Factors associated with delayed gastric emptying in patients with stent placement for malignant gastric outlet obstruction

Authors
Kenji Tominaga[1], Iruru Maetani[1], Hiroaki Shigoka[1], Shigefumi Omuta[1], Koichiro Sato[1], Sayo Ito[1], Yoshinori Saigusa[1], Tatsuya Gomi[2], Ehiichi Kohda[2]

Institutions
[1] Division of Gastroenterology and Hepatology, Department of Internal Medicine, Toho University Ohashi Medical Center, Tokyo, Japan
[2] Department of Radiology, Toho University Ohashi Medical Center, Tokyo, Japan

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Corresponding author:
Iruru Maetani, MD,
Division of Gastroenterology and Hepatology, Department of Internal Medicine,Toho University Ohashi Medical Center,
2-17-6 Ohashi, Meguro-ku,
Tokyo 153-8515,
Japan
mtnir50637@med.toho-u.ac.jp

Background and study aims: Delayed gastric emptying (DGE) is an important factor in determining the clinical outcome in patients with stent placement for malignant gastric outlet obstruction but the factors associated with DGE remain unclear. The aim of this study was to investigate whether clinicopathologic data could be used to identify the factors for DGE in such patients.

Patients and methods: A prospective, single-arm, observational clinical study was performed in a referral hospital in Japan. A total of 54 patients with stent placement for malignant gastric outlet obstruction were enrolled. A gastric emptying scintigraphy test was performed 1 week after stent placement. The relationship between DGE and clinicopathologic factors was investigated, and also the relationship between DGE and stent patency time, eating period (when the patient was able to maintain oral intake), and survival time.

Results: A total of 38.9% (21/54) of patients had DGE. The following were identified as independent predictive factors of DGE: opioid use (odds ratio, 5.32; 95% confidence interval [95%CI], 1.07–26.41; $p=0.04$), chemotherapy before stent placement (odds ratio, 8.03; 95%CI, 1.85–34.95; $p=0.006$), and smaller stent diameter (odds ratio, 13.59; 95%CI, 1.72–107.41; $p=0.01$). No relationship was found between DGE and the level of oral intake, stent patency time, eating period, and survival time.

Conclusions: The factors associated with DGE after stent placement include those associated with the patient's tumor as well as factors relating to their treatment, including stenting. The clinical and functional results after stent placement appear to be unrelated to the gastric emptying findings.

Introduction

Self-expandable metallic stent (SEMS) placement has been recommended for the treatment of malignant gastric outlet obstruction in those patients with poor performance status and/or short life expectancy [1–3]. The technical success rate of endoscopic placement of stents, defined as the successful deployment of the stent at the desired anatomic location, has ranged from 91% to 100%, [3]. The clinical success rate, defined as the relief of obstructive symptoms and/or improvement of oral intake, has ranged from 63% to 95%, [2–10]. Such discrepancies between technical success and clinical success are seen uniformly across prospective studies [3–10]. The main effect of stent placement in malignant gastric outlet obstruction is the re-establishment of the passage of food from the stomach to the jejunum. In view of the observed technical and clinical discrepancies, it is not likely that the re-establishment of passage is followed by a more rapid rate of gastric emptying in all patients treated [11].

The improvement of oral intake is a major parameter in palliative treatment following stent placement for malignant gastric outlet obstruction. Oral intake provides a means of evaluating the clinical effect of treatment regardless of disturbances in underlying gastric motility. Further knowledge of the factors that relate to delayed gastric emptying (DGE) in these patients could help with their clinical management.

Evaluation of the stent effect can be provided by measuring the rate of gastric emptying before and after stent placement [11,12]. Larssen et al. reported that treatment with stents resulted in improved gastric emptying in 76% (13/17) of patients with malignant gastric outlet obstruction, whereas gastric emptying was unchanged or worse in four patients (24%). The cause of the unimproved gastric emptying was not determined in that study, which used the 13C-octanoic acid

breath test (OBT) to measure the rate of gastric emptying [12]. The OBT is a simple, safe, radiation-free, and validated test for assessing gastric emptying if there is normal small-bowel absorption and pulmonary function [13].

Gastric emptying scintigraphy (GES) is commonly performed to evaluate patients with symptoms that suggest they have an alteration of gastric emptying and/or motility. GES has become the standard for the measurement of gastric motility in clinical practice, because it provides a physiologic, noninvasive, and quantitative measurement of gastric emptying [14]. DGE in patients with stent placement for malignant gastric outlet obstruction has been observed despite improvement of oral intake, when GES was performed with a liquid meal 1 week after stent placement [15]. The cause of the DGE could not be determined [15].

The aim of the present study was to investigate whether clinicopathologic data could identify the factors responsible for DGE in patients with stent placement for malignant gastric outlet obstruction.

Patients and methods

Patients

This study was designed as a prospective, single-arm, observational clinical study to evaluate the rate of gastric emptying in patients with stent placement for malignant gastric outlet obstruction. The patients were enrolled at Toho University Ohashi Medical Center, Tokyo, Japan between March 2004 and June 2007. Consecutive patients with malignant gastric outlet obstruction whose clinical conditions were deemed inoperable were considered for inclusion and underwent stent placement for palliative treatment. Malignant gastric outlet obstruction was confirmed by radiography, endoscopy, and by pathologic diagnosis. All patients underwent successful stent placement at the optimal position under endoscopic and fluoroscopic control. The exclusion criteria included any contraindication for esophagogastroduodenoscopy, suspected or impending perforation, and previous gastric, periampullary, or duodenal surgery. Patients with any of these contraindications were excluded from the study.

The clinical characteristics of the patients before stent placement and their outcomes after placement were evaluated. The following data were collected on patient background: age, sex, source of malignancy, disease stage [16], length of time from initial disease diagnosis to stent placement, site of stent placement (bridging the pylorus or duodenum only), Karnofsky Performance Status Scale (KPSS) score, absence or presence of ascites, absence or presence of peritoneal carcinomatosis, absence or presence of distant metastasis, previous or concurrent biliary stent placement, any kind of opioid use, chemotherapy before and after stent placement, radiotherapy before and after stent placement, stent type (covered or uncovered), stent diameter, stent length, and level of oral intake before stent placement [17].

The following outcome variables were recorded: highest KPSS score during the remaining lifespan after stent placement, level of oral intake 1 week after stent placement and highest level during the remaining lifespan after stent placement, adverse events [18], stent patency time, eating period when the patient was able to maintain an oral intake, and survival time.

Disease stage was classified according to the Union Intérnationale Contre le Cancer (UICC) TNM classification [16]. The presence of ascites and distant metastasis were diagnosed with ultrasonography and computed tomography scans prior to stent placement. Peritoneal dissemination was evaluated with ultrasonography and computed tomography scans and patients with a histologically proven malignancy were diagnosed with peritoneal carcinomatosis. The level of oral intake was measured using the Gastric Outlet Obstruction Scoring System (GOOSS) score: 0 = no oral intake; 1 = liquids only; 2 = soft solids; 3 = low-residue or full diet [17].

Adverse events were defined as events that prevented completion of the planned procedure and/or resulted in admission to hospital, prolongation of existing hospital stay, requirement for another procedure (needing sedation/anesthesia), or subsequent medical consultation [18].

Stent patency time was defined as the time from stent placement to an adverse event. Eating period was defined as the time from initiation of oral intake after stent placement until the time when the patient was unable to take oral solid or liquid meals finally before death or the patient's death. Survival time was defined as the time from stent placement to death.

This study was performed in accordance with the Helsinki Declaration and was approved by the ethics board of our hospital; written informed consent was obtained from all participating patients.

SEMSs characteristics

All stent placement procedures were performed by one investigator (I.M.) with several assistant endoscopists. The selection of stent type was at the discretion of the operator.

The following SEMSs were used: uncovered esophageal Ultraflex stents (Boston Scientific Corporation, Natick, Massachusetts, USA) [19], covered esophageal Ultraflex stents (Boston Scientific Corporation) [19], Niti-S D-type stents (uncovered) (Taewoong Medical Co., Ltd., Gimpo-si, Gyeonggi-do, Korea) [5], ComVi stents (covered) (Taewoong Medical Co., Ltd.), or SX-Ella stents (uncovered) (Ella-CS, Hradec Králové, Czech Republic). Two patients received two Niti-S D-type stents and one patient received two ComVi stents.

GES with a liquid meal

GES was performed 1 week after stent placement. After an overnight fast of at least 12 hours, the patient ingested a 200 mL liquid meal (Racol; EN Otsuka Pharmaceutical Co., Ltd., Iwate, Japan) that was radiolabeled with 37 MBq of 99mTc-diethylenetriaminepentaacetate (DTPA), as previously reported [15]. The 200 mL liquid meal consisted of 31.2 g of glucose (124.8 kcal), 4.46 g of fat (40.14 kcal), and 8.76 g of protein (35.04 kcal) with a total caloric value of 200 kcal (62.4 % carbohydrate, 20.1 % fat, 17.5 % protein, and 0 % fiber). Any prokinetic agents, anticholinergic medications, sedatives, or tranquilizers were discontinued from the time of stent placement until the GES was performed. Opioids were continued even after stent placement. Fasting plasma glucose was measured and recorded prior to GES. The optimal positioning and the full expansion of the stents had been confirmed by plain radiographs before the GES test.

All studies were performed using an SNC-510 R (Shimadzu Co., Ltd., Kyoto, Japan) or E.CAM (Toshiba Medical Systems Co., Ohtawara, Tochigi, Japan) gamma camera immediately after ingestion of the liquid meal at a rate of 30 second per frame for 120 minutes. Each patient was scanned in a supine position during the GES. Regions of interest were drawn manually for each image on the anterior image acquisitions, delineating the stomach boundary. Total stomach counts were measured from regions of interest [15].

The main parameter was gastric retention, which was defined as the percentage of the isotope remaining in the stomach at 2 hours. The normal range of values (mean ± 2 standard deviations [SDs]) of gastric retention at 2 hours for gastric emptying with the liquid meal were obtained from a prior study in 10 asymptomatic healthy volunteers (median age, 30 years; interquartile range [IQR] 25 – 36.5 years; eight men, two women) and was defined as 25.9 %±(2 × 12.5 %) [15, 20]. Thus values of gastric retention at 2 hours that exceeded 50.9 % were defined as DGE.

Evaluation

The relationship between delayed gastric emptying and the previously listed clinicopathologic factors was investigated. The relationship between GOOSS scores before stent placement, 1 week after placement, and the highest level during the remaining lifespan after placement was investigated. The relationship between DGE and stent patency time, eating period, and survival time was also investigated.

All follow-up procedures were performed according to usual medical practices and were continued until the patient's death at our hospital. Follow-up data were obtained by monthly interviews with the patient's general practitioner and relatives for patients who were followed-up at sites other than our hospital. Information about the situation at the time of death was also obtained from interviews.

Statistical analysis

KPSS scores before stent placement and the highest during the remaining lifespan after stent placement were analyzed using the Wilcoxon signed-rank test. GOOSS scores before stent placement, 1 week after placement, and the highest during the remaining lifespan after placement were analyzed using the Friedman test.

Clinicopathologic factors were analyzed using multiple logistic regression analysis. Comparison between groups was performed using the t test, the chi-squared test or the Fisher exact test. Factors with a p value < 0.1 in the univariate analysis were subsequently evaluated with multivariate analysis. The following variables were examined: age; sex; source of malignancy (gastric cancer or pancreatic/biliary tract/other cancers); site of stent placement (pylorus or duodenum only); KPSS score before stent placement (≤ 50 or ≥ 60); presence of ascites, peritoneal dissemination, or distant metastasis; previous or concurrent biliary stent placement; any kind of opioid use; chemotherapy beforestent placement and after; radiotherapy before stent placement and after; stent type (covered or uncovered); stent diameter (≥ 20 mm or 18 mm); stent length (≤ 100 mm or ≥ 120 mm) (including three patients who received two stents); and the level of oral intake before stent placement and 1 week after placement.

The relationship between DGE and stent patency time, eating period and survival time was analyzed using the Kaplan – Meier method. The significance of differences in rates between groups was compared using the log-rank test. Two-sided p values of < 0.05 were considered to be statistically significant. All statistical analyses were performed using the SPSS software (Version 19; SPSS, IBM SPSS Statistics).

Table 1 Patient demographics and clinical characteristics.

Patients, n	54
Age, mean ± SD, years	68.4 ± 12.7
Male; female, n	32; 22
Source of malignancy, n (%)	
Gastric cancer	30 (55.6)
Pancreatic cancer	16 (29.6)
Gallbladder cancer	3 (5.6)
Bile duct cancer	1 (1.9)
Duodenal cancer	1 (1.9)
Metastatic cancer	3 (5.6)
Disease stage,* n (%)	
Stage III	5 (9.3)
Stage IV	49 (90.7)
Time from initial disease diagnosis to stent placement, median (IQR), days	86 (25 – 227)
Site of stent placement, n (%)	
Bridging the pylorus	38 (70.4)
Duodenum only	16 (29.6)
Ascites, n (%)	28 (51.9)
Peritoneal carcinomatosis, n (%)	8 (14.8)
Distant metastasis, n (%)	39 (72.2)
Previous or concurrent biliary stent placement, n (%)	17 (31.5)
Opioid use, n (%)	13 (24.1)
Chemotherapy before stent placement, n (%)	24 (44.4)
Chemotherapy after stent placement, n (%)	23 (42.6)
Radiotherapy before stent placement, n (%)	2 (3.7)
Radiotherapy after stent placement, n (%)	4 (7.4)
Stent patency time, mean (95 %CI), days	247 (201 – 284)
Eating period after stent placement, median (IQR), days	101 (51 – 203)
Survival time after stent placement, median (IQR), days	107 (58 – 212)
Gastric retention at 2 hours, median (IQR), %	42 % (28 % – 70 %)
Delayed gastric emptying, n (%)	21 (38.9 %)

SD standard deviation, IQR interquartile range; 95 %CI, 95 % confidence interval
* Disease stage classified according to Union Intérnationale contre le Cancer (UICC) TNM classification (6th edition) [16].

Results

Patient demographics and clinical and SEMS characteristics

A total of 57 patients were initially enrolled in the study. Three of these patients were excluded from the study including two patients who vomited the liquid meal soon after intake, and one patient who required an excessively long time to drink the liquid meal. The remaining 54 patients were analyzed (mean age ± SD, 68.4 ± 12.7 years; 32 men and 22 women).

Two patients had a past history of cerebrovascular disease and 14 patients had diabetes mellitus. None of the patients were tobacco smokers. Patient demographics and clinical and SEMSs characteristics are summarized in **Table 1** and **Table 2**. The sources of malignant gastric outlet obstruction were gastric cancer in 30 patients (55.6 %), pancreatic cancer in 16 patients (29.6 %), gallbladder cancer in three patients (5.6 %), bile duct cancer in one patient (1.9 %), duodenal cancer in one patient (1.9 %), and metastatic cancer in three patients (5.6 %). Disease stages were stage III for five patients (9.3 %) and stage IV for 49 patients (90.7 %). Median duration from initial disease diagnosis to stent placement was 86 days (IQR, 25 – 227 days).

Table 2 Characteristics of self-expandable metallic stents.

Self-expandable metallic stent,* n	
Esophageal Ultraflex (uncovered)	3
Esophageal Ultraflex (covered)	5
Niti-S D-type (uncovered)	39
ComVi (covered)	8
SX-Ella (uncovered)	2
Stent diameter, 18/20/22 mm, n	8/47/2
Stent length, 70/80/100/120/135/140 mm, n	1/3/26/22/2/3

* Three patients received two stents each before gastric emptying scintigraphy.

The sites of stent placement were bridging the pylorus in 38 patients (70.4%) and the duodenum alone in 16 patients (29.6%). The median KPSS before stent placement was 60 (IQR, 60–70). The median highest KPSS after stent placement during the remaining lifespan of the patients was 70 (IQR, 70–80). Thus the KPSS improved after stent placement ($p<0.01$).

Ascites was found in 28 patients (51.9%), peritoneal carcinomatosis in eight patients (14.8%), and distant metastasis in 39 patients (72.2%). Regarding other treatments, 17 patients (31.5%) with obstructive jaundice underwent previous or concurrent biliary stent placement along with stent placement for malignant gastric outlet obstruction; 13 patients (24.1%) had used opioids for pain medication. Respectively, 24 (44.4%) and 23 (42.6%) patients had received chemotherapy before and after stent placement, and respectively 2 (3.7%) and 4 (7.4%) patients had received radiotherapy before and after stent placement.

Stent types and usage were as follows: uncovered esophageal Ultraflex stents, 3 in 3 patients; covered esophageal Ultraflex stents, 5 in 5 patients; Niti-S D-type stents (uncovered), 39 in 37 patients; ComVi stents (covered), 8 in 7 patients; and SX-Ella stents (uncovered), 2 in 2 patients (**Table 2**). Stent diameters were: esophageal Ultraflex, 18 mm; Niti-S D-type and ComVi stents, 20 mm; and SX-Ella, 22 mm. Stent lengths were: esophageal Ultraflex, 70 or 100 mm; Niti-S D-type and ComVi, 80, 100, 120, or 140 mm; and SX-Ella 135 mm.

Table GOOSS scores before stent placement were 0 for 40 patients (74.1%), 1 for 13 patients (24.1%), 2 for one patient (1.9%) and 3 for zero patients (0.0%). At 1 week after stent placement, the GOOSS scores had changed to 0 for one patient (1.9%), 1 for nine patients (16.7%), 2 for 30 patients (55.6%) and 3 for 14 patients (25.9%). The highest GOOSS scores during the remaining lifespan after stent placement were 0 for one patient (1.9%), 1 for one patient (1.9%), 2 for 14 patients (25.9%), and 3 for 38 patients (70.4%). This result indicated that impaired oral intake recovered with time after stent placement ($p<0.01$).

Table The following events were recorded. Adverse events occurred in 15 patients (27.8%): perforation, 1 (1.9%); stent fracture, 1 (1.9%); stent occlusion by tumor ingrowth, 5 (9.3%); stent occlusion by tumor overgrowth, 2 (3.7%); stent occlusion by hyperplasia, 2 (3.7%); stent occlusion by food impaction, 1 (1.9%); stent migration, 2 (3.7%); and bleeding occurred in 1 patient (1.9%). Placement of an additional stent was done in the 1 patient with stent fracture, in 4 of the patients with tumor ingrowth, in 2 patients with tumor overgrowth, in 2 patients with hyperplasia, and in 2 patients with migration. However 1 patient with perforation, 1 patient with tumor ingrowth, and 1 patient with bleeding did not undergo additional intervention because they had terminal disease and refused further intervention. The patient with food impaction was treated by endoscopic balloon clearance. All of the patients enrolled in this study died, whereupon the data were assessed.

GES with a liquid meal

Fasting plasma glucose was less than 200 mg/dL in all patients before performance of GES. Median gastric retention at 2 hours was 42% (IQR, 28–70%), and 21 patients (38.9%) had DGE.

Relationship between DGE and clinicopathologic factors

Variables that were significantly associated with DGE in the univariate analysis included ascites, opioid use, chemotherapy before stent placement, stent type, and stent diameter (**Table 3**). In the multivariate analysis, opioid use (odds ratio, 5.32; 95% confidence interval [95%CI], 1.07–26.41; $p=0.04$), chemotherapy before stent placement (odds ratio, 8.03; 95%CI, 1.85–34.95; $p=0.006$) and smaller stent diameter (odds ratio, 13.59; 95%CI, 1.72–107.41; $p=0.01$) were identified as statistically significant independent predictive factors of DGE (**Table 3**).

No relationship was found between DGE and the site of stent placement, the level of oral intake, or adverse effects.

Relationship between DGE and stent patency time, eating period, and survival time

The mean stent patency time was 247 days (95%CI, 201–284 days). The median eating period after stent placement was 101 days (IQR, 51–203 days). The median survival time after stent placement was 107 days (IQR, 58–212 days). No relationship was found between DGE and stent patency time ($p=0.33$), eating period ($p=0.73$), and survival time ($p=0.75$).

Discussion

Poor oral intake in patients with malignant gastric outlet obstruction may be attributed to underlying gastrointestinal motility disturbances caused by the following factors: a malignant tumor with or without neural involvement, anorexia caused by advanced malignancy, a poor performance status, ascites, distal obstruction secondary to peritoneal carcinomatosis, and side effects of opioids [15,21]. Some of these factors can cause delayed gastric emptying (DGE). Relatively high rates (55.6%) of gastric cancer patients with strictures of the gastric body and/or antrum were included in this study. Peristalsis was impaired in these patients from neoplastic neural involvement and from neoplastic invasion of the gastric body and/or antrum. No relationship was found between DGE and the source of malignancy.

Although DGE was not associated with the level of oral intake or with eating period, we have shown that 38.9% (21/54) of patients had delayed DGE at 1 week after stent placement for malignant gastric outlet obstruction. The factors associated with DGE were opioid use, chemotherapy before stent placement, and smaller stent diameter.

The present study has several limitations including the evaluation method for gastric emptying and it should be noted that this was not a comparative and multicenter study.

A standardized method for measuring gastric emptying by scintigraphy is recommended that uses imaging at 0, 1, 2 and 4 hours after a low fat, egg-white meal with a total ingested caloric value of 255 kcal [14,22]. In the present study, DGE was only documented at 1 week after stent placement, using modified gastric emptying scintigraphy (GES), with a liquid meal, imaging up to 2 hours, the patient maintaining a supine position, and comparing

Table 3 The relationship between gastric retention at 2 hours and clinicopathologic factors in patients with malignant gastric outlet obstruction after stent placement (n = 54).

	Gastric retention at 2 hours		Univariate analysis	Multivariate analysis		
Clinicopathologic factor	**Up to 50.9 % 33 patients**	**More than 50.9 % 21 patients**	***p* value***	**Odds ratio**	**95 %CI**	***p* value**
Age, mean ± SD, years	70.7 ± 14.4	64.9 ± 8.5	0.37	Not selected		
Male; female	19; 14	13; 8	0.75	Not selected		
Source of malignancy			0.45	Not selected		
Gastric cancer	17	13				
Pancreatic/biliarytract/other cancers	16	8				
Site of stent placement			0.60	Not selected		
Bridging the pylorus	23	16				
Duodenum alone	10	5				
Karnofsky performance status score before stent placement			0.40	Not selected		
0 – 50	26	18				
60 – 100	7	3				
Ascites			0.08	0.16		
No	19	7				
Yes	14	14				
Peritoneal dissemination			0.14	Not selected		
No	30	16				
Yes	3	5				
Distant metastasis			0.47	Not selected		
No	8	7				
Yes	25	14				
Previous or concurrent biliary stent placement			0.82	Not selected		
No	23	14				
Yes	10	7				
Opioid use			0.06	5.32	1.07 – 26.41	0.04
No	28	13				
Yes	5	8				
Chemotherapy before stent placement			0.01	8.03	1.85 – 34.95	0.006
No	23	7				
Yes	10	14				
Radiotherapy before stent placement			0.37	Not selected		
No	31	21				
Yes	2	0				
Stent type			0.03	0.24		
Covered	4	8				
Uncovered	29	13				
Stent diameter			0.03	13.59	1.72 – 107.41	0.01
≥ 20 mm	31	15				
18 mm	2	6				
Stent length			0.69	Not selected		
≤ 100 mm	16	9				
≥ 120 mm	17	12				
GOOSS scores before stent placement			0.39	Not selected		
0 – 1	33	20				
2 – 3	0	1				
GOOSS scores 1 week after stent placement			0.12	Not selected		
0 – 1	4	6				
2 – 3	29	15				

95 %CI, 95 % confidence interval; GOOSS, Gastric Outlet Obstruction Scoring System; SD, standard deviation.
* *P* values obtained using *t* test for age and from the chi-squared test or the Fisher exact test for other variables.

with a normal value of gastric retention at 2 hours that had been obtained from a prior study [15].

The effect of stent placement on the gastric emptying test could not be evaluated because the test was not also performed before stent placement [11,12]. Using analysis of 13C-octanoic acid breath test (OBT) results at 4 hours after a solid meal, Larssen et al. reported that 82.4% (14/17) of patients had DGE before stent placement whereas 52.9% (9/17) had DGE after stent placement [12]. The observation that the gastric emptying function was impaired even after stent placement suggests that patients with malignant gastric outlet obstruction may have dysmotility of the stomach. The approach of Larssen et al. elucidated the effect of the stent placement itself but did not identify the factors responsible for the DGE [12]. Our results further elucidate the factors responsible for DGE in patients with malignant gastric outlet obstruction after stent placement.

The results of the gastric emptying test maybe influenced by how soon the test is done after stent placement, because it is possible that the impaired gastric emptying still observed after placement in fact recovers with time. In a systematic review, the mean time to resumption of oral intake after stent placement was 4 days, and 48% of patients were able to resume a full diet, 39% tolerated soft solids, and 13% were on liquids only [2,3]. In the studies of both Piesman et al. and Costamagna et al., by day 5 after stent placement about 50% of patients had achieved an increase in GOOSS score of at least 1 point [7,10]. By day 7 after stent placement, 56% of patients reached a GOOSS score 2 or 3 in the Piesman et al. study, compared with 62% of patients in the Costamagna et al. study [7, 10]. Kim et al. reported that GOOSS scores were significantly greater 3 days after stent placement (median score 2, IQR 2–3) than before stent placement (median score 1, IQR 0–1; $p<0.001$) [23]. Canena et al. reported that resumption of solid food intake (GOOSS score 2–3) was achieved by 71.6% (53/74) patients within 5 days of stent placement [24]. In the present study, GES was performed 1 week after stent placement and 81.5% (44/54) of patients had a GOOSS score of 2–3.These results indicate an early resumption of oral food intake after stent placement. The level of oral intake was not associated with DGE in the present study, which is consistent with previous reports [12,15]. If gastric emptying is evaluated too early it may appear to be more delayed. Larssen et al. performed OBT within 1 week after stent placement [12] and therefore, the optimal timing of evaluation of gastric emptying in patients with malignant gastric outlet obstruction after stent placement remains unclear.

Liquid gastric emptying tests are generally not clinically useful, because normal gastric emptying of liquids is frequently maintained despite very severe gastroparesis for solids [25]. We used the liquid test meal in the present study, in anticipation of patients who could not ingest a solid meal at the time of GES and had DGE. In addition, a normal value obtained from a prior study in 10 asymptomatic healthy volunteers was used for reference in the present study [15]. Therefore, specific normal databases are needed for the specified meals before they are used [14].

Imaging times of 2 hours were used in the present study, but the data suggest that the 3-hour and 4-hour imaging times detect more abnormal gastric emptying in GES [14,25]. However Pathikonda et al. reported that gastric retention at 4 hours correlates well with gastric retention at 2 hours [26]. We therefore believe that the imaging times used in the present study were appropriate. In the OBT, the shorter collection period of 4 hours has been associated with longer estimates of the half emptying time (T1/2) and, therefore, the sampling period should be extended to 6 hours after dosing [27]. It is thus possible that in the OBT study by Larssen et al. the 4-hour sampling period led to relatively longer estimates of the T1/2 [12].

The use of T1 /2 of gastric emptying in GES measurements may be less accurate than measurement at fixed time points of retention percentages, particularly in individuals with very delayed gastric emptying. In those cases, extrapolation is needed to calculate the T1/2 if it is not actually reached during the test [14]. Therefore, we used gastric retention at 2 hours as the variable for evaluating gastric emptying.

The positioning of the patient during imaging can influence the result obtained for GES. Patients can move freely during the GES test and gamma camera images are usually obtained with the patient standing upright in front of the camera [14]. To ensure that all patients were evaluated under the same conditions, all of our patients were maintained in a supine position over a 2-hour period during the GES measurement. This was necessary because some patients were expected to become debilitated if they were required to stand upright in front of the camera. Patients who stayed in a supine position during GES imaging might show more delay in gastric emptying than if they were upright.

We used esophageal Ultraflex stents with some technical modifications because of a lack of enteral stents in Japan at that time. The clinical outcomes and adverse effects associated with Ultraflex stents were comparable with the stents designed for use in malignant gastric outlet obstruction [19]. The only differential effect of Ultraflex stents on gastric emptying was associated with stent diameter.

Larssen et al. reported that smaller stent diameter can contribute to DGE [12]. Our results support this finding, and therefore use of stents with a larger diameter may be preferable for better gastric emptying in patients with malignant gastric outlet obstruction, but the effects should be investigated in further studies.

Opioids were one of the factors associated with DGE in the present study; they might inhibit gastric emptying. This effect is presumed to occur as a result of enhanced gastric relaxation and increased pyloric tone [28]. It remains unclear how these pharmacological effects of opioids affect patients with malignant gastric outlet obstruction.

Chemotherapy is one of the causes of gastric dysmotility in patients with malignancy [29]. The present study showed that chemotherapy before stent placement is one of the factors associated with DGE. Recent studies have shown that chemotherapy is associated with prolonged stent patency in patients with malignant gastric outlet obstruction [4,23]. Chemotherapy both before and after stent placement is not associated with stent patency time (data not shown).

In addition, no relationship was found between chemotherapy before stent placement and the time from initial disease diagnosis to stent placement in the present study (data not shown). It is important to note that many studies consist of heterogeneous patient populations with various malignancies that are treated with an assortment of stents and chemotherapy agents. This heterogeneity makes it difficult to draw uniform conclusions with regard to efficacy [2]. Factors such as this will require further investigation regarding clinical outcomes.

Peritoneal disease is considered a relative contraindication to stent placement given the theoretical risk of multifocal obstruction. Mendelsohn et al. reported that peritoneal carcinomatosis should not be considered a contraindication for stent placement in selected patients with malignant gastric outlet obstruction [30]. Precise radiological diagnosis of peritoneal carcinomatosis

remains a challenge despite recent advances in imaging technology. In the present study, both ascites and peritoneal carcinomatosis were not associated with DGE after stent placement. The relative contribution of these factors might have been underestimated because of the broad diagnostic criteria of ascites and the strict diagnosis of peritoneal carcinomatosis in the present study. We have previously reported that patients with severe DGE have a shorter survival time but we did not observe shorter survival in patients with DGE in the present study [15]. In addition, there was no relationship between DGE and the level of oral intake and the eating period, that is the time for which patients could have oral intake of liquid or solid meals. Larssen et al. reported that there was no correlation between survival and the rate of gastric emptying before or after stent placement, nor was there a change in the rate of gastric emptying. Our results were consistent with those of Larssen et al. [12].

Prokinetic agents such as metoclopramide and domperidone are used in patients with malignant gastric outlet obstruction after stent placement, to reduce symptoms overall. However, there was no evidence that prokinetic agents improved DGE in patients with malignant gastric outlet obstruction after stent placement.

We propose that the use of larger-diameter stents for patients with malignant gastric outlet obstruction will prevent more DGE. A reduction in opioid treatment in malignant gastric outlet obstruction is not desirable because control of the patient's pain is just as important as an improvement in DGE.

In conclusion, we have shown that at 1 week after stent placement for malignant gastric outlet obstruction, 38.9% of patients (21/54) had DGE, and the factors associated with DGE were opioid use, chemotherapy before stent placement, and smaller stent diameter. These results indicate that the factors associated with DGE are not only those related to the patient's tumor but also factors relating to their treatment including stents. The clinical and functional results after stent placement appear to be unrelated to the gastric emptying findings.

Competing interests: None.

References

1 *Jeurnink SM*, *Steyerberg EW*, *van Hooft JE* et al. Surgical gastrojejunostomy or endoscopic stent placement for the palliation of malignant gastric outlet obstruction (SUSTENT study): a multicenter randomized trial. Gastrointest Endosc 2010; 71: 490 – 499 PubMed
2 *Fukami N*, *Anderson MA*, *Khan K* et al. The role of endoscopy in gastroduodenal obstruction and gastroparesis. Gastrointest Endosc 2011; 74: 13 – 21 PubMed
3 *Dormann A*, *Meisner S*, *Verin N* et al. Self-expanding metal stents for gastroduodenal malignancies: systematic review of their clinical effectiveness. Endoscopy 2004; 36: 543 – 550
4 *Kim JH*, *Song HY*, *Shin JH* et al. Metallic stent placement in the palliative treatment of malignant gastroduodenal obstructions: prospective evaluation of results and factors influencing outcome in 213 patients. Gastrointest Endosc 2007; 66: 256 – 264 PubMed
5 *Maetani I*, *Isayama H*, *Mizumoto Y*. Palliation in patients with malignant gastric outlet obstruction with a newly designed enteral stent: a multicenter study. Gastrointest Endosc 2007; 66: 355 – 360 PubMed
6 *van Hooft JE*, *Uitdehaag MJ*, *Bruno MJ* et al. Efficacy and safety of the new WallFlex enteral stent in palliative treatment of malignant gastric outlet obstruction (DUOFLEX study): a prospective multicenter study. Gastrointest Endosc 2009; 69: 1059 – 1066 PubMed
7 *Piesman M*, *Kozarek RA*, *Brandabur JJ* et al. Improved oral intake after palliative duodenal stenting for malignant obstruction: a prospective multicenter clinical trial. Am J Gastroenterol 2009; 104: 2404 – 2411 PubMed
8 *Kim CG*, *Choi IJ*, *Lee JY* et al. Covered versus uncovered self-expandable metallic stents for palliation of malignant pyloric obstruction in gastric cancer patients: a randomized, prospective study. Gastrointest Endosc 2010; 72: 25 – 32 PubMed
9 *van Hooft JE*, *van Montfoort ML*, *Jeurnink SM* et al. Safety and efficacy of a new non-foreshortening nitinol stent in malignant gastric outlet obstruction (DUONITI study): a prospective, multicenter study. Endoscopy 2011; 43: 671 – 675 PubMed
10 *Costamagna G*, *Tringali A*, *Spicak J* et al. Treatment of malignant gastroduodenal obstruction with a nitinol self-expanding metal stent: an international prospective multicentre registry. Dig Liver Dis 2012; 44: 37 – 43 PubMed
11 *Larssen L*, *Medhus AW*, *Hauge T*. Treatment of malignant gastric outlet obstruction with stents: an evaluation of the reported variables for clinical outcome. BMC Gastroenterol 2009; 9: 45 PubMed
12 *Larssen L*, *Hauge T*, *Medhus AW*. Stent treatment of malignant gastric outlet obstruction: the effect on rate of gastric emptying, symptoms, and survival. Surg Endosc 2012; 26: 2955 – 2960 PubMed
13 *Parkman HP*. Scintigraphy for evaluation of patients for GI motility disorders—the referring physician's perspective. Semin Nucl Med 2012; 42: 76 – 78 PubMed
14 *Abell TL*, *Camilleri M*, *Donohoe K* et al. Consensus recommendations for gastric emptying scintigraphy: a joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine. Am J Gastroenterol 2008; 103: 753 – 763 PubMed
15 *Maetani I*, *Ukita T*, *Tada T* et al. Gastric emptying in patients with palliative stenting for malignant gastric outlet obstruction. Hepatogastroenterology 2008; 55: 298 – 302 PubMed
16 *Sobin LH*, *Wittekind C* editors. International Union Against Cancer (UICC), TNM classification of malignant tumours. 6th edn New York: Wiley-Liss; 2002
17 *Adler DG*, *Baron TH*. Endoscopic palliation of malignant gastric outlet obstruction using self-expanding metal stents: experience in 36 patients. Am J Gastroenterol 2002; 97: 72 – 78 PubMed
18 *Cotton PB*, *Eisen GM*, *Aabakken L* et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc 2010; 71: 446 – 454 PubMed
19 *Maetani I*, *Tada T*, *Shimura J* et al. Technical modifications and strategies for stenting gastric outlet strictures using esophageal endoprostheses. Endoscopy 2002; 34: 402 – 406 PubMed
20 *House A*, *Champion MC*, *Chamberlain M*. National survey of radionuclide gastric emptying studies. Can J Gastroenterol 1997; 11: 317 – 321 PubMed
21 *Adler DG*. Enteral stents for malignant gastric outlet obstruction: testing our mettle. Gastrointest Endosc 2007; 66: 361 – 363 PubMed
22 *Tougas G*, *Eaker EY*, *Abell TL* et al. Assessment of gastric emptying using a low fat meal: establishment of international control values. Am J Gastroenterol 2000; 95: 1456 – 1462 PubMed
23 *Kim CG*, *Park SR*, *Choi IJ* et al. Effect of chemotherapy on the outcome of self-expandable metallic stents in gastric cancer patients with malignant outlet obstruction. Endoscopy 2012; 44: 807 – 812 PubMed
24 *Canena JM*, *Lagos AC*, *Marques IN* et al. Oral intake throughout the patients' lives after palliative metallic stent placement for malignant gastroduodenal obstruction: a retrospective multicentre study. Eur J Gastroenterol Hepatol 2012; 24: 747 – 755 PubMed
25 *Guo JP*, *Maurer AH*, *Fisher RS* et al. Extending gastric emptying scintigraphy from two to four hours detects more patients with gastroparesis. Dig Dis Sci 2001; 46: 24 – 29 PubMed
26 *Pathikonda M*, *Sachdeva P*, *Malhotra N* et al. Gastric emptying scintigraphy: is four hours necessary? J Clin Gastroenterol 2012; 46: 209 – 215 PubMed
27 *Choi MG*, *Camilleri M*, *Burton DD* et al. Reproducibility and simplification of 13C-octanoic acid breath test for gastric emptying of solids. Am J Gastroenterol 1998; 93: 92 – 98 PubMed
28 *De Schepper HU*, *Cremonini F*, *Park MI* et al. Opioids and the gut: pharmacology and current clinical experience. Neurogastroenterol Motil 2004; 16: 383 – 394 PubMed
29 *Donthireddy KR*, *Ailawadhi S*, *Nasser E* et al. Malignant gastroparesis: pathogenesis and management of an underrecognized disorder. J Support Oncol 2007; 5: 355 – 363 PubMed
30 *Mendelsohn RB*, *Gerdes H*, *Markowitz AJ* et al. Carcinomatosis is not a contraindication to enteral stenting in selected patients with malignant gastric outlet obstruction. Gastrointest Endosc 2011; 73: 1135 – 1140 PubMed