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Incidence and factors associated with stent dysfunction and pancreatitis after gastroduodenal stenting for malignant gastric outlet obstruction

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ABSTRACT

Background and study aims Endoscopic gastroduodenal stent (GDS) deployment is currently a standard treatment for malignant gastric outlet obstruction (mGOO) in patients with limited life expectancy; however, stent dysfunction (SD) and complicated pancreatitis often occur after GDS deployment. We investigated incidence and contributing factors of SD and complicated pancreatitis.

Patients and methods We retrospectively reviewed 203 patients who underwent initial GDS deployment for palliation of mGOO symptoms between October 2017 and July 2022, including 109 who underwent GDS deployment across the duodenal papilla (sub-cohort).

Results SDs, including tumor ingrowth (n = 26), kinking (n = 14), and migration (n = 13), occurred in 68 patients (33.5%). Cumulative SD incidence was 41.1% (95% confidence interval, 32.6–49.4%). SD incidence increased to 0.4%, 0.16%, and 0.06% per day at <8, 8–16, and >16 weeks, respectively. On multivariate analysis, Niti-S pyloric/duodenal stent deployment (sub-distribution hazard ratio [sHR] 0.26, $P = 0.01$) and survival length ≥ 90 days (sHR 2.5, $P = 0.01$) were respectively identified as favorable and risk factors significantly associated with SD. Pancreatitis developed in 14 patients (12.8%) in the sub-cohort, which had significantly higher parenchymal diameter ($P < 0.01$) and lower main pancreatic duct (MPD) caliber ($P < 0.01$) than the non-pancreatitis cohort. On multivariate analysis, MPD caliber <3 mm independently predicted pancreatitis (odds ratio 6.8, $P = 0.03$).

Conclusions Deployment of the Niti-S pyloric/duodenal stent, with conformability even for angulated strictures, significantly reduced the incidence of SD. Stent selection, life expectancy, and MPD caliber should be taken into consideration during decision-making for GDS deployment for mGOO.

Introduction

Malignant gastric outlet obstruction (mGOO) often occurs in patients with advanced upper digestive cancers, including gastric and pancreatobiliary cancers. It can lead to vomiting, dehydration, malnourishment, and an inability to tolerate chemotherapy and oral intake, severely impairing the quality of life [1]. Traditionally, treatment options for mGOO have comprised surgical (open/laparoscopic) gastroenterostomy (surgical gastrojejunostomy [GJ]), which is especially invasive for patients with end-stage disease. Therefore, endoscopic gastroduodenal stent deployment (GDS) is widely performed as an alternative treatment to surgical GJ, particularly in patients with an expected survival of less than 2 to 6 months or low performance status (non-tolerance for surgery) [2, 3, 4].

Endoscopic GDS deployment for mGOO may afford a shorter hospital stay, quicker resumption of oral intake, and lower total medical costs [5, 6]. In particular, this minimally invasive method is more suitable for terminal patients with limited survival [7, 8]. In addition, recent studies have shown excellent technical and clinical success rates for endoscopic GDS deployment, at 96% to 100% and 82% to 91%, respectively [9, 10, 11]. Therefore, endoscopic GDS deployment is typically performed in most patients with mGOO. However, endoscopic GDS deployment is associated with a high rate of stent dysfunction (SD) requiring reintervention. Further, adverse events (AEs), including pancreatitis, sometimes occur, leading to critical problems in pre-terminal patients. Moreover, the incidence of SDs and AEs may be increasing due to the currently advancing use of palliative chemotherapy and radiotherapy [12].

Several recent studies compared clinical outcomes between the deployment of uncovered self-expandable metal stents (UCSEMSs) and covered self-expandable metal stents (CSEMSs) [9, 13, 14, 15]. However, few studies have reported the clinical outcomes of each stent product and factors associated with each SD cause (e. g., ingrowth, migration, and kinking). Although we have discussed acute pancreatitis after endoscopic GDS deployment from a clinical standpoint [16, 17], few studies have described factors that are predictive of it. Therefore, we aimed to investigate the incidence of and factors associated with SD and complicated pancreatitis after endoscopic GDS deployment.

Patients and methods

Study patients

We retrospectively reviewed patients who underwent initial GDS deployment for palliation of mGOO symptoms between October 2017 and July 2022 at the National Cancer Center Hospital. Patients were included if they had GOO symptoms (appetite loss, nausea and/or vomiting with confirmed obstruction using endoscopy, fluoroscopy, and/or computed tomography [CT] due to a malignant obstruction located in the distal stomach or duodenum and were scheduled for initial GDS deployment for palliation of mGOO symptoms. Patients who underwent previous treatment for mGOO symptoms (i. e., GDS placement or surgical GJ) or simultaneous deployments with different GDS types were excluded from this study. In addition, patients who underwent simultaneous transpapillary procedures were excluded. A sub-cohort of those who underwent GDS deployment across the duodenal papilla was defined for the evaluation of pancreatitis incidence and its risk factors (**Supplementary Fig. S1**).

This study was approved by our institutional review board (No. 2018–149). The requirement for informed consent was waived because of the retrospective study design.

Equipment and procedures

The prescription of nonsteroidal anti-inflammatory drugs as preventive medicine was based on the judgment of the endoscopist. GDS deployment was performed using a direct-viewing or side-viewing duodenoscope under fluoroscopic guidance according to standard procedures. The main stenosis site was defined as the middle site of the stenosis based on CT, fluoroscopy, and endoscopy findings. Jejunal stenosis included surgically altered anatomy.

The CSEMS used in this study was the Niti-S ComVi pyloric/duodenal stent (Taewoong Medical Co, Ltd., Seoul, South Korea). We also used the following six UCSEMS products: HANAROSTENT Naturfit duodenal stent (Boston Scientific Corporation, Marlborough, Massachusetts, United States), Niti-S pyloric/duodenal stent (Taewoong Medical Co, Ltd.), WallFlex duodenal stent (Boston Scientific Corporation, Marlborough, Massachusetts, United States), NEXENT duodenal stent (Next Biomedical Co., Ltd., Incheon, South Korea), Evolution duodenal stent (Cook Medical Co., Ltd., Limerick, Ireland), and JENTLLY NEO duodenal stent (Japan Lifeline Co., Ltd., Tokyo, Japan). The GDSs were 8 to 12 cm in length and 20 mm in diameter for CSEMSs and 6 to 15 cm in length and 22 mm in diameter for UCSEMSs. Selection of the most appropriate stent length was based on the judgment and preference of the endoscopist; however, selection of stent products was based on the timing of sales launches. When multiple stents were deployed, the longest stent length was used for analysis.

Clinical outcomes and definitions

Clinical outcomes of GDS deployment were evaluated in terms of technical success, clinical success, oral intake status (evaluated using the GOO scoring system [GOOSS]), duration of stent patency (time to SD), cumulative incidence of SD, and AEs. The severity of GOO was assessed before and after stent placement using an adaptation of the GOOSS [18]. Technical success was defined as satisfactory GDS deployment and precise positioning at the obstruction site. Clinical success was defined as an improvement in the GOOSS score (≥ 1) and relief of GOO symptoms within 1 week after GDS placement. SD was defined as appetite loss, nausea, and/or vomiting with confirmation of re-obstruction using any imaging technique (endoscopy, fluoroscopy, and/or CT). The causes of SD (tumor ingrowth, migration, kinking, transection, overgrowth, insufficient expansion, and food impaction) were determined using imaging techniques (endoscopy, fluoroscopy, and/or CT). Stent migration was defined as stent dislocation relative to the initial deployment site. Duplicate causes were permitted for SD as-

sessment. AEs were defined as stent-related events other than SDs during the follow-up period. AEs were defined as early if they occurred within 30 days of the procedure and as late if after 30 days.

Definition of pancreatitis and hyperamylasaemia after stent deployment

Pancreatitis after GDS deployment was defined according to the criteria in Cotton et al. [19], which consist of a 3-fold rise in serum amylase above the upper limit of the norma l(ULN), along with abdominal pain 24 hours after endoscopic retrograde cholangiopancreatography that required>1 additional night of hospitalization. Elevation of serum amylase levels (3-fold above the ULN) without abdominal symptoms was defined as hyperamylasaemia.

Measurement of pancreatic parenchyma and main pancreatic duct diameters

The diameters of the pancreatic parenchyma and main pancreatic duct (MPD) were measured manually on axial CT images before GDS deployment (**Supplementary Fig. S2**). The maximum diameter of the pancreatic parenchyma without the main lesion was measured, and the MPD was measured upstream of the stenosis site.

Statistical analyses

Continuous variables are expressed as medians (interquartile ranges [IQRs]), and categorical variables are presented as numbers (percentages). Qualitative and quantitative differences between subgroups were evaluated using the χ^2 or Fisher's exact test for categorical parameters and the Mann-Whitney U test was used for continuous variables. Time to SD and overall survival (OS) were calculated as the time from GDS deployment to SD and final follow-up or death, respectively, using the Kaplan-Meier method. Differences in the cumulative incidences of SD and each SD cause were evaluated using Gray's test; death without SD was a competing risk due to preclusion of the occurrence of the primary event of interest (SD).

In univariate and multivariate analyses to evaluate risk factors for SD, the sub-distribution hazard ratio (sHR) with the 95% confidence interval (CI) were estimated using Fine-Gray sub-distribution hazard regression with adjustment for the competing risk of death without SD [20]. In addition, binary logistic regression was used to calculate the odds ratio (OR) with 95% CI for pancreatitis after GDS deployment in the sub-cohort of GDS deployment across the duodenal papilla. The optimal cut-off values of the predictive parameters for pancreatitis were calculated using the area under the receiver operating characteristic curve (AUC) and evaluated by binary logistic regression. Factors with $P<0.10$ on univariate analysis were further evaluated by multivariate analysis.

$P<0.05$ were considered statistically significant. Data were analyzed using SPSS (version 27.0; IBM Corp., Armonk, New York, United States) and R software (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics

Among 211 consecutive patients who underwent GDS deployment during the study period, eight were excluded for the following reasons: 1) GDS migration at the time of biliary stent deployment (n = 1); and 2) simultaneous deployment of different stent types (n = 7). Thus, 203 patients were enrolled in this study (**Supplementary Fig. S1**).

Pancreatic cancer was the most common etiology (67.5%). "Other cancers" as the etiology included lung cancer (n = 3), colon cancer (n = 3), breast cancer (n = 3), and other cancer types (n = 18). The main stenosis was the duodenum in 183 patients (90.1%), with the second portion (D2) as the most common site. Prior endoscopic sphincterotomy and biliary drainage were observed in 82 patients (40.4%) and 135 patients (66.5%), respectively. In total, 136 patients (70.0%) had a pre-GOOSS score ≤ 1, and 149 (73.4%) had a performance score ≤ 1. The median follow-up period was 72.5 days (IQR 35.0–163) and death was observed in 117 patients (57.6%). The median OS was 117 days (95%CI 73.6–160) (▶ **Table 1**).

Treatment and clinical outcomes

UCSEMSs and CSEMSs were deployed in 181 patients (89.2%) and 22 patients (11.5%), respectively. Technical success was achieved in 203 of 203 patients (100%) in the entire cohort. Clinical success was achieved in 162 of 178 patients (91.0%) with a pre-GOOSS score of 0, 1, or 2. The mean GOOSS score significantly improved from 1.4 to 2.5 ($P<0.01$) after deployment. SDs occurred in 68 patients (33.5%) due to ingrowth, kinking, and migration. The most common early AE was pancreatitis (14 patients, 6.9%), with mild, moderate, and severe pancreatitis in nine, three, and two patients, respectively. Late AEs included perforation (n = 2, 1.0%) and small bowel obstruction due to stent migration (n = 1, 0.5%) (▶ **Table 2**).

Stent patency and dysfunction factors

The median time to SD was 179 days (95%CI 114–244). The cumulative incidence of SD was 22.6% at Week 8, 31.3% at Week 16, and 41.9% overall (▶ **Fig. 1a** and **Supplementary Table S1**). The increase in the rate of SD incidence was 0.4% per day until Week 8, 0.16% from Weeks 8 to 16, and 0.06% after Week 16, reflecting a lower slope after Week 8 (▶ **Fig. 1a**). The cumulative incidence of SD was significantly lower with the Niti-S pyloric/duodenal stent than with other GDSs (17.8% vs 45.7% in total, $P<0.01$) and was insignificantly higher with CSEMS than with other UCSEMSs (61.9% vs 38.7%, $P=0.06$) (▶ **Fig. 1**). On multivariate analysis, Niti-S pyloric/duodenal stent deployment (sHR 0.26, 95%CI 0.10–0.70, $P<0.01$) and a survival length ≥ 90 days (sHR 2.28, 95%CI 1.15–4.52; $P=0.02$) were identified as factors significantly associated with SD (▶ **Table 3**).

Factors for each cause of stent dysfunction

Tumor ingrowth, with a cumulative incidence of 21.5% (95%CI 14.3–29.7%), was the most common dysfunction after placement, followed by migration (9.5%; 95%CI 5.2–15.4%) and kink-

▶ **Table 1** Patient characteristics in the entire cohort.

Overall, n = 203	Variables*
Age, years	64 (55–72)
Sex (M:F)	116:87
Primary disease	
▪ Pancreatic cancer	137 (67.5%)
▪ Biliary tract cancer	35 (17.2%)
▪ Other cancers	27 (13.3%)
▪ Gastric cancer	4 (2.0%)
Main stenosis site	
Duodenum	183 (90.1%)
▪ D1:D2:D3:D4	37:87:48:12
Stomach	9 (4.4%)
Jejunum	11 (5.9%)
EST before SEMS deployment	82 (40.4%)
Biliary drainage before SEMS deployment	135 (66.5%)
▪ Transpapillary drainage†	80 (39.4%)
▪ EUS-HGS†	41 (20.2%)
▪ EUS-CDS†	17 (8.4%)
GOOSS score before SEMS deployment (0:1:2:3)	23:113:42:25
Performance status (0:1:2:3:4)	37:112:45:9:0
Chemotherapy after SEMS deployment	86 (42.4%)
Opioid use	68 (33.5%)
Follow-up duration, days	72.5 (35.0–163)
Death	117 (57.6%)
Overall survival, median (days) (95%CI)‡	117 (73.6–160)

*Data are presented as n (%) or median (interquartile range).
†Duplicated numbers.
‡Kaplan-Meier estimation.
M, male; F, female; D1, bulb; D2, second portion; D3, third portion; D4, fourth portion; EST, endoscopic sphincterotomy; SEMS, self-expandable metal stent; EUS-HGS, endoscopic ultrasound-guided hepaticogastrostomy; EUS-CDS, endoscopic ultrasound-guided choledochoduodenostomy; GOOSS, Gastric Outlet Obstruction Scoring System; CI, confidence interval.

▶ **Table 2** Initial stent deployment and outcomes in the entire cohort.

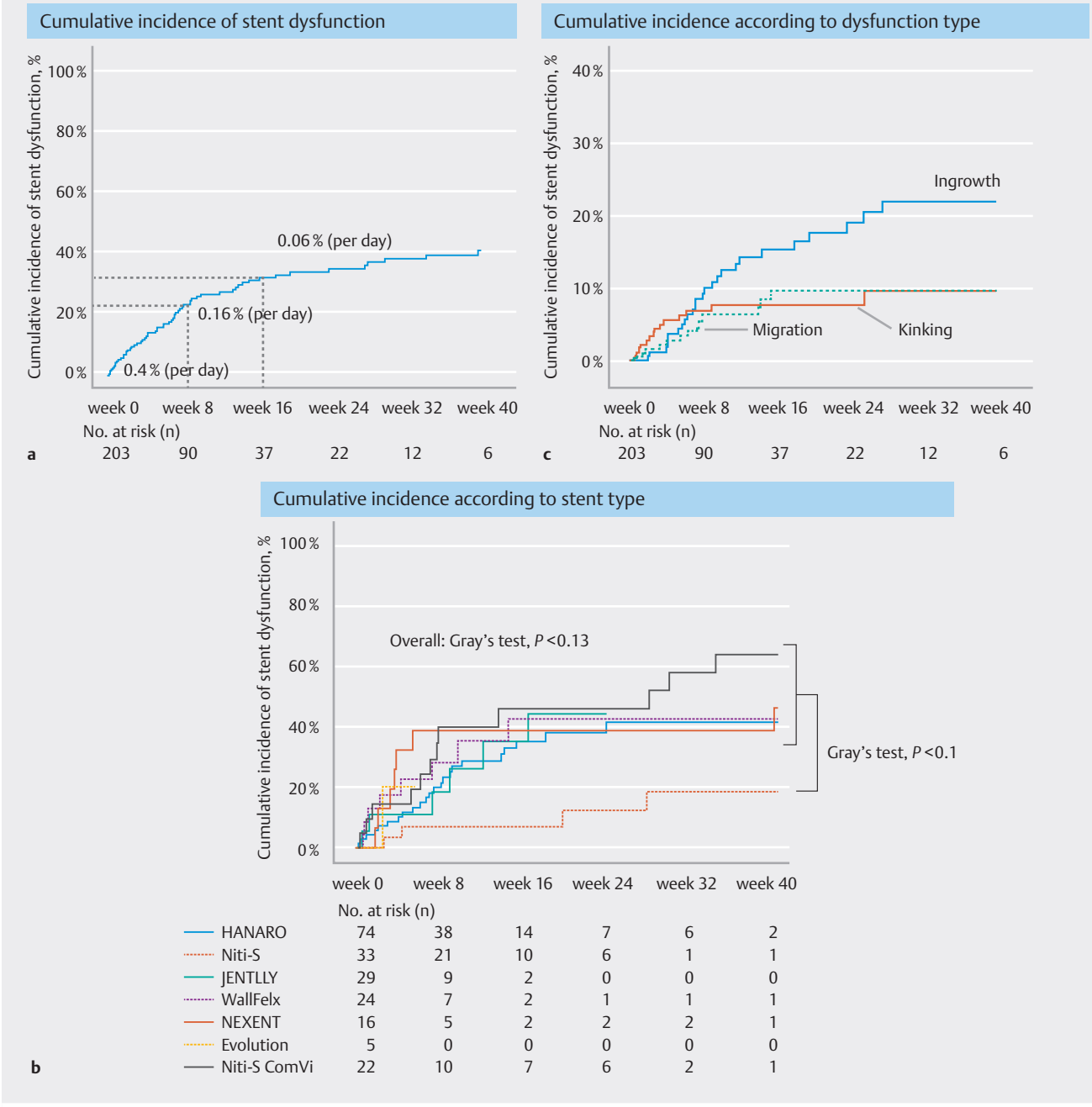
Overall, n = 203	Variables*
Technical success*	203 (100%)
Clinical success†	162 (91.0%)
GOOSS score after SEMS deployment (0:1:2:3)	1:14:70:118
NSAIDS use as preventive medicine	125 (61.6%)
Stent type (UCSEMS: CSEMS)	181: 22
UCSEMS	181 (89.2%)
▪ HANAROSTENT Naturfit duodenal stent	74 (36.5%)
▪ Niti-S pyloric/duodenal stent	33 (16.3%)
▪ JENTLLY NEO duodenal stent	29 (14.3%)
▪ WallFlex duodenal stent	24 (11.8%)
▪ NEXENT duodenal stent	16 (7.9%)
▪ Evolution duodenal stent	5 (2.5%)
CSEMS	
▪ Niti-S ComVi pyloric/duodenal stent	22 (11.5%)
Stent length (6 cm:8 cm:9 cm:10 cm:12 cm:15 cm)‡	4:23:8:51:136:4
Stent diameter (20 mm:22 mm)	22:181
Number of deployed stents (1:2:3)	156:36:11
Deployment across the duodenal papilla	121 (59.6%)
Stent dysfunction	68 (33.5%)
▪ Ingrowth/kinking/migration/food impaction/overgrowth/transection/insufficient expansion‡	26/14/13/11/8/8/6
Early adverse event (< 30 days)	18 (8.9%)
▪ Pancreatitis (mild/ moderate/ severe)§	14 (9/3/2) (6.9%)
▪ Jaundice and/or cholangitis§	3 (1.5%)
▪ Bleeding	2 (1.0%)
▪ Pneumonia	1 (0.5%)
Late adverse event (≥ 30 days)	3 (1.5%)
▪ Perforation	2 (1.0%)
Due to stent kinking	1 (0.5%)
▪ -Small bowel obstruction (due to stent migration)	1 (0.5%)

*Data are presented as n (%) or median (interquartile range).
†Technical success was defined as satisfactory SEMS placement and precise positioning at the obstruction site.
‡Clinical success was defined as an improvement in the GOOSS score (≥ 1) after stent deployment among patients with GOOSS scores of 0, 1, and 2 (n = 178).
§Duplicated numbers.
GOOSS, Gastric Outlet Obstruction Scoring System; SEMS, self-expandable metal stent; UCSEMS, uncovered self-expandable metal stent; CSEMS, covered self-expandable metal stent; NSAIDS, nonsteroidal anti-inflammatory drugs.

ing (9.2%; 95%CI 4.9–15.3%) (▶ **Fig. 1c**). The median onset of dysfunction was 42 days (IQR 15–70). Scatterplots indicating the onset timing and frequency of each SD cause are shown in ▶ **Fig. 2**.

Risk factors for each SD cause and risk stratification are shown in **Supplementary Table S2** and **Supplementary Fig. S3**. Tumor ingrowth was significantly associated with a survival length ≥ 90 days (sHR 3.58, 95%CI 1.35–9.51, $P = 0.01$). Tumor ingrowth did not occur in the CSEMS cohort (0/22).

Stent kinking was significantly associated with the NEXENT duodenal stent (sHR 5.65, 95%CI 1.77–18.0, $P < 0.01$). Stent migration was significantly associated with other cancers as the



▶ **Fig. 1** Cumulative incidence of stent dysfunction. **a** Cumulative incidence of all stent dysfunctions (SDs) in the entire cohort. The cumulative incidences of SD at Week 8, at Week 16, and overall were 22.6%, 31.3%, and 41.1%, respectively. **b** Cumulative incidence of SD with each stent type. The cumulative incidences of SD at Week 8, Week 16, and overall were 6.7%, 6.7%, and 17.8%, respectively, for Niti-S stents and 25.9%, 36.4%, and 45.7%, respectively, for other stents (Gray's test, P<0.01). The stent names are abbreviated as defined in **Supplementary Table S1**. **c** Cumulative incidence of each SD cause (ingrowth, kinking, and migration). The total cumulative incidences of ingrowth, kinking, and migration were 21.5%, 9.2%, and 9.5%, respectively.

etiology (sHR 3.23, 95%CI 1.0–10.5, P = 0.05), the bulb (D1) as the main stenosis site (sHR 3.84, 95%CI 1.34–11.0, P = 0.01), and CSEMSs (sHR 6.76, 95%CI 2.29–20.0, P<0.01). In the UCSEMS cohort, chemotherapy after deployment was insignificantly associated with stent migration (P = 0.06). In the CSEMS cohort, stent migration occurred in two of two patients with other cancers as the etiology and four of six patients with D1 as the main stenosis site; a significantly lower incidence of stent migration was observed in patients without these factors (sHR 0.06, 95%CI 0.01–0.47, P<0.01) (**Supplementary Table S3**).

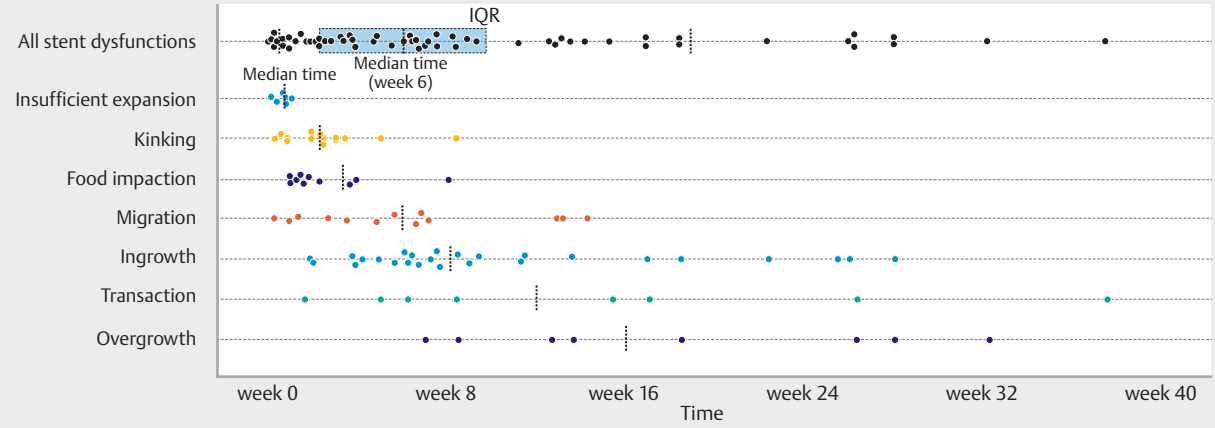
▶ **Table 3** Factors associated with stent dysfunction (Fine-Gray sub-distribution hazard regression).

Variables	Univariate sHR (95%CI)	*P* value	Multivariate adjusted sHR (95%CI)	*P* value
Age (per year)	1.0 (0.97–1.02)	0.69	–	–
Sex (M)	1.06 (0.63–1.78)	0.82	–	–
Primary cancer			–	–
▪ Pancreatic cancer	1.03 (0.59–1.79)	0.91	–	–
▪ Biliary tract cancer	1.33 (0.72–2.48)	0.37	–	–
▪ Other cancers	0.78 (0.32–1.87)	0.57	–	–
▪ Gastric cancer	NA	NA	–	–
Main stenosis site			–	–
Stomach	NA	NA	–	–
Duodenum			–	–
▪ D1 (bulb)	1.34 (0.76–2.34)	0.31	–	–
▪ D2 (second portion)	0.77 (0.46–1.28)	0.31	–	–
▪ D3 (third portion)	0.86 (0.46–1.61)	0.64	–	–
▪ D4 (fourth portion)	0.90 (0.28–2.88)	0.85	–	–
Jejunum	1.77 (0.73–4.24)	0.20	–	–
UCSEMS			–	–
▪ HANAROSTENT Naturfit duodenal stent	1.01 (0.60–1.68)	0.98	–	–
▪ Niti–S pyloric/duodenal stent	**0.29 (0.11–0.77)**	**0.01**	**0.26 (0.10–0.70)**	**< 0.01**
▪ JENTLLY NEO duodenal stent	1.06 (0.47–2.40)	0.89	–	–
▪ WallFlex duodenal stent	1.24 (0.58–2.67)	0.58	–	–
▪ NEXENT duodenal stent	1.46 (0.65–3.31)	0.36	–	–
▪ Evolution duodenal stent	0.66 (0.08–5.32)	0.70	–	–
CSEMS (Niti–S ComVi stent)	**1.94 (1.08–3.50)**	**0.03**	1.29 (0.70–2.36)	0.41
Multiple stenting (≥ 2 stents)	0.95 (0.52–1.75)	0.87	–	–
Stent length (≥ 12 cm)	1.04 (0.62–1.75)	0.89	–	–
GOOSS score before SEMS placement (≥ 2)	0.89 (0.52–1.52)	0.67	–	–
Performance status (≥ 2)	**0.56 (0.28–1.11)**	**0.10**	0.83 (0.39–1.73)	0.61
Chemotherapy after GDS deployment	**1.77 (1.06–2.94)**	**0.03**	0.91 (0.46–1.79)	0.78
Survival length (≥ 30 days)	1.71 (0.71–4.14)	0.23	–	–
Survival length (≥ 60 days)	1.79 (0.97–3.31)	0.06	–	–
Survival length (≥ 90 days)	**2.22 (1.33–3.70)**	**< 0.01**	**2.28 (1.15–4.52)**	**0.02**

sHR, sub-distribution hazard ratio; CI, confidence interval; M, male; NA, non-available data; UCSEMS, uncovered self-expandable metal stent; CSEMS, covered self-expandable metal stent; GOOSS, Gastric Outlet Obstruction Scoring System; GDS, gastric duodenal stent

Features and risk factors of complicated pancreatitis

Among 203 patients (entire cohort), those who did not undergo GDS deployment across the duodenal papilla (n = 82) and those who underwent simultaneous transpapillary procedures (n = 12) were not included in the sub-cohort of GDS deployment across the duodenal papilla. Thus, the sub-cohort comprised 109 patients. Pancreatitis complicated with GDS deployment developed in 14 patients (12.8%). The sub-cohort had a significantly larger parenchymal diameter (19.8 vs 14.2 mm, $P < 0.01$) and smaller MPD diameter (2.6 vs 5.8 mm, $P < 0.01$) than the non-pancreatitis cohort. In addition, a history of endoscopic sphincterotomy and biliary drainage, especially transpa-



▶ **Fig. 2** Time plot for each cause of each stent dysfunction. The median time to onset for any stent dysfunction (SD) was 42 days (IQR 15–70). The median times to onset for each SD cause are shown as dotted lines. The median days (number, duplicated) of insufficient expanding, kinking, food impaction, migration, ingrowth, transection, and overgrowth were 5.5 (n = 6), 17.5 (n = 14), 25.5 (n = 11), 42 (n = 14), 53 (n = 26), 88 (n = 8), and 119 (n = 8) days, respectively. IQR, interquartile range.

pillary drainage, had a lower frequency in the pancreatitis cohort than in the non-pancreatitis cohort. By contrast, the frequencies of CSEMS deployment and stent overlap (≥ 2 stents) on the papilla did not significantly differ between the pancreatitis cohort and non-pancreatitis cohort (**Supplementary Table S4**). The AUC in predicting pancreatitis was 0.76 (95%CI 0.65–0.86) for the parenchymal diameter and 0.78 (95%CI 0.67–0.89) for the MPD diameter, and the optimal cut-off values were 15.0 mm and 3.0 mm, respectively (**Supplementary Fig. S4**). On multivariate analysis, an MPD<3 mm was independently identified as the sole predictive factor for pancreatitis (odds ratio 6.8, 95%CI 1.17–39.4, $P = 0.03$) (▶ **Table 4**).

Discussion

In this study, we retrospectively evaluated incidence of and risk factors for SDs and complicated pancreatitis after GDS deployment for mGOO. Although recent studies have identified factors for SD, SDs have heterogeneous causes (ingrowth, migration, and kinking, among others). Therefore, we also indicated the onset time, frequency, and contributing factors for each SD cause in initial GDS deployment cases. In addition, from a clinical standpoint, we frequently encountered pancreatitis in cases of GDS deployment across the papilla. We also determined its incidence and predictive factors.

Overall, the incidence of SD was approximately 40%, which is similar to that in previous studies [9, 12, 13]. However, the incidence of SD was significantly lower with the Niti-S pyloric/duodenal stent than with other stents ($P<0.01$). Consistent with this, a randomized study reported the SD incidence as 24% with the Niti-S pyloric/duodenal stent and 64% with the WallFlex duodenal stent ($P<0.012$) [21]. The Niti-S pyloric/duodenal stent conforms better to angulated strictures because it is a hook-wire type with lower radial force (RF) and axial force (AF) compared with those with braided-type stents [22]. This characteristic likely might reduce the incidence of early SDs such as stent migration and kinking.

In a recent study, the median post-GDS deployment survival was 2.4 to 2.7 months, and mGOO was identified as a marker for poor survival in malignancy, regardless of the etiology [23]. In the present study, post-stent deployment median survival was slightly longer, at 117 days; however, the population that required intervention for mGOO had pre-terminal status. Most late-phase SDs are caused by tumor ingrowth and overgrowth, which can be relatively easily treated by secondary GDS deployment using the stent-in-stent technique [24]. However, in cases of pre-terminal status (predictive of a short life expectancy), it is important to prevent SDs in the early phase, including stent kinking and migration. Considering the high frequency of SDs up to Week 8, we performed a detailed investigation of the risk factors for stent kinking and migration in the early phase.

Incidence of stent kinking was significantly higher with the NEXENT duodenal stent than with the other stents. In general, the NEXENT duodenal stent has high AF and RF, similar to those of the WallFlex duodenal stent [25, 26]. The WallFlex duodenal stent has a flare system at the proximal area and can be fixed at the pylorus to reduce the risk of stent kinking. However, the present results suggest that the NEXENT duodenal stent does not have anti-kinking properties despite its high AF and RF.

Stent migration is a troublesome event because it is sometimes difficult to retrieve a migrated stent, leading to the possibility of gastrointestinal perforation or obstruction [27, 28, 29]. Previous studies have identified CSEMSs as a risk factor for stent migration [13, 14, 15], and preventing CSEMS migration remains challenging. The present findings indicate that CSEMS deployment has a significantly higher potential for stent migration in patients with other cancers as the etiology or D1 as the stenosis site. GDS deployment for D1 stenosis is affected not only by angulated strictures, but also by stomach peristalsis in general, which may explain this result. Further, other cancers

▶ **Table 4** Predictive factors associated with pancreatitis after GDS deployment across the duodenal papilla (multivariate binary logistic regression).

Predictive factors	GDS deployment across the duodenal papilla, n = 109					
	N	Pancreatitis, n (%)	Univariate OR (95%CI)	*P* value	Multivariate adjusted OR (95%CI)	*P* value
Age (per year)	–	–	0.95 (0.90–1.01)	0.10	–	–
Sex (M)	58	6 (10.3%)	0.62 (0.20–1.93)	0.41	–	–
Primary cancer						
▪ Gastric cancer	3	1 (33.3%)	3.58 (0.30–42.3)	0.31	–	–
▪ Pancreatic cancer	72	6 (8.3%)	0.33 (0.11–1.04)	0.06	1.77 (0.29–10.7)	0.54
▪ Biliary tract cancer	21	5 (23.8%)	2.96 (0.87–10.1)	0.08	–	–
▪ Other cancers	13	2 (15.4%)	1.15 (0.23–5.79)	0.86	–	–
CSEMS	9	2 (22.2%)	2.10 (0.39–11.3)	0.39	–	–
Stent overlap (≥ 2 stents) on the papilla	17	2 (11.8%)	0.90 (0.18–4.38)	0.89	–	–
Stent length (≥ 12 cm)	85	10 (11.8%)	0.67 (0.19–2.35)	0.53	–	–
Performance status (≥ 2)	29	3 (10.3%)	0.75 (0.19–2.92)	0.68	–	–
Pancreatic parenchyma diameter ≥ 15 mm	**57**	**12 (21.1%)**	**6.40 (1.36–30.2)**	**0.02**	4.93 (0.92–26.4)	0.06
MPD caliber<3 mm	**28**	**9 (32.1%)**	**6.92 (2.07–23.1)**	**<0.01**	**6.80 (1.17–39.4)**	**0.03**
EST before GDS deployment	46	3 (6.5%)	0.33 (0.09–1.26)	0.10	0.42 (0.10–1.78)	0.24
Biliary drainage history						
▪ Transpapillary drainage	43	3 (7.0%)	0.38 (0.10–1.43)	0.15	–	–
▪ EUS–HGS	32	4 (12.5%)	0.96 (0.28–3.31)	0.95	–	–
▪ EUS–CDS	14	1 (7.1%)	0.49 (0.06–4.03)	0.49	–	–
Diabetes mellitus*	53	4 (7.5%)	0.34 (0.10–1.15)	0.08	–	–
NSAIDS use as preventive medicine	73	9 (12.3%)	0.87 (0.27–2.82)	0.82	–	–
Regular opioid use	35	1 (2.9%)	0.14 (0.02–1.10)	0.06		

*Diabetes mellitus was diagnosed based on the following criteria: 1)) HbA1c ≥6.5% and/or 2) fasting blood sugar level ≥ 200 mg/dL within 2 months of stent deployment.
GDS, gastric duodenal stent; OR, odds ratio; CI, confidence interval; M, male, CSEMS, covered self-expandable metal stent; MPD, main pancreatic duct; EST, endoscopic sphincterotomy; GDS, gastric duodenal stent; EUS-HGS, endoscopic ultrasound-guided hepaticogastrostomy; EUS-CDS, endoscopic ultrasound-guided choledochoduodenostomy; NSAIDS, nonsteroidal anti-inflammatory drugs.

may compress the digestive tract indirectly by lymph node metastasis or a nodule of peritoneal dissemination, resulting in a reduction in stent adhesion. This is consistent with the results of a prospective study that reported CSEMSs as the only factor for migration to extrinsic tumors [9]. These results may help to determine whether CSEMSs should be deployed in patients with mGOO. CSEMSs might be permitted in cases such as direct invasion due to pancreatobiliary cancer and a relatively straight stricture in D3 to D4. Given that CSEMS deployment had the highest SD incidence (61.9%), however, we may need to deploy it only in specific cases, such as in tumor bleeding (to reduce bleeding by compression with the CSEMS). In addition, UCSEMS migration was occasionally observed. Chemotherapy after UCSEMS deployment was thought to be a risk because of relief of obstruction attributed to treatment. We should pay attention not only to CSEMSs but also to UCSEMSs, especially after chemotherapy.

In cases of GDS deployment across the papilla, pancreatitis developed with high frequency, at 12.8% (14 of 109 cases). This result is similar to that of a previous study, which reported an incidence of 10.6% (9 of 85) [30]. Despite the high incidence of complicated pancreatitis, its risk factors have not been previously investigated due to a lack of experience with GDS deployment and sufficient awareness of complicated pancreatitis. Our study found that the sub-cohort of GDS deployment across the duodenal papilla had a significantly higher parenchymal diameter and lower MPD caliber than the non-pancreatitis cohort. Particular attention should be paid to patients with an MPD caliber<3 mm, which was identified as an independent risk factor for pancreatitis; 32.1% of such patients (9/28) developed pancreatitis in the present study. GJ may be more suitable

for patients with an MPD caliber<3 mm with sufficient tolerance [7, 8]. In addition, recent studies have indicated a preference for endoscopic ultrasound-guided GJ, a relatively new and minimally invasive technique that provides rapid relief from GOO symptoms and is associated with low morbidity and long-term patency [31, 32, 33, 34]. This technique has a low risk of pancreatitis because it does not involve the pancreas; thus, it may be more suitable for patients at high risk of pancreatitis.

This study has certain limitations. First, it used a retrospective design, inherently reducing the statistical power and resulting in several biases. Measurement of the parenchymal width and MPD caliber were performed manually, leading to the potential for informative bias. In addition, several types of GDS were used. The selection of stent type depended on the timing of sales launches; the stent type was not selected randomly, leading to the potential for selection bias. Further, the number of pancreatitis events was relatively low. To evaluate the robustness of the SD and pancreatitis results, a larger study is required.

Conclusions

In conclusion, our study highlights the potential for selecting the Niti-S pyloric/duodenal stent to reduce the incidence of future SD. In addition, increased awareness of complicated pancreatitis after GDS deployment is needed. Stent selection, life expectancy, and MPD caliber should be considered during decision-making for GDS deployment for mGOO.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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