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Efficacy of Fully Covered Self-Expanding Metal Stents Removal versus Stent-in-Stent Techniques in Recurrent Malignant Distal Biliary Obstruction

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Abstract

Fully covered self-expandable metal stents (FCSEMSs) are widely used in managing malignant distal biliary obstruction (MDBO). However, recurrent biliary obstruction (RBO) has become a significant challenge due to improved patient survival with advanced chemotherapy. This multicenter retrospective cohort study evaluated revision techniques for FCSEMS dysfunction in 159 patients with MDBO initially treated with FCSEMSs. Patients were categorized into four groups based on the revision method: stent exchange with self-expandable metal stents (SEMS, n=53) or plastic stents (n=23), and stent-in-stent placement with SEMS (n=51) or plastic stents (n=32). All procedures achieved 100% technical and clinical success. The primary time to recurrent biliary obstruction (TRBO) showed no significant difference among the groups (mean: 148 days, 95% confidence interval [CI]: 127–170 days). However, secondary TRBO differed significantly (p=0.014): 161 days (SEMS, stent exchange), 53 days (plastic stent, stent exchange), 104 days (SEMS, stent-in-stent), and 67 days (plastic stent, stent-in-stent). Multivariate analysis revealed that stent-in-stent placement with SEMS increased the risk of RBO compared to SEMS stent exchange (hazard ratio [HR]: 6.53, 95% CI: 1.89–22.55, p=0.003). Additionally, revision within 180 days was associated with a higher risk of RBO (HR: 1.77, 95% CI: 1.10–2.86, p=0.019). Overall survival was comparable across all groups. These findings suggest that SEMS stent exchange after FCSEMS removal is an

effective revision method for RBO in MDBO, providing improved secondary stent patency without increasing adverse events or affecting overall survival.

Key words: Malignant distal biliary obstruction, Recurrent biliary obstruction, Revision method, Stent patency

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) guided biliary stenting is the primary therapeutic approach for biliary decompression in malignant distal biliary obstruction (MDBO)[1,2]. Advances in oncologic therapies have prolonged the survival of patients with pancreaticobiliary cancer, often surpassing the primary patency of the initial stent[3,4]. As a result, recurrent biliary obstruction (RBO) has become a significant clinical challenge. Fully covered self-expandable metal stents (FCSEMS) are increasingly preferred for initial intervention due to their removability and superior patency[5,6]. However, managing RBO after self-expandable metal stent (SEMS) occlusion often necessitates multiple interventions to restore biliary drainage. These interventions include mechanical cleaning, additional stent placement, or replacing the occluded stent with another SEMS or a plastic stent[7]. While SEMS are well established as the first-line treatment for MDBO, the optimal strategy for managing RBO remains unclear[7-9]. Current guidelines lack a standardized approach, although there is a general consensus that endoscopic reintervention is preferred over external drainage and that placing a new metal stent is the recommended strategy[1]. Some guidelines suggest that occluded FCSEMS should be removed and replaced with a new stent to maximize long-term patency[10]. However, recent studies indicate that the stent-in-stent technique may serve as an effective rescue therapy when an FCSEMS occludes in the setting of

MDBO[11]. To date, no large-scale clinical trials have definitively demonstrated that stent removal is superior to leaving the stent in place. Given this uncertainty, this study aims to evaluate the effects of various modification strategies following primary FCSEMS dysfunction in MDBO. Key outcomes, including stent patency, overall survival, and adverse event rates, were analyzed, with a particular focus on comparing SEMS versus plastic stents, covered versus uncovered SEMS, and different stent replacement techniques.

Results

Patient characteristics

This study included 159 patients with MDBO, with a mean age of 70 years (range: 36–89 years), and 81 patients (51%) were male. The most common cause of MDBO was pancreatic cancer (58%), followed by cholangiocarcinoma (26%) and ampullary cancer (6%). Baseline characteristics, including age, sex, cancer type, TNM stage, presence of duodenal strictures, and initial bilirubin levels, were comparable across all four groups ($p > 0.05$ for all comparisons) (**Table 1**). The mean length of biliary strictures was also similar among the groups (range: 25.6–30.1 mm, $p = 0.265$). To assess potential differences between stent exchange and stent-in-stent placement, we conducted a subgroup analysis. No significant differences were found in baseline characteristics between these two groups (**Supplementary table 1**, $p > 0.05$). Additionally,

considering the differences between covered and uncovered SEMS, we performed another subgroup analysis. No significant differences were observed in baseline characteristics between patients with covered SEMS and uncovered SEMS (**Supplementary table 2**, $p > 0.05$).

Primary and secondary biliary stent patency and outcomes

This study achieved 100% technical and clinical success rates across all intervention groups, demonstrating procedural efficacy (**Table 2**). Kaplan–Meier analysis showed no significant differences among the four groups in primary time to recurrent biliary obstruction (TRBO) (**Figure 1A**, log-rank test, $p = 0.185$). The mean primary TRBO across all patients was 148 days (95% CI: 127–170 days). Stent dysfunction patterns varied among groups. Ingrowth and overgrowth were more frequent in the stent-in-stent SEMS (58.9%) and stent-in-stent plastic stent (46.9%) groups ($p = 0.007$). Stone or sludge formation was most common in the stent exchange SEMS group (58.5%), although the difference among groups was not statistically significant ($p = 0.068$). Migration occurred exclusively in the stent exchange groups (22.6% in SEMS, 39.1% in plastic stents) and was absent in the stent-in-stent groups ($p < 0.001$). The mean secondary stent length was not significantly different across groups (range: 7.1–7.8 cm, $p = 0.218$). However, the secondary TRBO varied significantly among the groups ($p = 0.014$), with the longest duration in the stent exchange SEMS group (161 days), followed by stent-in-stent SEMS (104 days), stent-in-stent plastic stents (67 days),

and stent exchange plastic stents (53 days). Further Kaplan–Meier analysis confirmed significant distinctions in secondary TRBO (**Figure 1B**, $p < 0.001$). Further, no significant differences in postprocedural complications or overall survival rates were observed among the groups. The early complication rate (<1 month) was comparable across groups ($p = 0.973$), with acute cholangitis being the most common early complication (4.4–9.8%, $p = 0.870$). The late complication rate (≥1 month) also showed no significant differences ($p = 0.606$). The total complication rate ranged from 70.6% to 87.5% but did not significantly differ among groups ($p = 0.111$). The mean overall survival time was longest in the stent exchange SEMS group (478 days), followed by stent-in-stent plastic stents (434 days), stent exchange plastic stents (339 days), and stent-in-stent SEMS (337 days), though this difference was not statistically significant ($p = 0.259$). Kaplan–Meier curves for overall survival showed no significant differences (**Figure 2**, $p = 0.172$). The mean secondary TRBO was longer in the stent exchange group (128 days) compared to the stent-in-stent group (90 days), though this difference was not statistically significant ($p = 0.135$, **Supplementary table 3**). However, Kaplan–Meier analysis revealed a significant difference in secondary stent patency between the two groups (log-rank $p = 0.035$, **Supplementary figure 1**), indicating a potential advantage of stent exchange over stent-in-stent for prolonged secondary stent patency. The mean overall survival time was 439 days in the stent exchange group and 377 days in the stent-in-stent group, with no statistically significant

difference between the two (p = 0.325). Kaplan–Meier survival analysis further confirmed that there was no significant difference in overall survival between the two groups (log-rank p = 0.294, **Supplementary figure 2**). Secondary stent outcomes, complication rates, and overall survival were comparable between covered and uncovered SEMS within each revision method (**Supplementary table 4**). For the stent exchange group, the secondary TRBO was 186 days for covered SEMS and 121 days for uncovered SEMS (p = 0.265), and 109 days and 102 days, respectively, for the stent-in-stent group (p=0.812). The overall survival was also similar, with 550 days for covered SEMS and 406 days for uncovered SEMS in the stent exchange group (p = 0.270), and 314 days and 383 days, respectively, in the stent-in-stent group (p = 0.403). These findings indicate that secondary TRBO rates, complication rates, and survival outcomes do not significantly differ between covered and uncovered SEMS within each technique. Kaplan–Meier survival analysis also revealed no statistically significant differences in primary and secondary stent patency (p = 0.782, p = 0.498) or overall survival (p = 0.654, p = 0.276) based on the secondary stent insertion or stent exchange method in the stent-in-stent procedure using covered and uncovered SEMS (**Supplementary figures 3–6**).

Univariate and multivariate Cox regression analysis

Univariate and multivariate Cox regression analyses were performed to assess factors influencing secondary TRBO (**Table 3**). In univariate

analysis, revisions performed within 180 days were associated with a significantly increased risk of secondary TRBO (HR: 1.79, 95% CI: 1.13–2.84, p = 0.013). Primary stent dysfunction owing to migration was associated with a reduced risk of secondary TRBO (HR: 0.31, 95% CI: 0.13–0.75, p = 0.009). According to the revision method, stent exchange with plastic stents (median TRBO: 53 days) and stent-in-stent with plastic stents (median TRBO: 67 days) were associated with significantly higher risks of secondary TRBO compared to stent exchange with SEMS (HR: 3.62, 95% CI: 1.63–8.03 and HR: 3.58, 95% CI: 1.84–6.99, respectively). In multivariate analysis, adjusting for primary TRBO duration, cause of primary stent dysfunction, and cancer type, shorter primary TRBO (HR: 1.77, 95% CI: 1.10–2.86), stent migration (HR: 0.30, 95% CI: 0.13–0.68), and revision method were independently associated with secondary TRBO. Among revision strategies, stent exchange with plastic stents showed the highest risk of secondary TRBO (HR: 6.84, 95% CI: 2.63–17.80), followed by stent-in-stent with SEMS (HR: 6.53, 95% CI: 1.89–22.55) and plastic stents (HR: 2.69, 95% CI: 1.21–5.97). Cox regression analyses for overall survival demonstrated no significant differences among revision methods, indicating that the choice of revision strategy did not directly affect long-term survival outcomes (**Table 4**).

Discussion

Most prior studies in MDBO have focused on optimizing the initial stent

strategy, including the timing/sequence of metal stenting or comparisons of stent designs and coverage[12-14]. However, as patient survival improves and RBO becomes more frequent, an equally important and practical question is the optimal strategy for endoscopic revision after primary FCSEMS dysfunction. Comparative data guiding whether to remove and exchange the occluded FCSEMS versus performing a stent-in-stent approach—and whether to select metal versus plastic stents at revision—remain limited. The present multicenter study directly addresses this clinical decision point and provides comparative evidence favoring SEMS exchange after FCSEMS removal for improved secondary patency without compromising safety or survival. Overall the present study demonstrated that, stent replacement with SEMS was more effective in prolonging secondary stent patency compared to stent-in-stent or plastic stents in patients who developed RBO after using FCSEMS as a primary stent for MDBO.

Unlike uncovered SEMS, covered SEMS provide greater versatility, including options such as stent removal and reinsertion. This study aimed to compare and analyze differences in secondary TRBO and overall survival across various revision methods among patients with FCSEMS. Overall, we found a significant difference in secondary TRBO among the four groups: stent exchange with SEMS, stent-in-stent with SEMS, stent exchange with plastic stents, and stent-in-stent with plastic stents. Kaplan–Meier and univariate analyses confirmed the superiority of SEMS over plastic stents, consistent with previous studies[15-17]. However, multivariate analysis, incorporating variables from univariate analysis

and key clinical factors, demonstrated the superiority of stent exchange with SEMS over stent-in-stent with SEMS in secondary stent patency. While previous studies have reported on the effectiveness of stent-in-stent when metallic primary stents are occluded[7], this analysis identified that stent exchange is more effective when the primary stent is limited to FCSEMS. Overall survival analysis revealed that the revision methodology did not significantly influence survival duration. Multivariate analysis identified TNM stage, chemotherapy status, and jaundice as critical factors associated with cancer prognosis, thereby highlighting the need to prioritize these factors in cancer management[18,19]. Additionally, a significant correlation was found between shorter primary TRBO and decreased survival. Early SEMS occlusion may increase the risk of subsequent occlusion, likely influenced by tumor size, stenosis degree, or location[20,21]. Frequent drainage owing to shorter TRBOs can increase risks of further obstruction and cholangitis, ultimately reducing survival[22-24].

Although prior studies have reported more frequent cholecystitis and stent migration with covered SEMS[25], no significant differences in complication rates were observed in this study across procedure methods or SEMS types. These findings indicate that patient clinical characteristics, procedural experience, or recent advances in stent design may have contributed to these results. For example, a novel multi-hole fully covered SEMS was developed to reduce migration while maintaining removability, and a recent multicenter study reported favorable clinical outcomes with a low migration-related RBO rate and a

long time to RBO[26]. In addition, anti-reflux valve–equipped covered metal stents have been investigated to mitigate reflux-related RBO and showed longer TRBO compared with conventional covered metal stents[27]. Further research is thus required to identify risk factors for complications associated with covered SEMS. The results of this study emphasize the efficacy of using FCSEMS as the primary stent for MDBO, followed by stent exchange with SEMS as a revision strategy. A key question raised is the optimal timing for stent exchange. While exchange is clearly indicated when RBO criteria are met or stent dysfunction occurs, the average duration of stent exchange in this study was 4–5 months, with a range of 18 to 420 days. A thorough assessment of stent function around 4–5 months may facilitate the early detection of RBO or dysfunction, potentially improving patient outcomes by enabling timely intervention. Additionally, as FCSEMS has demonstrated stent patency for up to 14 months, assessing stent function at 1 year appears to be clinically important.

This study had limitations due to patient number imbalance between groups, and the small sample size made propensity score matching for equalization impossible. Furthermore, primary FCSEMS migration cannot be managed with a stent-in-stent approach, such cases were treated with stent exchange, reflecting a practical constraint of the revision strategy. Furthermore, the choice between FCSEMS and UCSEMS as the secondary stent was not protocolized and depended on the endoscopist’s discretion, which may have introduced heterogeneity in secondary SEMS selection. To strengthen these findings, future studies

should aim to enroll a larger, more balanced cohort, ideally in a multicenter setting, to enable more robust comparisons. Furthermore, growing interest in partially covered SEMS, which combine features of covered and uncovered stents, warrants investigation[28,29]. These stents may offer unique advantages and challenges in managing biliary strictures. Follow-up studies should explore the efficacy, safety, and specific indications of various covered SEMS types in clinical practice.

In conclusion, the present study showed when RBO occurs after initial placement of an FCSEMS for MDBO, stent exchange with SEMS offers an effective alternative, providing superior secondary stent patency without increasing adverse events or negatively impacting overall survival.

Methods

Study design and patients

This multicenter, retrospective study compared the efficacy and safety of various revision methods for RBO following FCSEMS insertion. Patients who underwent ERCP for MBO at participating tertiary referral centers between March 2013 and March 2023 were considered eligible. The inclusion criteria included: (1) adults aged ≥20 years, (2) unresectable MDBO, (3) initial stenting with FCSEMS, and (4) availability of follow-up after secondary stent placement with ascertainable outcomes until secondary stent dysfunction or censoring (death or last follow-up). Exclusion criteria included: (1) malignant hilar or intrahepatic duct stricture, (2) initial stent insertion with an uncovered SEMS, (3) loss to

follow-up after secondary stenting, (4) percutaneous procedures, (5) endoscopic ultrasound-guided procedures, and (6) contraindications to ERCP, pregnancy, or breastfeeding. The study endpoints were clinical outcomes, complications, and prognoses. A total of 159 patients with MDBO were included, including 76 patients treated with the stent exchange method and 83 with the stent-in-stent method. In the stent exchange group, 53 patients received SEMS and 23 plastic stents, whereas in the stent-in-stent group, 51 patients received SEMS and 32 plastic stents (**Figure 3**).

Ethics Approval

This multicenter retrospective study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board at each participating center. Gangnam Severance Hospital served as the coordinating center (IRB No. 3-2022-0248). The requirement for informed consent was waived due to the retrospective design, and all data were anonymized prior to analysis.

Procedure details and revision techniques

RBO was managed using two revision techniques: (1) stent replacement, involving removal of the existing FCSEMS followed by re-stenting, or (2) stent-in-stent, in which an additional stent was placed without removing the existing FCSEMS. In cases of primary FCSEMS migration, stent-in-stent placement was not feasible; therefore, these cases were managed with stent exchange followed by re-stenting. Stents used during reintervention included SEMS (covered or uncovered) and plastic stents.

The choice of stent type, length, and diameter was determined by an expert endoscopist, based on the patient's MBO characteristics. The selection of covered versus uncovered SEMS at revision was not standardized across centers and was determined by the endoscopist's clinical judgment, considering stricture characteristics and the anticipated trade-off between migration/removability and tumor ingrowth. ERCP was performed under sedation using diazepam, midazolam, pethidine, and/or propofol, following written informed consent. Duodenoscopes (JF260V or JF290V, Olympus, Tokyo, Japan) were used. The decision to perform balloon sweeping was made by the endoscopist, considering the presence of bile duct sludge or cholangitis.

Plastic stents included Advanix (Boston Scientific, USA) and Zimmon (Cook Medical, USA), with a diameter of 7 Fr and lengths of 5–15 cm. Commonly used uncovered SEMS included BONASTENT (SEWOON Medical, Korea) and Niti-S D-type (TaeWoong Medical, Korea), while covered SEMS included Hilzo (BCM Co., Korea) and HANAROSTENT (M.I.Tech, Korea). SEMS dimensions ranged from 8 to 10 mm in diameter and 4–10 cm in length, selected based on stricture length.

Outcome and definition

The primary outcome was secondary stent patency, defined as the TRBO according to the Tokyo criteria: the interval from stent deployment to dysfunction owing to migration, occlusion, or other causes requiring reintervention[30]. Patients without secondary stent dysfunction were censored at death or last follow-up. Overall survival was defined as the

interval from first stent deployment to death. Technical success was defined as successful stent deployment confirmed by imaging. Clinical success was characterized by a ≥50% reduction in total bilirubin and symptom improvement (e.g., jaundice, abdominal pain, fever) within 1 month[7]. Stent migration was assessed using abdominal radiography or CT, with confirmation performed during follow-up. Stent occlusion was diagnosed radiologically (cholangiography, CT, or MRI) in patients with recurrent cholangitis or jaundice, with causes identified via cholangiography or duodenoscopy. MDBO diagnosis and type were determined using established criteria[31,32]. Adverse events were evaluated based on the ESGE guidelines[33].

Statistical analysis

Continuous variables were summarized as means or medians with ranges, and categorical variables as counts and percentages. For comparisons among the four revision groups, continuous variables were analyzed using the Kruskal–Wallis test, and categorical variables were analyzed using the chi-square test or Fisher's exact test when expected cell counts were small. When an overall group comparison was statistically significant, post-hoc pairwise comparisons were performed with appropriate multiple-comparison adjustment (Dunn's test with Holm/Bonferroni correction for continuous variables; pairwise comparisons with Holm/Bonferroni adjustment for categorical variables). The Mann–Whitney U test was used only for pre-specified two-group subgroup comparisons. Stent patency and overall survival were

evaluated using the Kaplan–Meier method and compared using the log-rank test. Factors associated with secondary time to recurrent biliary obstruction (TRBO) and overall survival were assessed using univariate and multivariate Cox proportional hazards regression models, and results are presented as hazard ratios (HRs) with 95% confidence intervals (CIs). All tests were two-sided, and p values <0.05 were considered statistically significant. Statistical analyses were performed using SPSS version 25.0 and R version 4.2.1.

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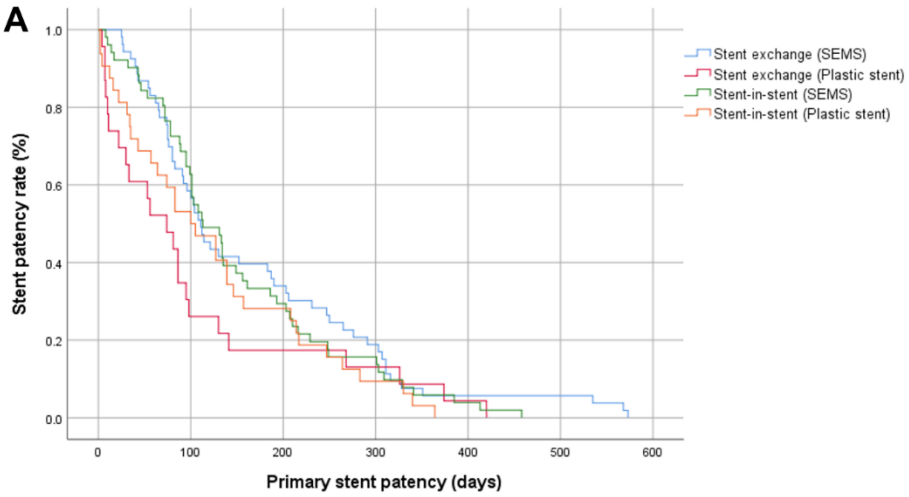
Competing Interests

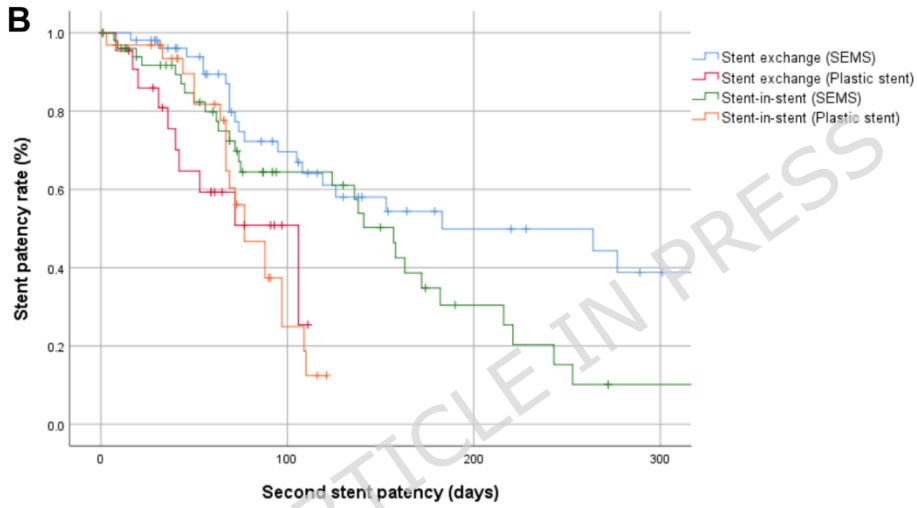
Authors declare no conflict of interests for this article.

Data availability

The datasets used and/or analyzed in this study are available from the corresponding author upon reasonable request.

FIGURE LEGENDS





Group	Stent patency (day)	Hazard ratio	95% CI	P-value
Stent exchange, SEMS	94	1.00	-	-
Stent exchange, Plastic stent	53	3.62	1.63-8.03	0.002
Stent-in-Stent, SEMS	75	1.72	0.98-3.02	0.059
Stent-in-Stent, Plastic stent	67	3.58	1.84-6.99	<0.001

Figure 1. Kaplan–Meier survival curves of primary and secondary stent patency according to the revision method.
(A) Kaplan–Meier survival curves of primary stent patency according to the revision method. The survival curves, as per the primary stent patency obtained by log-rank analysis, did not show any statistically significant differences ($p = 0.185$). **(B)** Kaplan–Meier survival curves for secondary stent patency following revision method. Survival curves were significantly different as per the secondary stent patency (log-rank analysis, $p < 0.001$). The stent exchange (SEMS) group demonstrated more favorable secondary stent patency compared to the plastic stent groups (hazard ratio [HR] 3.62; 95% confidence interval [CI] 1.63–8.03, and HR 3.58; 95% CI 1.84–6.99, respectively, $p = 0.002$ and $p < 0.001$). No statistical significance was observed between the SEMS group and the stent-in-stent [SEMS] group (HR 1.72; 95% CI 0.98–3.02, $p = 0.059$).

SEMS, self-expandable metallic stent

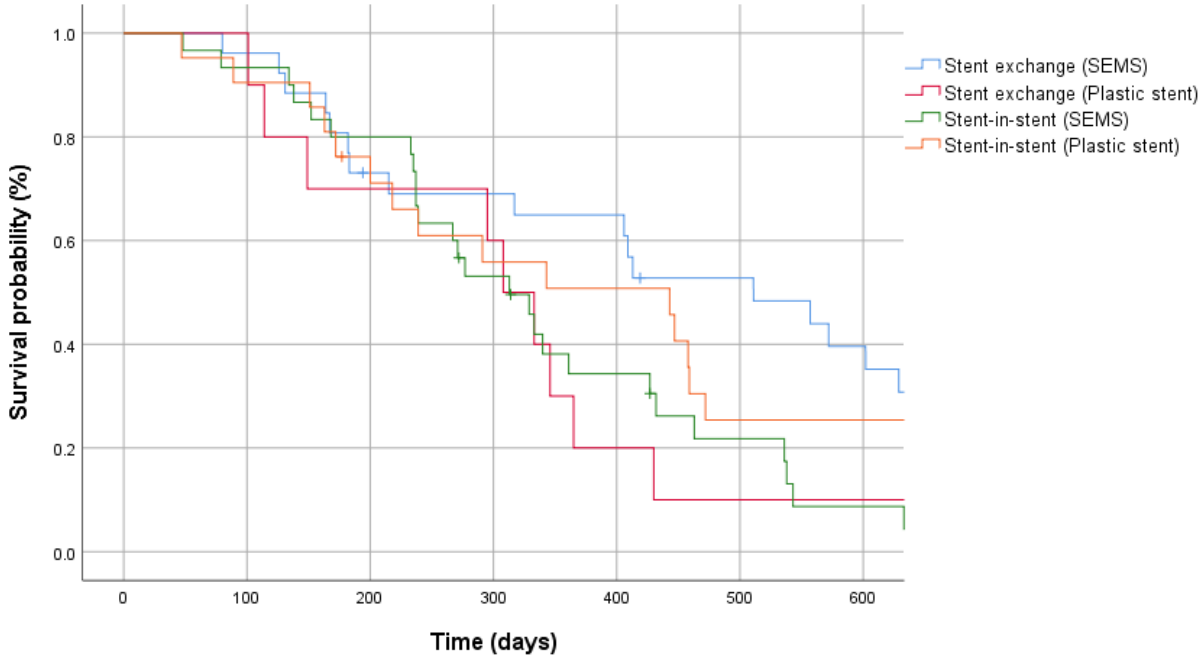


Figure 2. Kaplan–Meier survival curves of overall survival time
(A) Kaplan–Meier survival curves of the overall survival time according to the primary and secondary biliary stent type and method. The survival curves, as per the overall survival time obtained by log-rank analysis, did not indicate any statistically significant differences (p = 0.172). (B) Kaplan–Meier survival curves of the overall survival time according to the secondary stenting method. The survival curves according to the overall survival time obtained by log-rank analysis did not suggest any statistically significant differences (p = 0.294). SEMS, self-expandable metallic stent

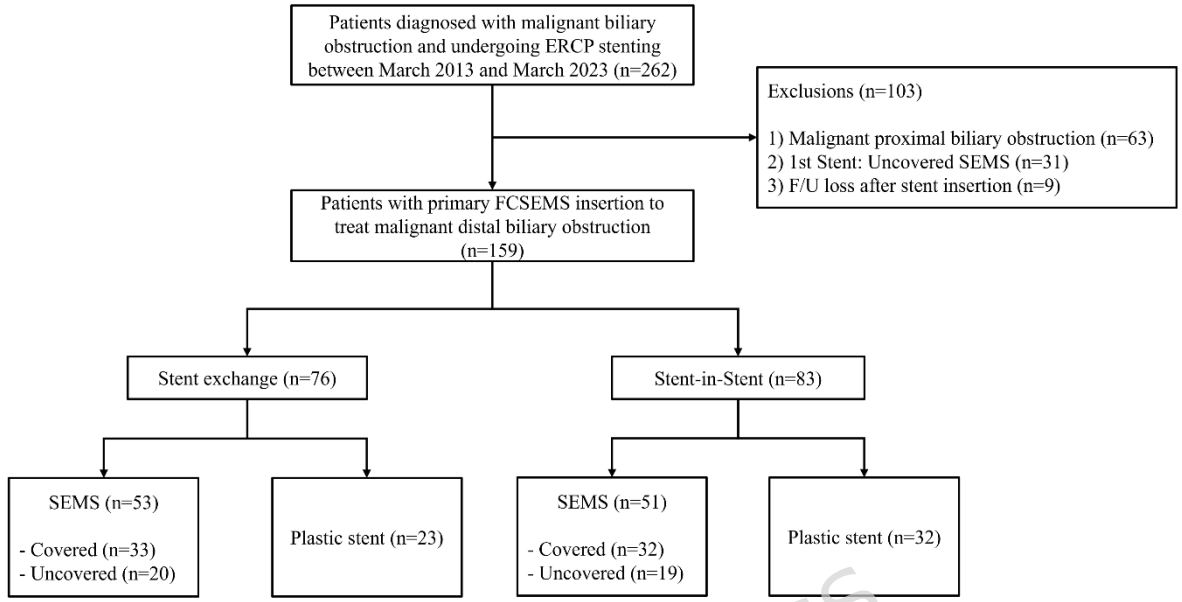


Figure 3. Flow diagram showing patient selection and categorization according to the primary stent and revision method. SEMS, self-expandable metal stents; FCSEMS, fully covered SEMS

Table 1. Baseline characteristics of patients and clinical outcomes according to the primary and secondary biliary stent type and method

	Stent exchange, SEMS (covered & uncovered) (n=53)	Stent exchange, plastic stent (n=23)	Stent-in-stent, SEMS (covered & uncovered) (n=51)	Stent-in-stent, plastic stent (n=32)	p-value
Age (range) (years)	71.8 (48–89)	70.5 (40–86)	69.6 (47–89)	67.9 (36–88)	0.323
Sex					
Male/female (n)	26/27	11/12	29/22	15/17	0.781
Diagnosis					
Pancreatic cancer, n (%)	33 (62.3)	10 (43.5)	30 (58.8)	19 (59.4)	0.492
GB cancer, n (%)	2 (3.8)	3 (13.0)	4 (7.8)	1 (3.1)	0.379
CBD cancer, n (%)	13 (24.5)	7 (30.4)	12 (23.5)	9 (28.1)	0.913
AOV cancer, n (%)	4 (7.5)	1 (4.3)	3 (5.9)	2 (6.3)	0.960
Metastatic disease, n (%)	1 (1.9)	2 (8.7)	2 (3.9)	1 (3.1)	0.556
TNM stage					
III, n (%)	23 (43.4)	10 (43.5)	23 (45.1)	17 (53.1)	0.387
IV, n (%)	30 (56.6)	13 (56.5)	28 (54.9)	15 (46.9)	0.387
Duodenal stricture, n (%)	4 (7.5)	0 (0.0)	0 (0.0)	2 (6.3)	0.139
Length of biliary stricture (mm)	26.7	29.6	25.6	30.1	0.265
CTx. ± CCRTx., n (%)	43 (81.1)	16 (69.6)	29 (56.9)	27 (84.4)	0.149
Total bilirubin (mg/dL)					
Baseline	7.0	6.7	7.6	6.8	0.886
Day 1	5.8	5.7	5.8	5.2	0.873
Day 28	1.4	2.1	1.4	2.1	0.282
Previous procedure†, n (%)	17 (32.1)	8 (34.8)	12 (23.5)	8 (25.0)	0.663

AOV, ampulla of vater; CBD, common bile duct; CCRTx., concurrent chemoradiotherapy; CTx., chemotherapy; GB, gallbladder; SEMS, self-expandable metallic stent; TNM, classification of malignant tumors

†Previous procedure indicates any prior ERCP-based biliary intervention (e.g., plastic stent placement or other biliary drainage) performed before index FCSEMS insertion.

Table 2. Primary and secondary biliary stent patency and outcomes according to stent type and method

	Stent exchange, SEMS (covered & uncovered) (n=53)	Stent exchange, plastic stent (n=23)	Stent-in-stent, SEMS (covered & uncovered) (n=51)	Stent-in-stent, plastic stent (n=32)	p-value
Primary stent outcome					
Primary stent length (cm), mean (min–max)	6.4 (4–8)	6.2 (4–9)	6.1 (4–8)	6.5 (4–8)	0.605
Primary TRBO (days), mean (95% CI)	171 (133–209)	106 (52–158)	154 (124–185)	128 (89–166)	0.108
Cause of stent dysfunction					
Ingrowth & overgrowth, n (%)	10 (18.8)	5 (21.7)	30 (58.9)	15 (46.9)	0.007
Stone & sludge, n (%)	34 (58.5)	9 (39.1)	21 (41.2)	17 (36.3)	0.068
Migration, n (%)	12 (22.6)	9 (39.1)	0 (0.0)	0 (0.0)	<0.001
Secondary stent outcome					
Secondary stent length (cm), mean (min–max)	7.1 (4–9)	7.8 (5–13)	7.5 (5–10)	7.7 (5–15)	0.218
Secondary TRBO (days), mean (95% CI)	161 (128–191)	53 (39–68)	104 (67–143)	67 (56–78)	0.014
Early complication (<1m)					
Acute pancreatitis, n (%)	0 (0.0)	1 (4.4)	0 (0.0)	1 (3.1)	0.265
Acute cholangitis, n (%)	4 (7.6)	1 (4.4)	5 (9.8)	3 (9.4)	0.870
Migration, n (%)	2 (3.8)	1 (4.4)	0 (0.0)	0 (0.0)	0.599
Total, n (%)	6 (11.3)	3 (13.0)	5 (9.8)	4 (12.5)	0.973
Late complication (≥1m)					
Acute pancreatitis, n (%)	1 (1.9)	0 (0.0)	3 (5.9)	1 (3.1)	0.520
Acute cholangitis, n (%)	29 (54.7)	10 (43.5)	27 (52.9)	19 (59.4)	0.705
Migration, n (%)	6 (11.3)	5 (21.7)	1 (2.0)	4 (12.5)	0.060
Total, n (%)	36 (67.9)	15 (65.2)	31 (60.8)	24 (75.0)	0.606
Total complication, n (%)	42 (79.3)	18 (78.3)	36 (70.6)	28 (87.5)	0.111
Overall survival time (day, mean)	478	339	337	434	0.259

SEMS, self-expandable metallic stent; TRBO, time to recurrent biliary obstruction

Table 3. Univariate and multivariate analysis of variables associated with secondary biliary stent patency

	n	Median (day)	Univariate analysis			Multivariate analysis		
			HR	95% CI	p-value	HR	95% CI	p-value
Diagnosis								
Pancreatic cancer	92	69	1.00		Ref.	1.00		Ref.
GB cancer	10	72	1.02	0.37–2.81	0.976	0.72	0.25–2.08	0.543
CBD cancer	41	61	1.11	0.70–1.76	0.657	0.91	0.52–1.59	0.728
AoV cancer	10	91	1.09	0.50–2.40	0.828	1.63	0.69–3.86	0.264
Metastasis	6	50	2.90	1.04–8.13	0.043	1.61	0.50–5.20	0.424
TNM stage								
III	73	65	1.00					
IV	86	72	1.13	0.71–1.79	0.605			
Length of biliary stricture								
≥25mm	74	69	1.00					
<25mm	85	63	0.98	0.60–1.60	0.919			
CTx. ± CCRTx.								
Yes	115	70	1.00					
No	44	65	1.44	0.88–2.36	0.148			
Total bilirubin (baseline)								
≤3mg/dL	66	63	1.00					
>3mg/dL	93	74	1.30	0.79–2.15	0.310			
Primary TRBO								
≥180days	47	93	1.00			1.00		
<180days	112	67	1.79	1.13–2.84	0.013	1.77	1.10–2.86	0.019
Cause of primary stent dysfunction								
Ingrowth & overgrowth	55	60	1.00		Ref.	1.00		Ref.
Stone, sludge	83	72	1.69	0.96–2.99	0.069	1.50	0.90–2.51	0.123
Migration	21	77	0.31	0.13–	0.009	0.30	0.13–0.68	0.004

				0.75				
Method								
Stent exchange, SEMS	53	94	1.00		Ref.	1.00		Ref.
Stent exchange, Plastic stent	23	53	3.62	1.63–8.03	0.002	6.84	2.63–17.8	<0.001
Stent-in-Stent, SEMS	51	75	1.72	0.98–3.02	0.059	6.53	1.89–22.55	0.003
Stent-in-Stent, Plastic stent	32	67	3.58	1.84–6.99	<0.001	2.69	1.21–5.97	0.015

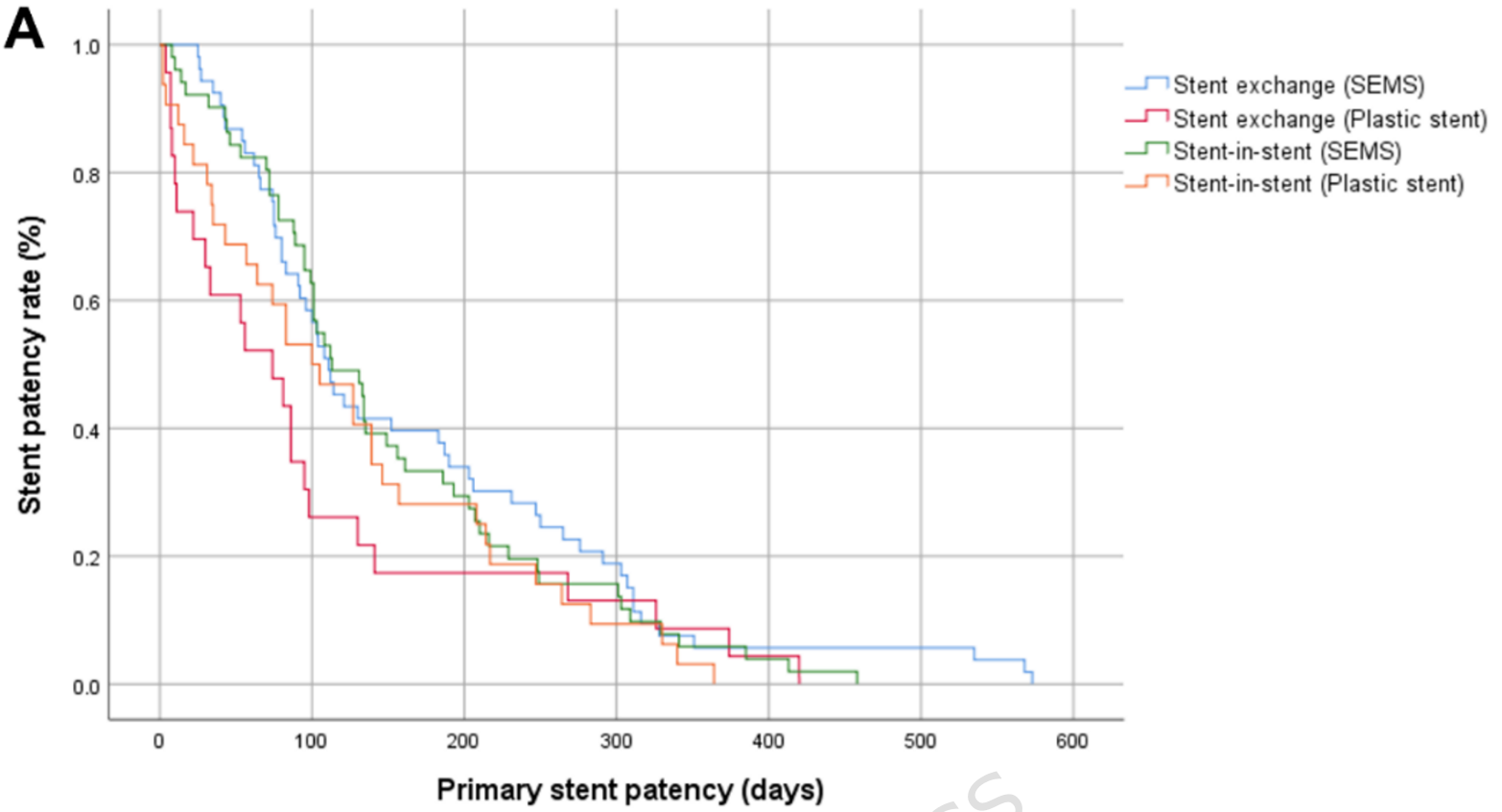
AOV, ampulla of vater; CBD, common bile duct; CCRTx., concurrent chemoradiotherapy; CTx., chemotherapy; GB, gallbladder; SEMS, self-expandable metallic stent; TNM, classification of malignant tumors; TRBO, time to recurrent biliary obstruction

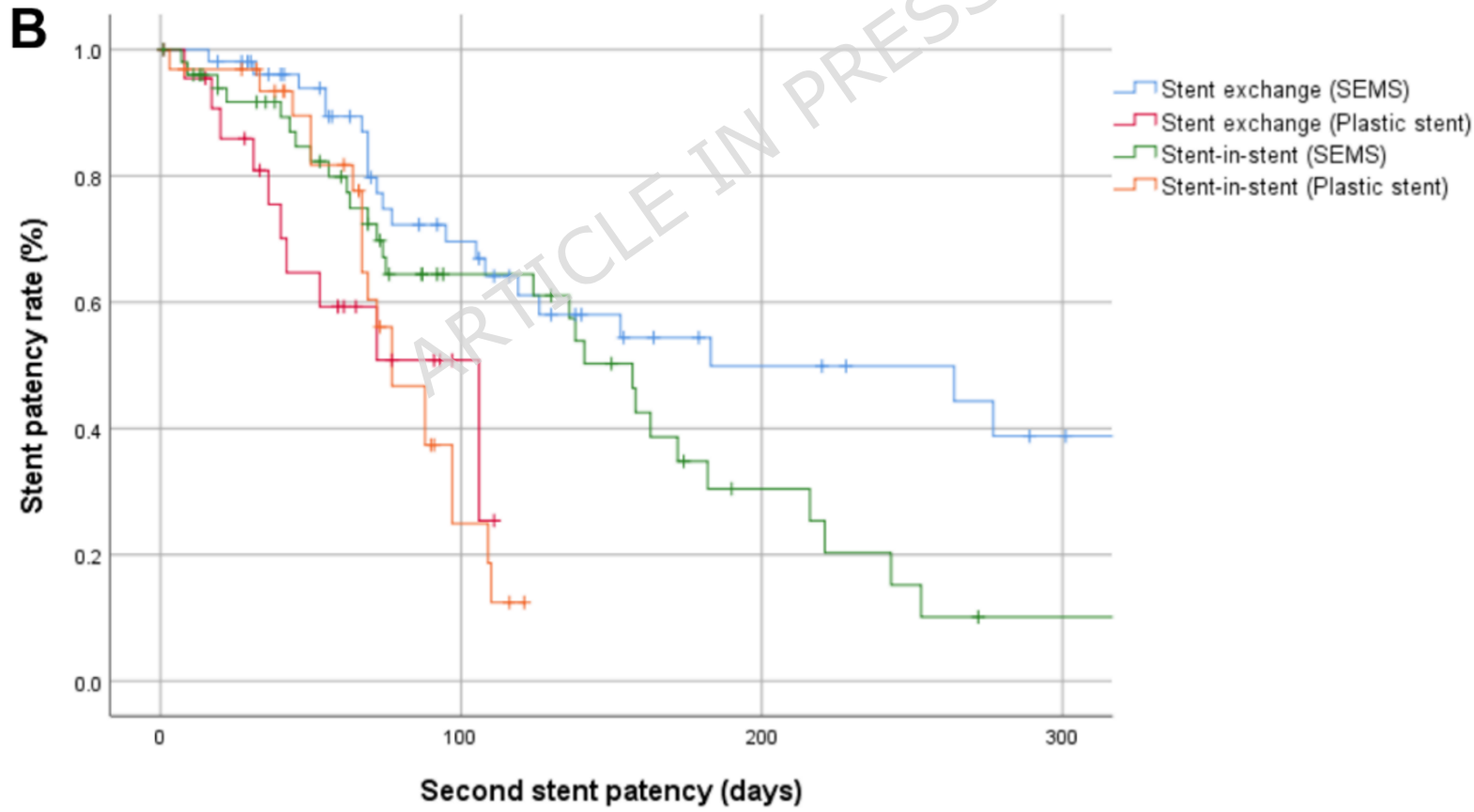
Table 4. Univariate and multivariate analysis of variables associated with overall survival time

	n	Median (day)	Univariate analysis			Multivariate analysis		
			HR	95% CI	p-value	HR	95% CI	p-value
Diagnosis								
Pancreatic cancer	92	348	1.00		Ref.	1.00		Ref.
GB cancer	10	173	1.51	0.36–6.35	0.573	3.68	0.79–17.15	0.097
CBD cancer	41	334	1.33	0.75–2.38	0.333	1.31	0.61–2.83	0.494
AoV cancer	10	546	0.71	0.12–4.17	0.705	0.65	0.11–3.68	0.624
Metastasis	6	158	1.64	0.87–3.10	0.129	1.66	0.89–3.10	0.109
TNM stage								
III	73	385	1.00		0.079	1.00		0.009
IV	86	333	1.61	0.95–2.75		2.26	1.23–4.16	
Length of biliary stricture								
≥25mm	74	342	1.00		0.853			
<25mm	85	353	0.93	0.44–1.97				
CTx. ± CCRTx.								
Yes	115	362	1.00		0.253	1.00		0.005
No	44	253	1.41	0.78–2.53		4.04	1.51–10.78	
Total bilirubin (baseline)								
≤3mg/dL	66	356	1.00		0.050	1.00		0.049
>3mg/dL	93	324	1.75	1.00–3.05		1.755	1.00–3.07	
Primary TRBO								
≥180days	47	474	1.00		0.005	1.00		0.019
<180days	112	280	2.46	1.32–4.60		1.77	1.10–2.86	
Cause of primary stent dysfunction								
Ingrowth & overgrowth	55	294	1.00		Ref.			
Stone, sludge	83	338	0.88	0.48–1.58	0.659			
Migration	21	385	0.76	0.30–1.93	0.557			
Method								
Stent exchange, SEMS	53	396	1.00		Ref.	1.00		Ref.
Stent exchange, Plastic stent	23	348	0.80	0.35–1.83	0.591	0.83	0.31–2.22	0.704
Stent-in-Stent, SEMS	51	285	1.30	0.45–3.77	0.630	1.35	0.41–4.43	0.625

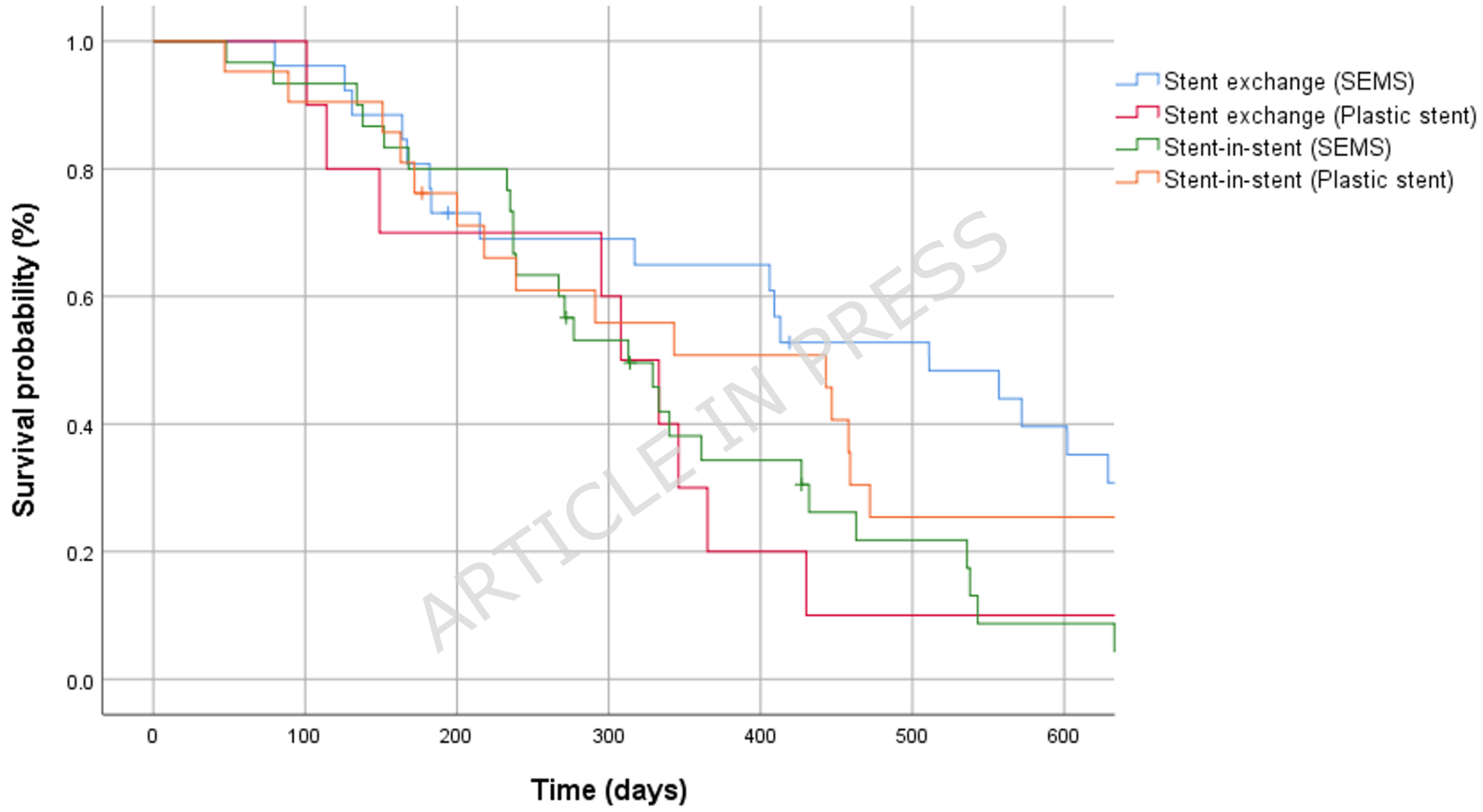
Stent-in-Stent, Plastic stent	32	334	1.59	0.89–2.86	0.120	1.17	0.58–2.36	0.658

AOV, ampulla of vater; CBD, common bile duct; CCRTx., concurrent chemoradiotherapy; CTx., chemotherapy; GB, gallbladder; SEMS, self-expandable metallic stent; TNM, classification of malignant tumors; TRBO, time to recurrent biliary obstruction





Group	Stent patency (day)	Hazard ratio	95% CI	P-value
Stent exchange, SEMS	94	1.00	-	-
Stent exchange, Plastic stent	53	3.62	1.63-8.03	0.002
Stent-in-Stent, SEMS	75	1.72	0.98-3.02	0.059
Stent-in-Stent, Plastic stent	67	3.58	1.84-6.99	<0.001



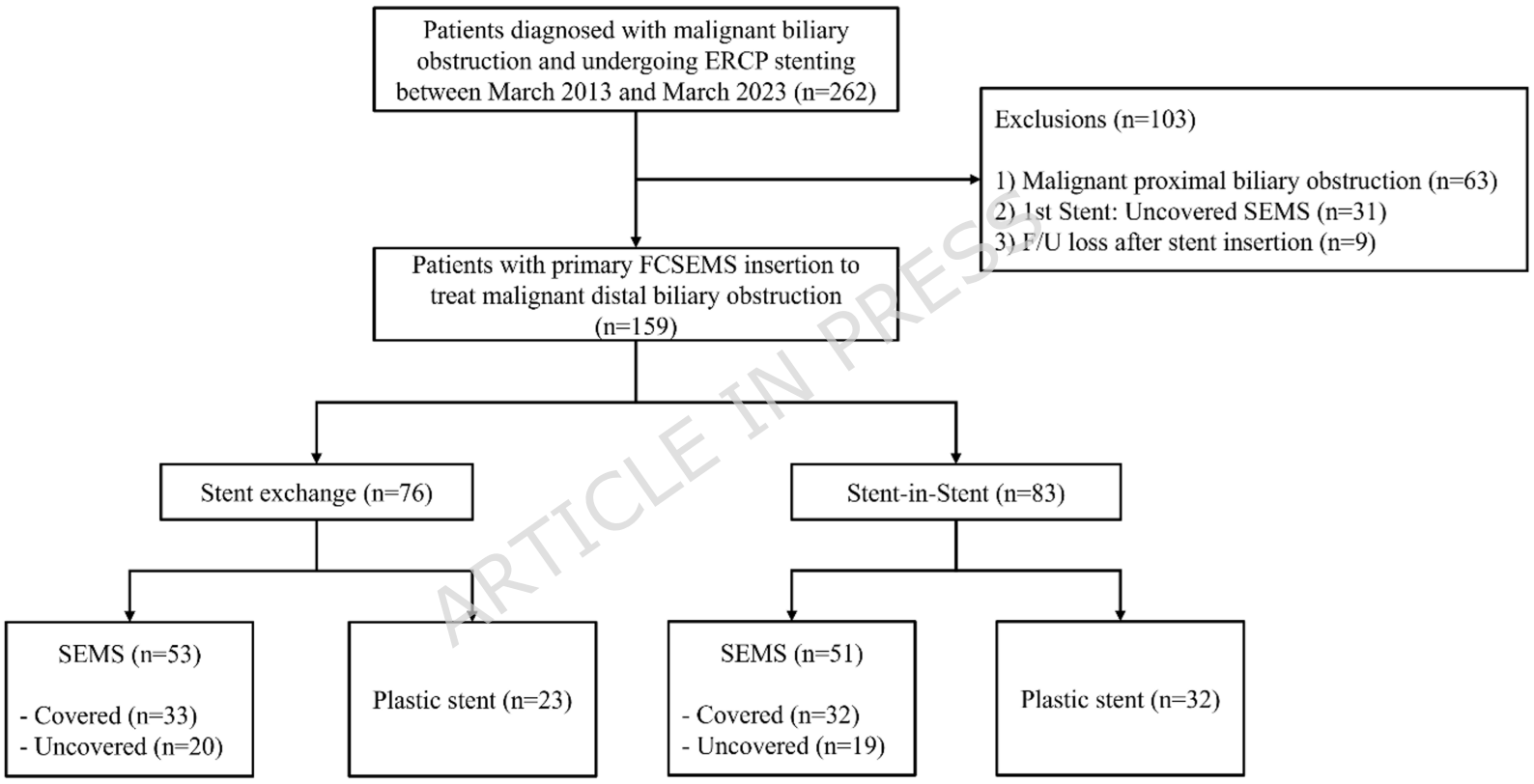


Table 1. Baseline characteristics of patients and clinical outcomes according to the primary and secondary biliary stent type and method

	Stent exchange, SEMS (covered & uncovered) (n=53)	Stent exchange, plastic stent (n=23)	Stent-in-stent, SEMS (covered & uncovered) (n=51)	Stent-in-stent, plastic stent (n=32)	p-value
Age (range) (years)	71.8 (48–89)	70.5 (40–86)	69.6 (47–89)	67.9 (36–88)	0.323
Sex					
Male/female (n)	26/27	11/12	29/22	15/17	0.781
Diagnosis					
Pancreatic cancer, n (%)	33 (62.3)	10 (43.5)	30 (58.8)	19 (59.4)	0.492
GB cancer, n (%)	2 (3.8)	3 (13.0)	4 (7.8)	1 (3.1)	0.379
CBD cancer, n (%)	13 (24.5)	7 (30.4)	12 (23.5)	9 (28.1)	0.913
AOV cancer, n (%)	4 (7.5)	1 (4.3)	3 (5.9)	2 (6.3)	0.960
Metastatic disease, n (%)	1 (1.9)	2 (8.7)	2 (3.9)	1 (3.1)	0.556
TNM stage					
III, n (%)	23 (43.4)	10 (43.5)	23 (45.1)	17 (53.1)	0.387
IV, n (%)	30 (56.6)	13 (56.5)	28 (54.9)	15 (46.9)	0.387
Duodenal stricture, n (%)	4 (7.5)	0 (0.0)	0 (0.0)	2 (6.3)	0.139
Length of biliary stricture (mm)	26.7	29.6	25.6	30.1	0.265
CTx. ± CCRTx., n (%)	43 (81.1)	16 (69.6)	29 (56.9)	27 (84.4)	0.149
Total bilirubin (mg/dL)					
Baseline	7.0	6.7	7.6	6.8	0.886
Day 1	5.8	5.7	5.8	5.2	0.873
Day 28	1.4	2.1	1.4	2.1	0.282
Previous procedure†, n (%)	17 (32.1)	8 (34.8)	12 (23.5)	8 (25.0)	0.663

AOV, ampulla of vater; CBD, common bile duct; CCRTx., concurrent chemoradiotherapy; CTx., chemotherapy; GB, gallbladder; SEMS, self-expandable metallic stent; TNM, classification of malignant tumors

†Previous procedure indicates any prior ERCP-based biliary intervention (e.g., plastic stent placement or other biliary drainage) performed before index FCSEMS insertion.

Table 2. Primary and secondary biliary stent patency and outcomes according to stent type and method

	Stent exchange, SEMS (covered & uncovered) (n=53)	Stent exchange, plastic stent (n=23)	Stent-in-stent, SEMS (covered & uncovered) (n=51)	Stent-in-stent, plastic stent (n=32)	p-value
Primary stent outcome					
Primary stent length (cm), mean (min–max)	6.4 (4–8)	6.2 (4–9)	6.1 (4–8)	6.5 (4–8)	0.605
Primary TRBO (days), mean (95% CI)	171 (133–209)	106 (52–158)	154 (124–185)	128 (89–166)	0.108
Cause of stent dysfunction					
Ingrowth & overgrowth, n (%)	10 (18.8)	5 (21.7)	30 (58.9)	15 (46.9)	0.007
Stone & sludge, n (%)	34 (58.5)	9 (39.1)	21 (41.2)	17 (36.3)	0.068
Migration, n (%)	12 (22.6)	9 (39.1)	0 (0.0)	0 (0.0)	<0.001
Secondary stent outcome					
Secondary stent length (cm), mean (min–max)	7.1 (4–9)	7.8 (5–13)	7.5 (5–10)	7.7 (5–15)	0.218
Secondary TRBO (days), mean (95% CI)	161 (128–191)	53 (39–68)	104 (67–143)	67 (56–78)	0.014
Early complication (<1m)					
Acute pancreatitis, n (%)	0 (0.0)	1 (4.4)	0 (0.0)	1 (3.1)	0.265
Acute cholangitis, n (%)	4 (7.6)	1 (4.4)	5 (9.8)	3 (9.4)	0.870
Migration, n (%)	2 (3.8)	1 (4.4)	0 (0.0)	0 (0.0)	0.599
Total, n (%)	6 (11.3)	3 (13.0)	5 (9.8)	4 (12.5)	0.973
Late complication (≥1m)					
Acute pancreatitis, n (%)	1 (1.9)	0 (0.0)	3 (5.9)	1 (3.1)	0.520
Acute cholangitis, n (%)	29 (54.7)	10 (43.5)	27 (52.9)	19 (59.4)	0.705
Migration, n (%)	6 (11.3)	5 (21.7)	1 (2.0)	4 (12.5)	0.060
Total, n (%)	36 (67.9)	15 (65.2)	31 (60.8)	24 (75.0)	0.606
Total complication, n (%)	42 (79.3)	18 (78.3)	36 (70.6)	28 (87.5)	0.111
Overall survival time (day, mean)	478	339	337	434	0.259

SEMS, self-expandable metallic stent; TRBO, time to recurrent biliary obstruction

Table 3. Univariate and multivariate analysis of variables associated with secondary biliary stent patency

	n	Median (day)	Univariate analysis			Multivariate analysis		
			HR	95% CI	p-value	HR	95% CI	p-value
Diagnosis								
Pancreatic cancer	92	69	1.00		Ref.	1.00		Ref.
GB cancer	10	72	1.02	0.37–2.81	0.976	0.72	0.25–2.08	0.543
CBD cancer	41	61	1.11	0.70–1.76	0.657	0.91	0.52–1.59	0.728
AoV cancer	10	91	1.09	0.50–2.40	0.828	1.63	0.69–3.86	0.264
Metastasis	6	50	2.90	1.04–8.13	0.043	1.61	0.50–5.20	0.424
TNM stage								
III	73	65	1.00					
IV	86	72	1.13	0.71–1.79	0.605			
Length of biliary stricture								
≥25mm	74	69	1.00					
<25mm	85	63	0.98	0.60–1.60	0.919			
CTx. ± CCRTx.								
Yes	115	70	1.00					
No	44	65	1.44	0.88–2.36	0.148			
Total bilirubin (baseline)								
≤3mg/dL	66	63	1.00					
>3mg/dL	93	74	1.30	0.79–2.15	0.310			
Primary TRBO								
≥180days	47	93	1.00			1.00		
<180days	112	67	1.79	1.13–2.84	0.013	1.77	1.10–2.86	0.019
Cause of primary stent dysfunction								
Ingrowth & overgrowth	55	60	1.00		Ref.	1.00		Ref.
Stone, sludge	83	72	1.69	0.96–2.99	0.069	1.50	0.90–2.51	0.123
Migration	21	77	0.31	0.13–	0.009	0.30	0.13–0.68	0.004

				0.75				
Method								
Stent exchange, SEMS	53	94	1.00		Ref.	1.00		Ref.
Stent exchange, Plastic stent	23	53	3.62	1.63–8.03	0.002	6.84	2.63–17.8	<0.001
Stent-in-Stent, SEMS	51	75	1.72	0.98–3.02	0.059	6.53	1.89–22.55	0.003
Stent-in-Stent, Plastic stent	32	67	3.58	1.84–6.99	<0.001	2.69	1.21–5.97	0.015

AOV, ampulla of vater; CBD, common bile duct; CCRTx., concurrent chemoradiotherapy; CTx., chemotherapy; GB, gallbladder; SEMS, self-expandable metallic stent; TNM, classification of malignant tumors; TRBO, time to recurrent biliary obstruction

Table 4. Univariate and multivariate analysis of variables associated with overall survival time

	n	Median (day)	Univariate analysis			Multivariate analysis		
			HR	95% CI	p-value	HR	95% CI	p-value
Diagnosis								
Pancreatic cancer	92	348	1.00		Ref.	1.00		Ref.
GB cancer	10	173	1.51	0.36–6.35	0.573	3.68	0.79–17.15	0.097
CBD cancer	41	334	1.33	0.75–2.38	0.333	1.31	0.61–2.83	0.494
AoV cancer	10	546	0.71	0.12–4.17	0.705	0.65	0.11–3.68	0.624
Metastasis	6	158	1.64	0.87–3.10	0.129	1.66	0.89–3.10	0.109
TNM stage								
III	73	385	1.00		0.079	1.00		0.009
IV	86	333	1.61	0.95–2.75		2.26	1.23–4.16	
Length of biliary stricture								
≥25mm	74	342	1.00		0.853			
<25mm	85	353	0.93	0.44–1.97				
CTx. ± CCRTx.								
Yes	115	362	1.00		0.253	1.00		0.005
No	44	253	1.41	0.78–2.53		4.04	1.51–10.78	
Total bilirubin (baseline)								
≤3mg/dL	66	356	1.00		0.050	1.00		0.049
>3mg/dL	93	324	1.75	1.00–3.05		1.755	1.00–3.07	
Primary TRBO								
≥180days	47	474	1.00		0.005	1.00		0.019
<180days	112	280	2.46	1.32–4.60		1.77	1.10–2.86	
Cause of primary stent dysfunction								
Ingrowth & overgrowth	55	294	1.00		Ref.			
Stone, sludge	83	338	0.88	0.48–1.58	0.659			
Migration	21	385	0.76	0.30–1.93	0.557			
Method								
Stent exchange, SEMS	53	396	1.00		Ref.	1.00		Ref.
Stent exchange, Plastic stent	23	348	0.80	0.35–1.83	0.591	0.83	0.31–2.22	0.704
Stent-in-Stent, SEMS	51	285	1.30	0.45–3.77	0.630	1.35	0.41–4.43	0.625

Stent-in-Stent, Plastic stent	32	334	1.59	0.89–2.86	0.120	1.17	0.58–2.36	0.658

AOV, ampulla of vater; CBD, common bile duct; CCRTx., concurrent chemoradiotherapy; CTx., chemotherapy; GB, gallbladder; SEMS, self-expandable metallic stent; TNM, classification of malignant tumors; TRBO, time to recurrent biliary obstruction