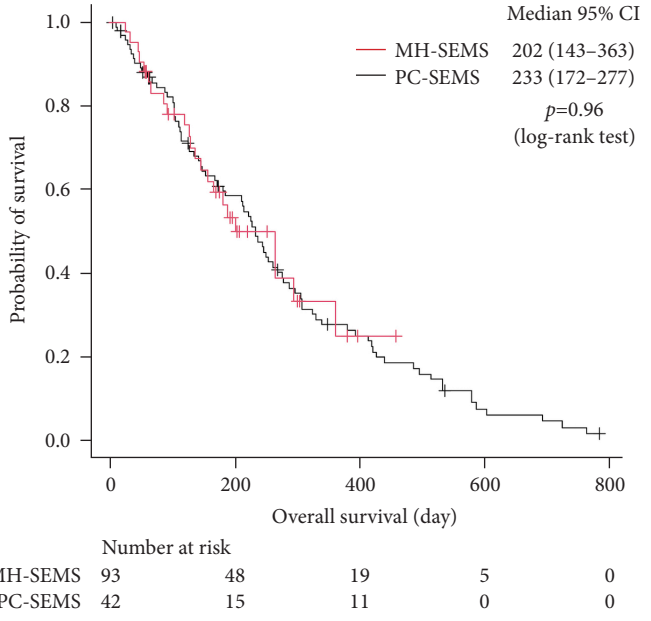

Fig. 4. Kaplan–Meier curve showing the overall survival (OS) duration of patients. There was no significant difference in the OS duration between the MH-SEMS and PC-SEMS groups. MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent; CI, confidence interval.

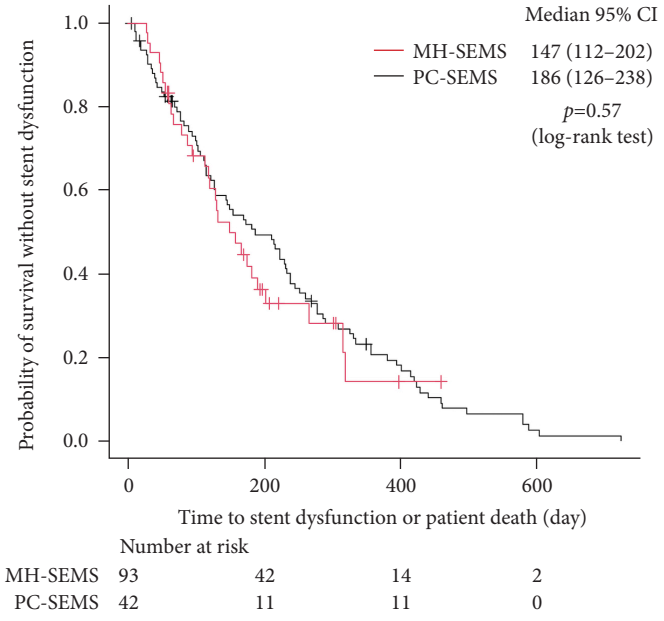

Fig. 5. Kaplan–Meier curve showing the cumulative patient survival without stent dysfunction. There was no significant difference in the cumulative time to stent dysfunction or patient mortality between the MH-SEMS and PC-SEMS groups. MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent; CI, confidence interval.

significantly between the two groups. Some patients in the MH-SEMS and PC-SEMS groups presented with cholecystitis. However, the incidence and severity did not differ significantly between the two groups. All cholecystitis cases were assumed to be caused by SEMS placement. Imaging studies confirmed no cases of cholecystitis due to gallstones, even in patients with gallstones. Furthermore, there were no significant differences in the incidence rates and severity of other AEs, including pancreatitis, nonobstructive cholangitis, liver abscess, and bleeding. In this study, none of the patients died of AEs.

Risk factors of cholecystitis

Of 131 patients with an intact gallbladder, 11 (8.4%) developed cholecystitis. Risk factors for cholecystitis were also analyzed (Table 6). In the univariate analysis, tumor invasion of the cystic duct was the only significant risk factor of cholecystitis (odds ratio, 5.49; 95% confidence interval, 1.50–20.10; p=0.010). Subgroup analysis of 95 patients (PC-SEMS group, n=65; MH-SEMS group, n=30) was performed. In this subgroup analysis, 36 patients with tumor invasion into the cystic duct were excluded (Table 7). No cases of cholecystitis occurred in the MH-SEMS group. However, compared to the PC-SEMS group, no significant difference in the incidence of cholecystitis was observed.

Table 4. Univariate and multivariate analyses for time to recurrent biliary obstruction (n=135)

	Univariate		Multivariate	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Patient factors				
Age (yr), >72 (n=58)/≤72 (n=77)	1.90 (0.94–3.86)	0.074	1.45 (0.65–3.23)	0.36
Sex, male (n=67)/female (n=68)	0.73 (0.37–1.43)	0.36		
ECOG PS, ≥1 (n=85)/0 (n=50)	2.20 (0.32–4.20)	0.034	1.71 (0.76–3.88)	0.20
Status of pancreatic cancer				
Unresectable metastasis (n=74)/others (n=61)	0.60 (0.30–1.20)	0.15		
Unresectable locally advanced (n=35)/others (n=100)	1.24 (0.62–2.48)	0.54		
Duodenal invasion, yes (n=61)/no (n=/74)	1.96 (1.01–3.82)	0.048	2.05 (1.01–3.82)	0.046
Stent factors				
MH-SEMS (n=42)/PC-SEMS (n=93)	1.66 (0.80–3.42)	0.17	1.63 (0.76–3.50)	0.21
Stent length, ≥8 cm (n=62)/<8 cm (n=73)	0.59 (0.29–1.18)	0.14		
Previous drainage history, yes (n=31)/no (n=94)	1.19 (0.61–2.33)	0.61		
Chemotherapy				
Chemotherapy, no (n=53)/yes (n=82)	2.08 (1.00–4.34)	0.051	1.68 (0.74–3.82)	0.21
Therapeutic effect, PD or BSC (n=64)/PR or SD (n=71)	1.53 (0.73–3.22)	0.26		
Chemotherapy not including GnP or BSC (n=76)/including GnP (n=59)	1.48 (0.73–3.01)	0.28		

HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; PS, performance status; MH-SEMS, multi-hole self-expandable metal stent; PC-SEMS, partially covered self-expandable metallic stent; PD, progressive disease; BSC, best supportive care; PR, partial response; SD, stable disease; GnP, gemcitabine/nab-paclitaxel.

Table 5. Adverse events

AE	All patients (*n*=135)	MH-SEMS group (*n*=42)	PC-SEMS group (*n*=93)	*p*-value
Rate of adverse events	37 (27.2)	13 (31.0)	24 (25.5)	0.54
Pancreatitis	11 (8.1)	2 (4.8)	9 (9.6)	0.50
Grade, mild/moderate/severe	9/2/0	2/0/0	7/2/0	1.00
Cholecystitis (in patients with an intact gallbladder)	11 (8.4)	3 (7.1)	8 (9.0)	1.00
Grade, mild/moderate/severe	2/7/2	1/1/1	1/6/1	0.28
Non-occlusive cholangitis	14 (10.3)	6 (14.3)	8 (8.5)	0.36
Grade, mild/moderate/severe	4/6/4	1/3/2	3/3/2	0.82
Liver abscess	10 (7.4)	4 (9.5)	6 (6.4)	0.63
Grade, mild/moderate/severe	0/0/10	0/0/4	0/0/6	1.00
Hemorrhage	2 (1.5)	1 (2.4)	1 (1.1)	0.52
Grade, mild/moderate/severe	0/1/1	0/0/1	0/1/0	1.00

Values are presented as number (%) or number only.
MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent.

Table 6. Risk factors of cholecystitis after stent placement (univariate analysis)

Variable	OR (95% CI)	*p*-value
Patient factors		
Age (yr), ≤74 (*n*=69)/>74 (*n*=62)	1.64 (0.46–5.89)	0.45
Sex, male (*n*=66)/female (*n*=65)	0.34 (0.15–1.92)	0.34
ECOG performance status, ≥1 (*n*=79)/0 (*n*=52)	1.17 (0.32–4.20)	0.81
Gallstone, present (*n*=27)/absent (*n*=104)	1.50 (0.37–6.08)	0.57
Maximum diameter of the CBD, <12 (*n*=75)/≥12 mm (*n*=56)	2.45 (0.68–8.82)	0.17
Status of pancreatic cancer		
Unresectable local advanced (*n*=35)/others (*n*=96)	2.74 (0.78–9.65)	0.12
Duodenal invasion, yes (*n*=60)/no (*n*=71)	0.41 (0.11–1.64)	0.21
Biliary stricture length ≥16 mm (*n*=74)/<16 mm (*n*=57)	0.64 (0.18–2.20)	0.48
Tumor invasion of cystic duct, yes (*n*=36)/no (*n*=95)	5.49 (1.50–20.10)	0.010
Tumor invasion to the feeding artery, yes (*n*=33)/no (*n*=98)	1.12 (0.28–4.52)	0.87
Stent factors		
MH-SEMS (*n*=42)/PC-SEMS (*n*=89)	0.46 (0.095–2.24)	0.34
Stent length, ≥8 cm (*n*=59)/<8 cm (*n*=72)	1.02 (0.30–3.52)	0.98
Stent across the orifice of the cystic duct, yes (*n*=100)/no (*n*=31)	1.43 (0.29–7.02)	0.66
Others		
Stent placement in acute cholangitis, yes (*n*=26)/no (*n*=105)	1.81 (0.43–7.53)	0.42
Previous drainage history, yes (*n*=38)/no (*n*=93)	0.91 (0.23–3.63)	0.90
Treatment with chemotherapy, yes (*n*=81)/no (*n*=50)	3.00 (0.62–14.50)	0.17

OR, odds ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; CBD, common bile duct; MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent.

Table 7. Cholecystitis in patients without tumor invasion to the cystic duct

	MH-SEMS group (*n*=30)	PC-SEMS group (*n*=65)	*p*-value
With cholecystitis	0 (0)	4 (6.2)	0.30
Without cholecystitis	30 (100.0)	61 (93.8)	

Values are presented as number (%).
MH-SEMS, multi-hole self-expandable metallic stent; PC-SEMS, partially covered self-expandable metallic stent.

DISCUSSION

This study compared the novel MH-SEMS and conventional PC-SEMS to assess the use of the MH-SEMS in patients with MDBO caused by PC. The two types of stents did not differ in terms of TRBO or safety. The type of SEMS used did not affect TRBO, and only duodenal invasion caused by PC was identified as a factor that significantly shortened TRBO. However, our results showed that if AEs such as RBO and cholecystitis occurred, MH-SEMS could be removed while maintaining the same level of anti-migration effects as PC-SEMS.

Recent advancements in chemotherapy for PC have improved local tumor control.[21,22] The causes of RBO include tumor ingrowth and sludge obstruction. However, stent migration cannot be ignored in the context of the increasing number of PC patients with long-term survival. To prevent C-SEMS migration, a previous study showed the usefulness of conventional PC-SEMS with the bare ends of the SEMS[6,7] or novel C-SEMSs with anchoring fins.[23] Recently, another study attempted to fix the distal end of a C-SEMS to the duodenal mucosa using an endoscopic hemostatic clip.[24] However, these approaches pose potential risks that make stent removal challenging. Conversely, although broadly classified as a PC-SEMS, the novel MH-SEMS evaluated in this study can be eliminated if AEs develop. In 7 (16.3%) of the 43 patients who underwent MH-SEMS placement, the stents were successfully removed without any AEs. The endoscopic treatment options for RBO after C-SEMS placement include mechanical cleaning, additional stent placement, and stent exchange. C-SEMSs are advantageous because they can be easily removed. Stent exchange is the most common clinical choice for treating RBO. Jirapinyo et al.[25] showed that stent replacement was superior to additional stent placement and mechanical cleaning.

In contrast, in our study, the median TRBO and overall incidence of RBO did not differ significantly. However, RBO caused by tumor ingrowth was slightly more likely to occur in MH-SEMS. This may be attributed to the presence of side holes in the cover membrane in MH-SEMS, which facilitate tumor growth into the stent lumen more readily than in PC-SEMS. Moreover, the MH-SEMS group had a slightly lower 12-month non-obstruction rate than the PC-SEMS group (33.9% vs. 60.9%). Furthermore, in this study, the TRBO of the MH-SEMS was shorter than that previously reported.[14] Kulpatcharapong et al.[14] reported that the TRBO of an MH-SEMS was 479 days. However, their study included patients with different cancer types, such as cholangiocarcinoma, in addition to PC, and the OS of these patients was longer than that of patients in our study. Our study included only patients with MDBO attributed to unresectable PC, and these differences in background factors may have affected TRBO. In contrast, Takeda et al.[26] recently reported the MH-SEMS results in patients with MDBO due to unresectable PC. Unlike the aforementioned report from Thailand, Takeda et al.[26] reported that the TRBO for MH-SEMS was significantly shorter than that for conventional fully C-SEMS at 101 days. Takeda et al.[26] highlighted that multiple small ingrowths occur via the side hole of the MH-SEMS, which can easily cause blockage of the antegrade bile flow. However, their study included a smaller number of cases than ours and did not evaluate the therapeutic effects of chemotherapy. Nevertheless, TRBO of MH-SEMS varies substantially depending on the report, and more prospective studies with larger numbers of cases are needed in the future. Additionally, in the latest Tokyo Criteria 2024,[17] stent removal caused by AEs possibly related to the stent itself was considered RBO. Therefore, stents that can be removed may have a higher incidence of RBO than those that cannot.

However, cholecystitis after C-SEMS placement cannot be neglected. Risk factors for the development of cholecystitis after C-SEMS placement include tumor invasion into the cystic duct, presence of gallstones, and diameter of the common bile duct.[8-10,27] Specifically, tumor invasion into the cystic duct is the strongest risk factor for the development of cholecystitis.[28] The usefulness of prophylactic endoscopic gallbladder stenting (EGBS)[8] and endoscopic ultrasonography-guided gallbladder drainage[29] has been reported in recent years. However, the development of cholecystitis after C-SEMS placement remains challenging to prevent completely. In our study, tumor invasion of the cystic duct was the strongest risk factor for the development of cholecystitis, and the use of MH-SEMS was not associated with a decreased risk of developing cholecystitis. In contrast, in our study, none of the patients in the MH-SEMS group developed cholecystitis in the absence of tumor invasion into the cystic duct. Therefore, the efficacy of MH-SEMS in preventing cholecystitis cannot be judged solely based on this study; thus, further studies should be conducted. However, as presented in the previous text, the MH-SEMS can be removed even if cholecystitis develops. In our study, there was one case of severe cholecystitis in the MH-SEMS group, which improved after stent removal and EGBS placement.

Furthermore, the possibility of pancreatitis after SEMS placement should not be disregarded. In our study, only of 1/127 pa-

tients underwent endoscopic sphincterotomy (ES) before SEMS placement. Whether ES before SEMS placement reduces the risk after SEMS placement remains controversial. Onnekink et al.[30] conducted a randomized controlled trial and found no preventive effect of ES before C-SEMS placement in patients with MDBO. Hayashi et al.[31] also argued that ES before C-SEMS placement is unnecessary in cases of pancreatic duct obstruction, such as pancreatic head cancer. In our study, pancreatitis developed in only 8.1% of patients with PC who received SEMS placement, and all cases were mild or moderate and resolved with conservative treatment. None of the patients required SEMS removal due to pancreatitis. These findings are consistent with those of previous studies by Onnekink et al.[30] and Hayashi et al.[31]

In addition, cost-effectiveness is a key factor in SEMS drainage of MDBO. As of 2024, both MH-SEMS and PC-SEMS are sold in Japan at the same price (227,000 JPY), indicating that the initial placement costs are identical. However, the overall cost-effectiveness depends on multiple factors, including the frequency of RBO, treatments required for RBO management, and endoscopic reintervention strategies. Further studies are needed to determine which stent type offers superior cost-effectiveness, considering their similar clinical outcomes.

The current study had several limitations. First, this study had a retrospective design. Notably, PC-SEMS were primarily used in the first half of the study period, whereas MH-SEMS were used more frequently in the second half. Although the proportion of patients who received nanoliposomal irinotecan chemotherapy was slightly higher in the MH-SEMS group, the difference was not statistically significant. Furthermore, as shown in Table 1 and Figure 4, patient characteristics and survival rates did not differ significantly between the MH-SEMS and PC-SEMS groups. The details of the ERCP procedure were similar in both groups. However, stent selection bias may have existed. Second, our sample size was small, potentially limiting the detection of statistically significant differences in key outcomes related to MH-SEMS and PC-SEMS performance, such as cholecystitis incidence after stent placement and stent removal success. Third, the two stents were of the same braided type. However, the manner in which the stent wires were braided differed. This variation in the mechanical properties of the stent body may have influenced our results.

In conclusion, the clinical outcomes of MH-SEMS and PC-SEMS in patients with MDBO caused by PC were similar.

Conflicts of Interest

The authors have no potential conflicts of interest.

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Author Contributions

Conceptualization: KKi, SA; Data curation: SA, FT, JH, KKa, AM, YM, YO, TI; Formal analysis: KKi, SA; Investigation: KKi, SA; Methodology: KKi, SA; Project administration: KKi, SA; Resources: KKi, SA; Supervision: HY; Validation: KKi, SA; Visualization: KKi, SA; Writing–original draft: SA, KKi; Writing–review & editing: all authors.

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