Recent advancements in stent therapy in patients with malignant gastroduodenal outlet obstruction

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Abstract: Gastric outlet obstruction (GOO) is one of severe comorbidities caused by many kinds of malignant diseases and is associated with not only degradation of patients' quality of life but also mortality. Although surgical bypass is one of the main therapies for malignant GOO, it is often difficult to perform in end-stage patients. The deployment of self-expandable metallic stents (SEMSs) has recently become a viable alternative to surgical bypass for malignant GOO. This technique is less invasive and more effective, particularly in patients with poor prognoses. Many reports have referred to the feasibility, effectiveness, and safety of the placement of SEMSs for malignant GOO. According to these reports, the rates of technical and clinical success were reported to be relatively high and the rate of adverse events to be acceptable. However, precautions against severe adverse events such as massive bleeding and perforation are necessary. Several reports have described the differences in clinical results among different kinds of SEMSs. The presence of a covered design for SEMSs may affect the patency of SEMSs and the rate of stent dysfunction. Selection of the SEMS according to axial force may affect successful achievement of long patency of SEMSs and avoidance of gastroduodenal perforation at the bending site of the duodenum. Compared with high technical success rates nearing 100%, clinical success rates were usually lower than technical success. Therefore, determination of predictive factors for failure of clinical success is important. Several papers reported that low performance status could be associated with failure of clinical success. However, the association of clinical success with other factors such as carcinomatosa and ascites remains controversial, which is a problem to be solved. Reintervention with SEMS using the stent-in-stent method after stent dysfunction can be performed effectively as well as placement of the first SEMS.

Keywords: Gastric outlet obstruction (GOO); stent; adverse event; prediction; reintervention

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Introduction

Gastric outlet obstruction (GOO) leads to refractory vomiting, nausea, and poor oral food intake caused by tumors growing around the duodenum in those with pancreatic, biliary tract, duodenal and gastric cancer. In addition to such abdominal cancers, extra-abdominal cancers with lymph node metastasis and peritoneal dissemination of advanced cancers can cause malignant GOO. Surgical bypass traditionally has been a main treatment for malignant GOO and has been useful and feasible, especially in patients with a good performance status (1). However, performing a surgical procedure in end-stage patients is sometimes difficult.

Recently, the endoscopic placement of self-expandable metallic stents (SEMSs) has been developed as a viable

treatment for malignant GOO as an alternative to surgical bypass. Endoscopic placement of a SEMS for patients with malignant GOO is less invasive, can shorten the duration of hospitalization, and enable patients to resume oral intake earlier in comparison with a surgical procedure (2-4).

Many reports have referred to the feasibility, effectiveness, and safety of the deployment of SEMSs for malignant GOO. Recently, in addition to these reports, several reports have described differences in clinical results among the kinds of SEMSs and predictive factors for successful resumption of oral intake after deployment of a SEMS. We herein review the current literature concerning endoscopic treatment using SEMSs for patients with malignant GOO.

Clinical results

Table 1 shows clinical results of prospective and multicenter studies of endoscopic treatment using SEMS for patients with malignant GOO. These reports show a technical success rate for the endoscopic deployment of a SEMS in patients with malignant GOO ranging from 95–100% (*Table 1*) (5-18). Reasons for unsuccessful deployment of a SEMS included unsuccessful passage of the guidewire or stent delivery system because of severity of the stricture (8,12), perforation during the procedure (9,16), insufficient deployment (11), and functional problems with SEMSs (6). Though definitions of clinical success differ slightly among studies, the rates of clinical success, which are indicated by an improvement in the GOO ranged from 77–94% (5-18). Median survival after deployment of a SEMS was reported to be approximately 3 months or less in most reports. Though Endo *et al.* reported a longer survival period, all of their study patients had gastric cancer, which might account for this result (15).

Adverse events

The reported rate for adverse events including stent dysfunction after deployment of SEMS for patients with malignant GOO is 15–48% (*Table 1*) (5-18). The rates of stent dysfunction and other adverse events are 5-40% and 0–23%, respectively. Though the rate of stent dysfunction is less than 30% in most reports, the rate reported Nassif *et al.* was 40% (5). In this report, "primary stent dysfunction" defined as unsuccessful SEMS dilation occurred in 8 patients (13%). However, unsuccessful dilation of a SEMS is no longer a frequent adverse event because of recent progress in the function of SEMSs.

Bleeding and perforation are severe adverse events associated with mortality; however, few reports exist regarding fatal bleeding after deployment of a SEMS. Matsumoto *et al.* reported a fatal case due to massive gastrointestinal tract bleeding on day 43 after deployment of SEMS (19). They concluded that the disruption of the artery occurred in the necrotic portion of the tumor caused by SEMS deployment and bacterial infection. We need to take precautions against massive bleeding caused by mechanical pressure as a late complication after SEMS deployment in cases of a tumor involving an artery. Ge *et al.* described delayed migration of a WallFlex enteral stent with subsequent visceral perforation four months after SEMS deployment, which was connected with shrinking of the tumor by chemotherapy (20). Several reports did not find evidence of perforation as an adverse event (8,10-12,14,18), and the risk of perforation is thought to be low. However, when it occurs perforation is directly associated with mortality, therefore, special attention should be paid to the possibility of perforation with a SEMS. As to another rare adverse event, Javaid *et al.* reported a case of fracture of a covered SEMS (21). The position of placement of a SEMS is sometimes associated with adverse events. Liu *et al.* reported the rate of acute pancreatitis in patients undergoing SEMS placement across the duodenal papilla at the rate of 11% (9/35) (22). Multivariate analysis revealed that the presence of a stent bridging the duodenal papilla [odds ratio (OR) =18.48; 95% CI, 2.298–148.48; P=0.006] was an independent predictor of acute pancreatitis.

Covered metallic stents (CMS) *vs.* uncovered metallic stents (UCMS)

Table 2 shows the results of comparisons between CMS and UCMS in a prospective study and four randomized controlled trials (23-27). The technical and clinical success rates were similar between CMS and UCMS in all of these reports. As an adverse event, the migration rate was significantly lower in the UCMS group in three of these five reports (23-25). However, Maetani *et al.* reported that there was no significant difference in the migration rate between CMS and UCMS because the 15-mm uncovered portion at both ends of the UCMS prevented stent migration (26). Lee *et al.* also reported no significant difference in the migration rate between CMS and UCMS because of the anti-migration properties of CMS (27). On the other hand, the rate of tumor ingrowth or overgrowth in CMS was

Table 1 Clinical results of placement of SEMS for the patients with malignant GOO

Author	Year	Design	No. of patients	Stent	Technical success (%)	Clinical success (%)	Median patency or eating period (days) [range]	Median survival (days) [range]	Stent dysfunction (%)	Other adverse events (%)
Nassif *et al.* (5)	2003	M	63	Wallstent, Choo	95	92	39	49	40	8
Telford *et al.* (6)	2004	M	176	Wallstent	98	84	146 [65–202]	97 [62–116]	6	9
Graber *et al.* (7)	2007	P, M	51	Wallstent	98	84	NA	72 [9–515]	24	12
Kim *et al.* (8)	2007	P, M	213	S&G Biotech	94	94	270 [234–413]	99 [78–121]	18	3
Maetani *et al.* (9)	2007	M	37	Niti-S	97	94	NA	118	5	11
Piesman *et al.* (10)	2009	P, M	43	WallFlex	100	80	NA	49	20	13
van Hooft *et al.* (11)	2009	P, M	51	WallFlex	98	84	307	62	14	14
van Hooft *et al.* (12)	2011	P, M	52	Niti-S	96	77	NA	82 [31–135]	25	23
Costamagna *et al.* (13)	2012	P, M	202	WallFlex	98	91	184 [109–266]	94 [79-112]	14	7
Sasaki *et al.* (14)	2013	M	42	WallFlex	100	83	90 [33–129]	99 [54–180]	26	2
Endo *et al.* (15)	2014	P, M	20	NA	100	94	NA	186	30	0
Miyabe *et al.* (16)	2015	M	152	Ultraflex, Niti-S, WallFlex	98	94	94 [56–180]	109 [61–195]	14	11
Kato *et al.* (17)	2016	M	125	Niti-S, WallFlex	100	92	72 [3–775]	75 [3–775]	16	13
Sasaki *et al.* (18)	2016	P	39	WallFlex	100	92	NA	50 [25–152]	8	10

M, multicenter; P, prospective; NA, not available.

Table 2 Comparison of clinical results between placement of CMS and UCMS

Author	Year	Design	No. of patients		Technical success (%)		Clinical success (%)		Migration (%)			Ingrowth or overgrowth (%)			Re-intervention (%)			Median patency or eating period (days) [range]	
			CMS	UCMS	CMS	UCMS	CMS	UCMS	CMS	UCMS	P	CMS	UCMS	P	CMS	UCMS	P	CMS	UCMS
Lee *et al.* (23)	2009	P	70	84	100	100	99	96	17	0	0.0001	3	17	0.066	21	14	>0.05	75	73
Kim *et al.* (24)	2010	RCT	40	40	100	100	95	90	32	8	0.027	3	44	<0.001	NA	NA		98 [62–134]	91 [67–116]
Lim *et al.* (25)	2014	RCT	66	68	100	100	100	98	14	0	0.003	7	21	0.016	22	21	0.999	95 [56–133]	92 [62–121]
Maetani *et al.* (26)	2014	RCT	31	31	100	100	87	94	6	0	0.99	0	19	0.02	NA	NA		68	88
Lee *et al.* (27)	2015	RCT	51	51	98	96	94	86	10	5	0.491	7	38	0.001	24	39	NS	NA	NA

P, prospective study; RCT, randomized controlled trial; CMS, covered metallic stents; UCMS, uncovered metallic stents; NA, not available; NS, not significant.

significantly lower than for UCMS in all reports shown in *Table 2*, which is an advantage of CMS. However, the rates of re-intervention and stent patency between CMS and UCMS were similar in these reports except for that of Lee *et al.* (27). Lee *et al.* reported that the CMS group had a significantly longer cumulative duration of stent patency compared with the UCMS group (27), though all patients undergoing deployment of SEMS had gastric cancer. Minata *et al.* reviewed several studies about comparison between CMS and UCMS. There was a higher migration rate in CMS compared to UCMS in the palliation of malignant GOO. Nevertheless, covered SEMS had lower obstruction rates. There was no significant difference in technical success, clinical success, complications, bleeding, perforation, stent fracture and need for reintervention (28).

Metallic stents with different axial forces

The patency of a SEMS deployed for patients with biliary stricture is related to its axial force, which is connected with kinking of the bile duct (29). Similarly, the use of SEMSs with a low axial force for patients with malignant GOO is thought to be likely to decrease the risk of stent dysfunction caused by kinking because of the angulation of the duodenum. Okuwaki *et al.* compared two types UCMS with different axial forces: a Niti-S pyloric/duodenal stent (Taewoong Medical, Gimpo, Korea) and a WallFlex duodenal stent (Boston Scientific, Marlborough, MA, USA) (30). The Niti-S pyloric/duodenal stent is thought to have lower axial force. The median time to recurrent duodenal obstruction was significantly longer in the Niti-S group than in the WallFlex group, and the incidence of stent dysfunction was lower in the Niti-S group. Kato *et al.* compared the same two types of UCMS as did Okuwaki *et al.* (17). Though there was no significant difference in patency and the rate of stent dysfunction between the two groups, the clinical success rate in the Niti-S group was significantly higher than in the WallFlex group. However, the survival period between the two groups was similar in both studies. Because of the small number of patients in the currently available studies or their retrospective design, a larger prospective clinical trial is needed to confirm the superiority of using SEMSs with lower axial force for duodenal obstruction.

Predictive factors for clinical success

Despite of high successful rate of technical success of SEMS placement for the patients with malignant GOO, it is a problem to be resolved that all patients with technical success cannot achieve clinical success. Several reports concluded that performance status is a dependent predictive factor associated with clinical success (31-34). Yamao *et al.* reported that three or more stenosis sites (OR =6.11; P<0.01) predicted clinical success in addition to the performance status. Several reports reported that the presence of ascites or peritoneal dissemination was thought to be a predictive factor for the unsuccessful resumption of oral intake after the deployment of SEMS (31,32,34,35). However, there are differences among these reports. Sasaki *et al.* reported that not carcinomatosis but ascites (OR =3.28; 95% CI, 1.23–9.05; P=0.02) was a predictor associated with resumption of oral intake. On the other hands, Hori *et al.* and Sato *et al.* concluded that not ascites but carcinomatosis was a dependent predictive factor associated with clinical success. Mendelsohn *et al.* analyzed the results of placement of SEMS for malignant GOO in patients with or without carcinomatosis and concluded that there were no statistically significant differences between the two groups with regard to clinical outcomes or reintervention rates (P=0.95, 0.34, respectively). In addition, there was no statistically significant difference in the rate of clinical success between carcinomatosis patients with no/small ascites and those with moderate/severe ascites (P=0.7) (36).

Results of reinterventions

Few reports have analyzed the results of reinterventions for stent dysfunction after placement of SEMSs for malignant GOO. Stent dysfunction occurred in the range of 5–30% in patients with SEMS placement (*Table 1*). Kim *et al.* reported the results of stent-in-stent placements performed in 48 patients with stent dysfunction (37). The technical success rate and the clinical success rate were 97.9% and 95.8%, respectively. The median patency was 27.4 weeks (IQR, 21.6–51.0 weeks). No adverse events in addition to stent dysfunction occurred. Sato *et al.* reported technical and clinical success rates of 100% and 85.7%, respectively, for stent-in-stent placements performed in 14 patients (32). Median stent patency was 172 days (range, 4–205 days). Although no severe complications such as massive bleeding and perforation were shown in those reports, Sasaki *et al.* reported a high rate of severe adverse events (38). The technical success rate and the clinical success rate were 100% and 86.2%, respectively, in the 29 patients undergoing stent-

in-stent placement of a secondary stent. The median oral intake period was 3.0 months (95% CI, 2.1–4.1 months). As a severe adverse event, gastrointestinal perforation occurred at the rate of 13.8%, which was quite high. The authors hypothesized that some SEMS properties (e.g., axial force) might be enhanced when secondary gastroduodenal SEMSs are placed by the stent-in-stent technique. They noted that one way to prevent gastrointestinal perforation was to choose a lower axial-force SEMS for a gastroduodenal SEMS inserted at the bending site (supraduodenal angle or intraduodenal angle) as a secondary stent.

Conclusions

The success rate for the placement of a SEMS for malignant GOO was sufficient. The rate of adverse events is admissible, however, severe adverse events sometimes occur. UCMS are preferable to CMS in avoiding stent migration, while CMS is preferable to UCMS in avoiding tumor ingrowth or overgrowth. Selection of a SEMS with a lower axial force may be important to achieve long patency and to avoid gastroduodenal perforation at the bending site of the duodenum. Clinical success rates were usually lower than technical success rates and a predictive factor for failure of clinical success is lower performance status. The role of other factors such as carcinomatosa and ascites remains controversial. Both technical and clinical success rates for placement of a secondary SEMS after dysfunction of a previously placed stent is similar to those for placement of the first SEMS.

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Footnote

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