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Long-term outcomes of duckbill-type anti-reflux metal stents versus conventional covered metal stents in reinterventions after covered biliary metal stent dysfunction in unresectable pancreatic cancer

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Abstract

Background The use of duckbill-type anti-reflux metal stents (DMS) in reinterventions after covered metal stent (CMS) dysfunction has been reported in patients with distal malignant biliary obstruction (MBO). However, the superiority of DMS over conventional CMS (c-CMS) has not been established. Therefore, we conducted this retrospective study to evaluate the long-term efficacy and safety of DMS as a second stent in comparison with c-CMS.

Methods We investigated consecutive patients with distal MBO due to unresectable pancreatic cancer who underwent reintervention after dysfunction of initial biliary CMS at our institution. We compared causes of recurrent biliary obstruction (RBO), time to RBO (TRBO), adverse events (AEs), and reintervention rates of DMS and c-CMS in this stenting.

Results A total of 76 patients were included (DMS 41 and c-CMS 35). While overall RBO rates were similar between the two groups (46% vs. 63%, $p=0.172$), RBO due to non-occlusion cholangitis tended to be less frequent in the DMS group than in the c-CMS group (2% vs. 14%, $p=0.089$). Median TRBO was significantly longer in the DMS group (286 days vs. 112 days, $p=0.029$). DMS was identified as the only significant risk factor for TRBO (hazard ratio, 0.52; $p=0.044$). Overall AE rates were significantly lower in the DMS group (2% vs. 23%, $p=0.010$), with non-occlusion cholangitis being the most common AE in the c-CMS group. Endoscopic reintervention was successfully performed in all patients in both groups, despite failed stent removal in 15% of patients in DMS group.

Conclusions DMS was associated with a significantly longer TRBO and lower rate of AEs compared with c-CMS in reinterventions after initial CMS dysfunction. DMS may be preferable to c-CMS as a second stent after biliary CMS dysfunction.

Keywords Anti-reflux metal stent · Covered metal stent · Distal malignant biliary obstruction · Pancreatic cancer · Recurrent biliary obstruction

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Abbreviations

MBO	Malignant biliary obstruction
PC	Pancreatic cancer
SEMS	Self-expandable metal stent
CMS	Covered metal stent
RBO	Recurrent biliary obstruction
c-CMS	Conventional covered metal stent
ARMS	Anti-reflux metal stent
ARV	Anti-reflux valve
DMS	Duckbill-type anti-reflux metal stent
ENBD	Endoscopic nasobiliary drainage
NSAIDs	Nonsteroidal anti-inflammatory drugs
TRBO	Time to recurrent biliary obstruction
AE	Adverse event
OS	Overall survival
ECOG	Eastern Cooperative Oncology Group
PS	Performance status
HR	Hazard ratio
CI	Confidence interval

Distal malignant biliary obstruction (MBO) is a common clinical manifestation of pancreatic cancer (PC). Endoscopic placement of self-expandable metal stents (SEMS) has become the standard treatment for unresectable distal MBO due to longer stent patency compared to plastic stents [1–3]. Covered SEMS were developed to prevent stent occlusion due to tumor ingrowth [4]. However, stent occlusion of covered metal stents (CMS) due to sludge and food impaction remains a significant problem, especially for patients at high risk of recurrent biliary obstruction (RBO), including patients with duodenal invasion, those treated with an indwelling duodenal stent, and those who undergo SEMS placement as a reintervention after conventional CMS (c-CMS) dysfunction [5–8]. Duodenobiliary reflux, which frequently becomes an issue when SEMS are placed across the papilla, is a major cause of sludge formation and food impaction, which in turn can lead to stent dysfunction [9].

Several types of anti-reflux metal stents (ARMSs) have been developed to reduce risks associated with duodenobiliary reflux, including stent occlusion and non-occlusion cholangitis [10–16]. Although ARMS has been associated with a lower rate of stent occlusion compared to conventional SEMS in several studies, reported results have not been consistent. A recent meta-analysis showed that ARMS was associated with a lower rate of stent occlusion and a higher rate of stent migration, resulting in similar rate of stent dysfunction [17]. In our pilot study of 30 patients receiving a duckbill-type anti-reflux metal stent (DMS) who are also included in this study, we demonstrated that DMS achieved a significantly longer stent patency compared to c-CMS as reintervention for CMS dysfunction [18]. However, the study had several limitations including the lack of a control group and a relatively short follow-up period, resulting in an overall RBO rate of only 30%.

Therefore, we conducted this retrospective study to evaluate the long-term efficacy and safety of DMS in comparison with c-CMS as a second stent after initial CMS dysfunction in patients with unresectable PC.

Methods

Patients

We conducted a single-center retrospective study of consecutive patients with distal MBO due to unresectable PC who underwent reintervention after CMS dysfunction at our institution between May 2015 and July 2021. Only patients who developed RBO of the initial c-CMS and subsequently underwent CMS placement via the papilla were included in this study. Excluded patients were as follows: (1) patients who had a history of more than one biliary SEMS placement, (2) patients who received an uncovered metal stent or ARMS as the initial SEMS, (3) patients who received a SEMS above the papilla, (4) patients with surgically altered anatomy, and (5) patients with a concomitant hilar biliary obstruction. The selection of the type of SEMS was mainly based on the time period the patient received the second SEMS. In general, c-CMS was used between May 2015 and May 2019, while DMS was mainly used between June 2019 and July 2021. Written informed consent of the procedure was obtained from all patients. This study was approved by the ethics committee of our institution (Institutional Review Board number: 2022-GB-012).

ARMS and c-CMS

The ARMS used in this study was a fully covered laser-cut type SEMS with a 12.5 mm duckbill-shaped anti-reflux valve (ARV) attached to the distal end (Kawasumi Duckbill Biliary Stent, Kawasumi Laboratories Inc., Tokyo, Japan). The stent is made of nitinol wire and an expanded polytetrafluoroethylene membrane that extends beyond the distal end to create the duckbill-shaped ARV. The ARV is usually closed to prevent the reflux of the duodenal content into the bile duct, but opens when the bile duct pressure increases. Radio-opaque gold markers are located at both the proximal and distal end of the metal part to facilitate the recognition of the stent under fluoroscopy or endoscopic view. DMS with a diameter of 10 mm and lengths of 60 or 80 mm were used in this study. The delivery system was 9 Fr in diameter.

The c-CMS used in this study were as follows: HANAROSTENT Biliary (M.I.Tech, Soul, Korea), Evolution

Biliary Controlled-Release Stent – Fully Covered (Cook Medical, Bloomington, USA), Niti-S SUPREMO stent (Taewoong Medical, Soul, Korea).

Endoscopic procedures

ERCP was performed using a therapeutic duodenoscope (JF260, TJF260; Olympus Medical Systems, Tokyo, Japan) under moderate sedation with intravenous pethidine and midazolam. In general, the occluded SEMS was removed using a rat tooth forceps or snare forceps and an endoscopic nasobiliary drainage (ENBD) tube was placed to control cholangitis in the first session. After cholangitis had subsided, we subsequently deployed a SEMS under fluoroscopic and endoscopic guidance after balloon sweeping of the bile duct using an extraction balloon catheter (Multi-3 V Plus Extraction Balloon, Olympus Medical Systems, Tokyo, Japan) in the second session. The length of SEMS was determined based on cholangiographic findings. As for DMS, the distal end of the metal part was placed 5–10 mm below the papilla to completely expose the ARV into the duodenum. All patients had undergone endoscopic sphincterotomy at the time of initial CMS placement. Prophylactic rectal nonsteroidal anti-inflammatory drugs (NSAIDs) were used at the discretion of each endoscopist, and prophylactic pancreatic stenting was not performed in any of the patients.

Study endpoints and definitions

The primary outcome of this study was time to RBO (TRBO). Secondary outcomes included technical success, functional success, causes of RBO, non-RBO rates at 3, 6, and 12 months after SEMS placement, adverse events (AEs), and overall survival (OS). Outcomes of SEMS were basically evaluated according to Tokyo Criteria 2014 [19]. However, non-occlusion cholangitis was also considered as RBO when endoscopic biliary drainage was necessary to treat cholangitis, while it was considered as an AE when it improved with antibiotics without requiring any endoscopic interventions. Technical success was defined as successful deployment of a SEMS in the intended location with sufficient coverage of the stricture, whereas functional success was defined as a 50% decrease in or normalization of serum bilirubin level within 14 days after stent placement. When serum bilirubin level was normal due to prior ENBD placement, functional success was defined as no exacerbation of serum bilirubin level after stent placement. RBO was defined as a composite endpoint of either occlusion or migration. TRBO was defined as the time from stent placement to RBO occurrence. Patients who were lost to follow up or alive at the end of the study period, underwent stent removal, or died without RBO were treated as censored cases at the time of the last follow up, stent removal, or death. Stent removal due to AEs or conversion surgery and death without RBO were treated as competing events in the competing risk analysis. OS was defined as the time from stent placement to death. AEs were categorized as early ($\leq$30 days after SEMS placement) or late ($\geq$31 days after SEMS placement) [19] and the severity of AEs was graded according to the American Society of Gastrointestinal Endoscopy lexicon guidelines [20]. Duodenal invasion was diagnosed by the endoscopist at the time of SEMS placement. The amount of ascites was evaluated using the most recent computed tomography scan before SEMS placement and was categorized according to the Japanese Classification of Gastric Carcinoma [21]: none, ascites undetected by computed tomography; mild, ascites localized in only one area such as the pelvic cavity; moderate, ascites neither mild nor severe; and severe, ascites throughout the abdominal cavity. Follow-up data were confirmed until April 30, 2022.

Statistical analysis

Continuous variables are presented as median (interquartile range) and were compared using Mann–Whitney U test. Categorical variables are described as absolute numbers (proportions) and were analyzed using χ 2 test or Fisher's exact test as appropriate. TRBO and OS were estimated using the Kaplan–Meier method and compared using the log-rank test. The Cox proportional hazards model was used to identify risk factors for TRBO. Time to previous SEMS dysfunction was categorized into two groups: those shorter and longer than the median time period. Factors with *P*-values <0.20 were considered to be potential risk factors and were included in the multivariate analysis. The Cox proportional hazards model was also used to evaluate the treatment effect of DMS on TRBO in specific subgroups, with hazard ratios (HRs) shown in a forest plot. As the Kaplan–Meier method censors patients when competing events occur, we performed a competing risk analysis to estimate the cumulative incidence of RBO in the presence of competing risks [22]. The cumulative incidence was compared using the Gray's test [23]. *P*-values <0.05 were considered statistically significant. Statistical analysis was carried out using the EZR software version 1.40 [24].

Results

Patient characteristics

Seventy-six consecutive patients with unresectable PC who underwent reintervention after initial CMS dysfunction were included in this study. Forty-one patients received DMS (DMS group) and 35 patients received a conventional CMS (c-CMS group) as the second SEMS. Patient characteristics

Table 1 Baseline characteristics of patients who received DMS or c-CMS in reinterventions after prior SEMS dysfunction

		DMS $n=41$	c-CMS $n=35$	P value
Age, years		66 (57–72)	65 (62–74)	0.680
Sex	Male	17 (41%)	21 (60%)	0.167
ECOG PS	0/1/2	23 (56%)/14 (34%)/4 (10%)	19 (54%)/ 11 (31%)/ 5 (14%)	0.893
Tumor status				> 0.999
Locally advanced		13 (32%)	12 (34%)	
Metastatic		28 (68%)	23 (66%)	
Duodenal invasion	Yes	10 (24%)	6 (17%)	0.575
Co-existing duodenal metal stent	Yes	3 (7%)	2 (6%)	> 0.999
Ascites	Moderate to severe	8 (20%)	5 (14%)	0.761
Peritoneal dissemination	Yes	8 (20%)	1 (3%)	0.033
Post-cholecystectomy	Yes	2 (5%)	3 (9%)	0.657
Anti-tumor treatment before SEMS placement				0.405
Chemotherapy		39 (95%)	31 (89%)	
1st line/2nd line/3rd line		23 (56%)/ 14 (34%)/ 2 (5%)	18 (51%)/ 12 (34%)/ 1 (3%)	
Best supportive care		2 (5%)	4 (11%)	
Median time to prior SEMS dysfunction, days		168 (115–290)	205 (110–312)	0.453
Causes of prior SEMS dysfunction				
Occlusion		16 (39%)	11 (31%)	0.631
Sludge		13 (32%)	9 (26%)	
Food impaction		3 (7%)	2 (6%)	
Stent migration		17 (41%)	22 (63%)	0.071
Inward migration		1 (2%)	6 (17%)	
Outward migration		16 (39%)	16 (46%)	
Non-occlusion cholangitis		8 (20%)	2 (6%)	0.097

Continuous variables are expressed as median (interquartile range) and categorical variables are expressed as absolute numbers (proportions). *DMS* duckbill-type anti-reflux metal stent, *c-CMS* conventional covered metal stent, *SEMS* self-expandable metal stent, *ECOG* Eastern Cooperative Oncology Group, *PS* performance status

of the DMS and c-CMS groups are summarized in Table 1. Duodenal invasion and duodenal metal stents were present in ten (24%) and three (7%) patients, respectively, in the DMS group and in six (17%) and two (6%) patients, respectively, in the c-CMS group. Moderate to severe ascites was observed in eight patients (20%) in the DMS group and five patients (14%) in the c-CMS group. Peritoneal dissemination was more frequently observed in the DMS group (20% vs. 3%, $p=0.033$). Other parameters including anti-tumor treatment before SEMS placement and median time to prior SEMS dysfunction (168 days vs. 205 days, $p=0.453$) were not significantly different between the two groups. As for the causes of prior SEMS dysfunction, the DMS group tended to have a higher rate of non-occlusion cholangitis (20% vs. 6%, $p=0.097$) and a lower rate of stent migration (41% vs. 63%, $p=0.071$) compared to the c-CMS group.

Procedural characteristics and AEs

Details on procedural characteristics and AEs are shown in Table 2. All patients received stents with a diameter of 10 mm, except for one patient in the c-CMS group who received a stent with a diameter of 12 mm (Niti-S SUPREMO stent). Stents used in both groups were generally 6 to 8 cm in length. Sphincterotomy had been previously performed in all patients in both groups. Prophylactic rectal NSAIDs was used in five (12%) and three (9%) patients in the DMS and c-CMS groups, respectively. The technical success rate was 100% in both groups and the functional success rate was not significantly different between the two groups (100% vs. 97%, $p=0.461$). The percentage of patients who received chemotherapy after SEMS placement was also similar between the two groups.

Early AEs occurred in one patient (mild pancreatitis) in the DMS group and five patients (moderate cholecystitis: 1, mild non-occlusion cholangitis: 4) in the c-CMS group ($p=0.089$). Late AEs occurred in three cases, all in the c-CMS group (severe pancreatitis and mild non-occlusion cholangitis: 1, moderate cholecystitis: 1, mild non-occlusion cholangitis: 1) ($p=0.093$). AEs were significantly less common in the DMS group compared to the c-CMS group (2% vs. 23%, $p=0.010$), with non-occlusion cholangitis being

Table 2 Procedural characteristics and adverse events of patients who received DMS or c-CMS as reintervention after prior SEMS dysfunction

		DMS $n=41$	c-CMS $n=35$	P value
Procedural characteristics				
Stent diameter, mm	10/12	41 (100%)/ 0	34 (97%)/1 (3%)	0.461
Stent length, cm	4/5/6/7/8	0/0/29 (71%)/0/12 (29%)	1 (3%)/2 (6%)/18 (51%)/5 (14%)/9 (26%)	0.012
Prior history of sphincterotomy	Yes	41 (100%)	35 (100%)	> 0.999
Prophylactic rectal NSAIDs	Yes	5 (12%)	3 (9%)	0.719
Technical success		41 (100%)	35 (100%)	> 0.999
Functional success		41 (100%)	34 (97%)	0.461
Anti-tumor treatment after SEMS placement		34 (83%)	29 (83%)	> 0.999
Adverse events		1 (2%)	8 (23%)	0.010
Early adverse events		1 (2%)	5 (14%)	0.089
Pancreatitis		1 (2%)	0	
Cholecystitis		0	1 (3%)	
Non-occlusion cholangitis		0	4 (11%)	
Late adverse events*		0 (0%)	3 (9%)	0.093
Pancreatitis		0	1 (3%)	
Cholecystitis		0	1 (3%)	
Non-occlusion cholangitis		0	2 (6%)	

Categorical variables are expressed as absolute numbers (proportions). *One patient in the c-CMS group developed both pancreatitis and non-occlusion cholangitis at different times. *DMS* duckbill-type anti-reflux metal stent, *c-CMS* conventional covered metal stent, *NSAIDs* nonsteroidal anti-inflammatory drugs, *SEMS* self-expandable metal stent

Table 3 Recurrent biliary obstruction after second biliary SEMS placement

	DMS $n=41$	c-CMS $n=35$	P value
Occlusion	8 (20%)	7 (20%)	> 0.999
Sludge	8 (20%)	6 (17%)	
Food impaction	0	1 (3%)	
Migration	10 (24%)	10 (29%)	0.795
Inward migration	2 (5%)	1 (3%)	
Outward migration	8 (20%)	9 (26%)	
Complete migration	6 (15%)	4 (11%)	
Incomplete migration	2 (5%)	5 (14%)	
Non-occlusion cholangitis	1 (2%)	5 (14%)	0.089
Total	19 (46%)	22 (63%)	0.172

Categorical variables are expressed as absolute numbers (proportions). *DMS* duckbill-type anti-reflux metal stent, *c-CMS* conventional covered metal stent, *SEMS* self-expandable metal stent

the most common AE in the c-CMS group. Overall frequency of non-occlusion cholangitis was also significantly lower in the DMS group (0% vs. 17%, $p=0.007$).

Outcomes of DMS and c-CMS

During a median follow-up period of 304 days (112–459 days) in the DMS group and 245 days (135–533 days) in the c-CMS group ($p=0.967$), RBO occurred in 41 patients (Table 3). Overall RBO rates were not significantly different between the two groups (46% vs. 63%, $p=0.172$). Stent migration was the most common cause of RBO in both groups (24% vs. 29%), followed by stent occlusion (20% vs. 20%). Inward migration occurred in two and one patient in the DMS and c-CMS groups, respectively, while outward migration occurred in eight (complete migration: 6, incomplete migration: 2) and nine (complete migration: 4, incomplete migration: 5) patients in the DMS and c-CMS groups, respectively. Non-occlusion cholangitis was less frequently observed in the DMS group (2% vs. 14%, $p=0.089$), although the difference was not statistically different. At the time of reintervention, the ARV was torn in seven of the nine patients (78%) in the DMS group who experienced RBO due to occlusion or non-occlusion cholangitis.

Kaplan–Meier curves of OS and TRBO are shown in Fig. 1. Median OS was similar between the two groups (357 days vs. 245 days, $p=0.358$). Median TRBO was significantly longer in the DMS group (286 days vs. 112 days, $p=0.029$). The non-RBO rates at 3, 6, and 12 months were 86%, 64%, and 36%, respectively, in the DMS group, and 69%, 35%, and 21%, respectively, in the c-CMS group.

Univariate and multivariate analyses of risk factors for TRBO are summarized in Table 4. Multivariate analysis identified DMS as the only independent predictor of TRBO (HR, 0.52; 95% confidence interval [CI], 0.28–0.98; $P=0.044$).

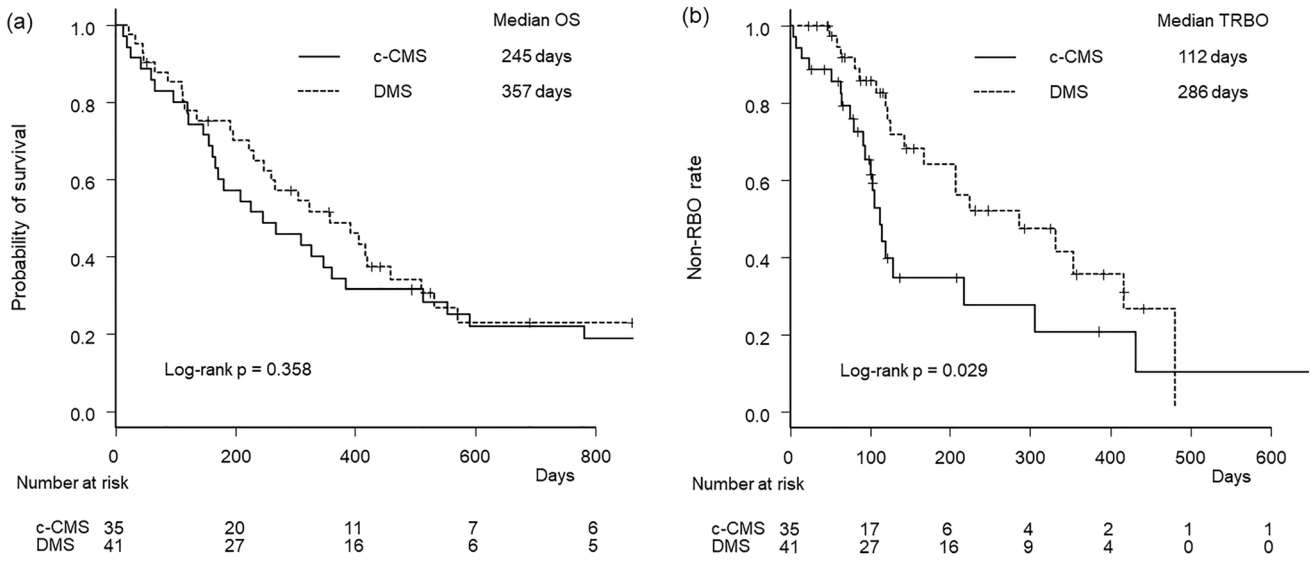

Fig. 1 Kaplan–Meier curves by stent group. **a** Overall survival. **b** Time to recurrent biliary obstruction. *DMS* duckbill-type anti-reflux metal stent, *c-CMS* conventional covered metal stent, *OS* overall survival, *RBO* recurrent biliary obstruction, *TRBO* time to recurrent biliary obstruction

Table 4 Univariate and multivariate analyses for time to recurrent biliary obstruction

		Univariate			Multivariate		
		HR	95% CI	*P* value	HR	95% CI	P value
Age	> 70 years	0.89	0.46–1.75	0.745			
Sex	Male	1.42	0.76–2.66	0.269			
ECOG PS	0	0.67	0.35–1.28	0.228			
Tumor status	Metastatic	1.38	0.72–2.66	0.335			
Time to previous SEMS dysfunction	≤ 200 days	1.32	0.71–2.47	0.385			
Co-existing duodenal metal stent	Yes	3.12	0.72–13.4	0.127	2.52	0.58–10.9	0.217
Duodenal invasion	Yes	1.58	0.71–3.51	0.262			
Ascites, moderate to massive	Yes	1.32	0.50–3.51	0.577			
Peritoneal dissemination	Yes	1.23	0.29–5.33	0.778			
Chemotherapy after SEMS placement	Yes	0.69	0.16–3.05	0.625			
Type of SEMS	DMS	0.50	0.27–0.94	0.032	0.52	0.28–0.98	0.044

ECOG Eastern cooperative oncology group, *PS* performance status, *SEMS* self-expandable metal stent, *DMS* duckbill-type anti-reflux metal stent, *HR* hazard ratio, *CI* confidence interval

Figure 2 shows the forest plot of HRs for TRBO according to subgroups. The treatment effect significantly favored the DMS group in several subgroups including males, metastatic disease, time to previous SEMS dysfunction ≤ 200 days, and absent or mild ascites.

Figure 3 shows the cumulative incidence of RBO. The cumulative incidence of RBO was lower in the DMS group (HR 0.55, 95% CI, 0.31–1.01, $p = 0.052$), although the difference was not statistically different.

Reintervention after RBO of DMS and c-CMS

Reintervention was performed in 19 patients (six patients experienced complete distal migration) in the DMS group. DMS removal was attempted in 13 patients and was successful in 11 patients (85%). Three patients presented with a duodenal stricture (type I: 1, type III: 2). All three patients underwent simultaneous duodenal stenting and endoscopic ultrasound-guided biliary drainage (hepaticogastrostomy: 1, choledochoduodenostomy: 2). Of the remaining 16 patients, 15 underwent CMS placement and one underwent endoscopic ultrasound-guided hepaticogastrostomy.

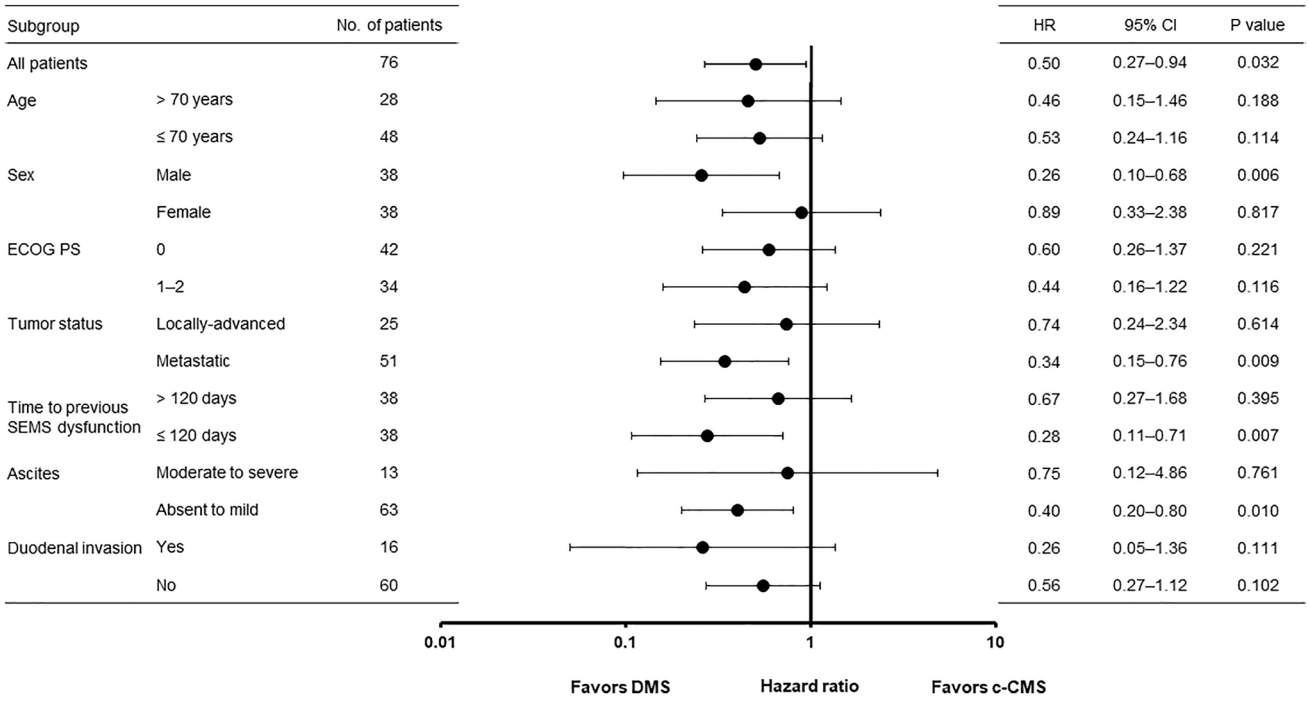

Fig. 2 Forest plot of hazard ratios for time to recurrent biliary obstruction in subgroups. *DMS* duckbill-type anti-reflux metal stent, *c-CMS* conventional covered metal stent, *SEMS* self-expandable metal stent, *ECOG* Eastern Cooperative Oncology Group, *PS* performance status, *HR* hazard ratio, *CI* confidence interval

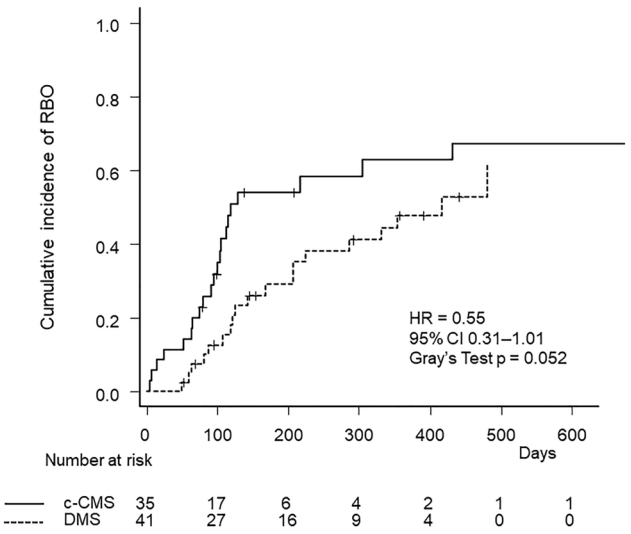

Fig. 3 Cumulative incidence of recurrent biliary obstruction by stent group. *DMS* duckbill-type anti-reflux metal stent, *c-CMS* conventional covered metal stent, *RBO* recurrent biliary obstruction, *HR* hazard ratio, *CI* confidence interval

Reintervention was performed in 22 patients (four patients experienced complete distal migration) in the c-CMS group. c-CMS removal was successful in all attempted cases. Fourteen underwent CMS replacement, two underwent endoscopic ultrasound-guided hepaticogastrostomy, one underwent uncovered SEMS placement, two underwent plastic stent placement, and three underwent endoscopic nasobiliary drainage.

Discussion

This study evaluated the long-term efficacy and safety of DMS compared to c-CMS in reinterventions after biliary CMS dysfunction in unresectable PC patients with distal MBO. We demonstrated that DMS was associated with a significantly longer TRBO (286 days vs. 112 days, $p=0.029$) and lower rate of AEs, especially overall frequency of non-occlusion cholangitis (0% vs. 17%, $p=0.007$), compared with c-CMS. DMS was identified as an independent risk factor for longer duration of TRBO. DMS led to prolonged TRBO in several subgroups including males, metastatic disease, time to previous SEMS dysfunction ≤ 200 days, and absent or mild ascites. Even when accounting for competing risks, the cumulative incidence of RBO was lower in the DMS group (HR 0.55, $p=0.052$), although the difference was not statistically different. At the time of reintervention, the ARV was torn in seven of the nine patients (78%) in the DMS group who experienced RBO due to occlusion or non-occlusion cholangitis. Endoscopic reintervention was successfully performed in all patients in both groups, despite

failed stent removal in two of the 13 patients (15%) in the DMS group.

Secondary SEMS placement after SEMS dysfunction is challenging and results have been mixed [7, 8, 25]. Duodenobiliary reflux and risk of stent migration due to predilation of the biliary stricture during prior SEMS placement are unsolved issues in this setting. ARMS was developed to prevent duodenobiliary reflux, thereby reducing the risk of non-occlusion cholangitis. Despite the promising results of several braided-type ARMS [10–15], a recent meta-analysis concluded that ARMS had a lower rate of stent occlusion but a higher rate of stent migration compared to conventional SEMS [17]. Thus, adding an anti-migration system to ARMS appears to be a logical way to prolong TRBO. The DMS used in this study is a laser-cut type ARMS with a duckbill-type ARV, whose efficacy was reported in two previous studies [16, 18]. As laser-cut type SEMS are considered to have a lower risk of stent migration compared to braided-type SEMS, we speculated that DMS may achieve longer TRBO than braided-type ARMS.

In the present study, DMS showed superiority over c-CMS in terms of both stent patency and safety after stent dysfunction of the initial CMS. Overall rate of AEs was significantly lower in the DMS group (2% vs. 23%, $p=0.010$), which was attributable to the significantly lower rate of non-occlusion cholangitis (0% vs. 17%, $p=0.007$). This may suggest that DMS was effective in preventing cholangitis resulting from duodenobiliary reflux. Although overall RBO rates were not significantly different between the two groups, median TRBO was significantly longer in the DMS group (286 days vs. 112 days, $p=0.029$), with a consistently higher non-RBO rates at 3, 6, and 12 months (86%, 64%, and 36%, vs. 69%, 35%, and 21%). Compared to our results, Kin et al. [16] reported a higher early AE rate of 10% (cholangitis: 2, pancreatitis: 1) and a slightly shorter median TRBO (261 days) and lower non-RBO rates at 3 and 6 months (75% and 62%). This could be explained by the difference in patient and procedural characteristics. First, our study only included unresectable PC patients who received DMS as a second stent for reintervention. Second, we generally inserted an ENBD tube in the first session and subsequently deployed DMS after balloon sweeping of the bile duct in the second session, which may reduce the risk of cholangitis.

The current study highlights several issues to be resolved to further improve stent patency of DMS. Despite its laser-cut design, stent migration occurred in 24% of the patients (inward migration: 2, outward migration: 8) in this study, which rate was higher compared to the results reported in a meta-analysis (16%) [17] and the study by Kin et al. (7%) [16]. The discrepancies between studies may be explained by differences in patient characteristics and the follow-up period. Our study only included cases in which the biliary stricture was dilated and loosened by the initial CMS. The median follow-up period of DMS was 304 days in this study, which was considerably longer than Kin et al.'s report (5 months) [16]. The etiology of MBO and the administration of chemotherapy after SEMS placement [26] might also affect the rate of stent migration. In any case, the introduction of an effective anti-migration system should be considered to lower the risk of stent migration. The durability of the ARV is another important matter. At the time of reintervention, the ARV was found to be torn in 78% of RBO cases resulting from occlusion or non-occlusion cholangitis during a median follow-up period of 143 days (range, 49–286 days). A previous in vitro study reported that a morphological change of ARV was caused by the duodenal pH environment, leading to stent dysfunction [27]. Development of a new ARV which is not affected by the duodenal pH environment might be necessary to improve the durability of the ARV. Reintervention after DMS dysfunction is another controversial issue for debate. DMS was successfully removed in 85% of the patients (11/13) in this study, compared to only 67% (6/9) in the study by Kin et al. [16], which included SEMS-naïve patients. Thus, caution may be warranted when using DMS in SEMS-naïve patients. When the DMS cannot be removed at the time of reintervention, biliary cannulation through the stent mesh of DMS [28] or conversion to endoscopic ultrasound-guided intervention may be effective salvage methods for biliary drainage.

We acknowledge several limitations in this study. This was a retrospective study from a single institution with a limited sample size. The efficacy of DMS was evaluated only in patients who received DMS as a reintervention for prior CMS dysfunction. Therefore, the efficacy and safety of DMS in SEMS-naïve patients is unknown.

In conclusion, we found that DMS was associated with a significantly longer TRBO and lower rate of AEs than c-CMS when used in reinterventions after initial CMS dysfunction. DMS was identified as an independent risk factor for longer duration of TRBO. A randomized controlled trial with a larger sample size is needed to further confirm the promising results of the present study.

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Declarations

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