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Food passage following proximal gastrectomy with double-tract reconstruction and its effect on nutritional status in early gastric cancer: a prospective single-center cohort study

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Purpose: Laparoscopic proximal gastrectomy with double-tract reconstruction (LPG-DTR) expectedly results in improved nutritional status and less body weight loss than conventional total gastrectomy in upper-third gastric cancer. This study aimed to investigate the food passage patterns following LPG-DTR and its effect on nutritional outcomes up to 1 year after surgery.
Methods: This prospective cohort study recruited 10 patients with early gastric cancer scheduled for LPG-DTR. Nutritional indices and body composition were assessed every 3 months up to 12 months. Liquid and solid food transits were evaluated with fluoroscopic upper gastrointestinal study and radionuclide scintigraphy, respectively.
Results: At 12 months, patients exhibited a body weight loss of 14.5% ± 3.6%. The main passage routes for liquid and solid foods differed, primarily via the interposed jejunum for liquids, whereas via both tracts for solids. The median half-life of solid food emptying from the remnant distal stomach was 105.1 minutes (range, 50.8–2,194.2 minutes), and duodenal passage of solid food was noted in 9 of 10 patients. Those with gastric half-emptying time >3 hours demonstrated greater weight loss (19.5% ± 1.4% *vs*. 12.5% ± 1.1%, P = 0.024) and more pronounced reduction in serum albumin levels (–0.5 ± 0.3 g/dL *vs*. 0.0 ± 0.2 g/dL, P = 0.024) after 12 months.
Conclusion: LPG-DTR demonstrated varying food passage patterns depending on the food contents and delayed solid food emptying from the remnant stomach was associated with more substantial weight loss.
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Key Words: Gastrectomy, Gastric emptying, Nutritional status, Radionuclide imaging, Stomach neoplasms

INTRODUCTION

Along with the growing number of early gastric cancer (EGC) cases in Korea, there has been a consistent effort to improve the long-term quality of life in patients with EGC over the last decades [1]. One of the issues is performing proximal gastrectomy (PG) instead of standard total gastrectomy (TG) in patients with EGC located in the upper third of the stomach.

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The oncologic safety of PG in EGC has been guaranteed in previous studies, and PG is considered less invasive and more function-preserving than TG given the distal part of the stomach is preserved [2-6]. However, the relatively high incidence of reflux esophagitis and anastomotic stenosis following esophagogastric anastomosis has been the main obstacle to the widespread adoption of PG [7]. The modification of the reconstruction method was suggested to overcome these drawbacks, and one of these alternatives is a double-tract reconstruction (DTR) [8,9].

The presumed benefit of PG with DTR compared with TG can be summarized as follows: less body weight loss, improved nutritional status, and consequently better postoperative quality of life (QOL). Advocates of PG have argued that preserving the distal part of the stomach enables superior nutritional and weight maintenance as opposed to TG [10]. However, only a few studies have investigated the postoperative functional and nutritional outcomes following PG with DTR, and previous studies have presented conflicting results [11-15].

Thus, this study aimed to investigate food passage patterns following laparoscopic PG with DTR (LPG-DTR) and its effect on the nutritional outcomes up to 1 year after surgery.

METHODS

Patients

This prospective single-center cohort study recruited 10 patients who underwent LPG-DTR between January 2017 and March 2018 at Kyungpook National University Chilgok Hospital, Daegu, Korea. The patients were eligible for the study when they satisfied the following criteria: (1) pathologically proven gastric cancer, (2) clinical stage I (cT1N0M0) according to the American Joint Committee for Cancer 8th edition, which was assessed with endoscopy and/or endoscopic ultrasonography and abdominal CT, and (3) tumor localization in the upper third of the stomach. Patients who had a history of surgery, except for laparoscopic cholecystectomy, or previous radiotherapy in the upper abdomen, those with EGC meeting the absolute indication for endoscopic resection, and those with Eastern Cooperative Oncology Group performance status of ≥2 were excluded.

This study was approved by the Institutional Review Board of Kyungpook National University Chilgok Hospital before participant accrual (No. 2017-01-013), and written informed consent was obtained from all patients before study enrollment. All procedures were carried out in accordance with relevant guidelines and regulations.

Surgical procedures

According to the institutional practice guidelines, LPG-DTR was performed for patients where at least 50% of the gastric volume could be preserved. During LPG, the extent of lymph node dissection followed the Japanese Gastric Cancer Treatment Guidelines, and D1+ lymph node dissection was conducted. The lymph nodes along the right gastric artery and right gastroepiploic artery were preserved to secure the blood supply to the remnant stomach. The hepatic branch of the vagus nerve was saved whenever possible to preserve pyloric function; however, it was not mandatory. The gastrointestinal passage was restored in a double-tract fashion. Gastrojejunostomy and jejunojejunostomy were established extracorporeally via mini-laparotomy, and linear-stapled esophagojejunostomy was performed intracorporeally under the laparoscopic view. The distances between esophagojejunostomy and both the gastrojejunostomy and jejunojejunostomy were approximately 15 and 20 cm, respectively, and further procedures were described in detail elsewhere [12].

Follow-up

All demographic data including age, sex, body weight, height, and laboratory test results were collected prospectively. Data on surgical information such as operating time, blood loss, hospital stay, and presence of postoperative complications were also gathered.

Patients were followed up every 3 months up to 1 year after surgery. The nutritional status of the patients was evaluated with laboratory tests and body composition using bioelectrical impedance analysis (InBody770, InBody Co., Ltd.) at every visit. Liquid and solid food passages were separately measured 6 months after surgery. At 12 months, an endoscopic evaluation was conducted to assess esophageal reflux and evaluate the remnant stomach.

Evaluation of food transit

To evaluate liquid and solid food passages through the remnant stomach and duodenum, food passage studies were scheduled 6 months after surgery when patients can well tolerate normal diets. All patients were evaluated after overnight fasting. First, a fluoroscopic upper gastrointestinal study with 100 mL of gastrografin swallow was conducted to evaluate the liquid passage. Imaging began immediately following the ingestion of gastrografin, and continuous images were acquired in the upright position at 60 seconds until the whole ingested contrast was emptied into the small bowel below the jejunojejunostomy. The passage of the contrast medium was measured qualitatively to identify the main route of the liquid passage via the jejunum or remnant stomach. In addition, whether the contrast medium passed through the duodenum beyond the pyloric ring after filling the remnant distal stomach was evaluated.

To assess solid food passage and emptying, radionuclide scintigraphy imaging with radio-labeled egg albumin was

performed. The 2 liquid eggs were mixed with 3 mCi technetium-99m (99mTc)-diethylenetriamine pentaacetic acid and cooked in the microwave. The egg mixture was stirred once or twice during cooking and cooked for approximately 5 minutes until it had the texture of steamed eggs. The cooked eggs were administered orally, and the patients were asked to consume the meal within 10 minutes. Immediately upon meal ingestion, the patient was placed in front of the gamma camera in a supine position, for 0 minutes, and radioactivity was measured over the whole abdomen. Scintigraphy images were acquired over 40 minutes, and a frame image was collected approximately every minute. The regions of interest corresponding to the remnant distal stomach were outlined in the frame image, and radioactivity was counted on each image and expressed as the percentage of the ingested activity to measure the period of nuclide attenuation. Considering the half-life of 99mTc, the half-emptying curves (actual and fitting curves) of the isotopes were depicted by the computer analyzing system to estimate the gastric half-emptying time (GET) of the solid food containing the nuclide.

Statistical analysis

Statistical analyses were performed using the IBM SPSS Statistics ver. 25.0 (IBM Corp.). The differences in the laboratory results and body composition between the baseline and each postoperative follow-up time point were analyzed using paired t-tests. The association between food passage patterns and postoperative nutritional outcomes was assessed using the Pearson correlation test. Postoperative weight loss and nutritional indices were compared between the subgroups using the Mann-Whitney U-test. Two-sided P-values were calculated, and a P-value < 0.05 was considered statistically significant.

Table 1. Clinicopathologic characteristics of the patients

Characteristic	Data
No. of patients	10
Age (yr)	65.5 ± 10.3
Sex, male:female	6:4
Preoperative ESD	1 (10.0)
Body mass index (kg/m^2)	24.2 ± 3.3
Operation time (min)	266.7 ± 56.8
Length of hospital stay (day)	7.1 ± 2.8
Postoperative complications[a], within 30 days	
Grade I	1 (10.0)
Grade II	1 (10.0)
Grade IIIa	1 (10.0)
Tumor size (cm)	1.9 ± 0.6
PRM (cm)	2.2 ± 1.7
DRM (cm)	2.8 ± 2.3
No. of retrieved nodes	34.0 ± 8.2
Pathologic stage[b]	
Stage IA	10 (100)

Values are presented as number only, mean ± standard deviation, or number (%).
ESD, endoscopic submucosal dissection; PRM, proximal resection margin; DRM, distal resection margin.
[a]Postoperative complications were classified according to the Clavien-Dindo classification.
[b]Pathologic stage followed the American Joint Committee for Cancer, 8th edition.

RESULTS

Overall, 12 patients initially gave informed consent to participate in the study before surgery, and 2 of them withdrew their consent following enrollment. Ultimately, a total of 10 patients completed the scheduled examination and were included in the final analyses.

The mean age of the patients was 65.5 ± 10.3 years, and one of them was referred for curative surgery following incomplete endoscopic resection (Table 1). According to the final pathologic report, the mean number of retrieved lymph nodes was 34.0 ± 8.2, and none of the patients had metastatic lymph nodes. All patients were diagnosed with stage IA gastric cancer. An esophagojejunal anastomotic leak developed in 1 patient, which was diagnosed at the initial outpatient clinic visit 2 weeks after surgery and was managed with percutaneous abscess drainage and endoscopic stenting. Another patient was diagnosed with esophagojejunal anastomotic stenosis 4 months after surgery and required repeated endoscopic balloon dilatation.

Laboratory results

The changes in the nutritional indices were analyzed based on the serum levels at each time point in all patients, irrespective of supplementation. The nutritional indices demonstrated a statistically significant decrease in the serum vitamin B12 levels in the early postoperative period up to 6 months compared with the baseline, which recovered to the baseline level at 9 months and thereafter, and only 1 patient required supplementation for overt deficiency (Fig. 1). The total protein level was significantly decreased at 9 and 12 months compared with the baseline level. The serum albumin, ferritin, and hemoglobin levels tended to decrease; however, the difference compared with the baseline levels was not statistically significant. Two patients were administered oral iron supplementation for 3 months during the 12-month follow-up period; the first patient, diagnosed with iron deficiency anemia preoperatively, was prescribed oral iron immediately after surgery, and the second patient (case 6 in Table 2) experienced compromised oral intake secondary to anastomotic stenosis, subsequently developing iron deficiency anemia necessitating oral iron supplementation.

Body composition

Patients showed a significant reduction in body mass index

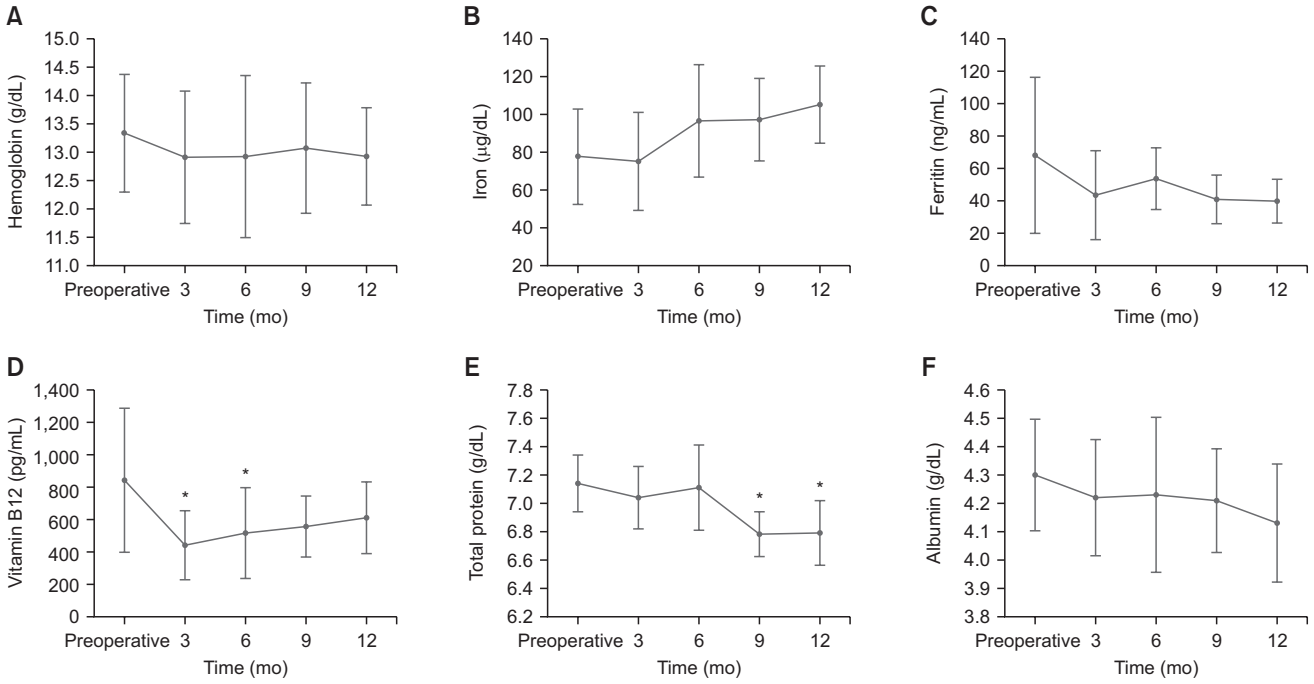

Fig. 1. Changes in the laboratory nutritional indices during the follow-up. (A) Hemoglobin, (B) iron, (C) ferritin, (D) vitamin B12, (E) total protein, and (F) albumin. Data are plotted as means with 95% confidence intervals. *P < 0.05 compared with the preoperative level.

Table 2. Liquid and solid food passage after laparoscopic proximal gastrectomy with double-tract reconstruction

Case No.	Age (yr)	Sex	Body mass index (kg/m^2)	Upper gastrointestinal contrast swallow series (liquid)			Gastric emptying scintigraphy (solid)	
				Stomach filling	Duodenal passage	Main route	Emptying half-time (min)	Duodenal passage
1	56	Male	26.2	(+), delayed	(–)	Jejunum	131.4	(+)
2	49	Male	27.3	(+)	(+)	Both	84.1	(+)
3	63	Male	25.0	(+)	(+)	Both	378.9	(+)
4	75	Male	23.9	(+)	(+), delayed	Jejunum	50.8	(+)
5	72	Female	22.5	(+)	(+)	Both	56.5	(+)
6	80	Male	25.4	(+)	(–)	Jejunum	Not estimated[a]	(+)
7	71	Male	21.9	(+), delayed	(+), delayed	Jejunum	2,194.2	(±), minimal
8	70	Female	17.9	(+)	(–)	Jejunum	105.1	(+)
9	52	Female	22.4	(+)	(+), delayed	Both	95.3	(+)
10	67	Female	29.6	(–)	(–)	Jejunum	613.7	(+)

[a]The half-time of gastric emptying could not be properly measured because of esophagojejunal stenosis.

(BMI) during the follow-up from 24.1 ± 3.1 kg/m^2 to 20.6 ± 2.6 kg/m^2 at 12 months (P < 0.001), and this corresponded to the 14.5% ± 3.6% loss of initial body weight. Body composition analysis by bioelectric impedance test showed that the decrease in BMI was mainly attributed to fat mass reduction, whereas fat-free mass was well-maintained during the follow-up (Fig. 2).

Food passage after surgery

In the upper gastrointestinal contrast study, the liquid contrast mostly passed through the interposed jejunum rather than via the remnant distal stomach (Table 1, Fig. 3A). The contrast passed into the duodenum through the pyloric ring in 6 of 10 patients, and passage was delayed in half of these patients.

In gastric emptying scintigraphy, the tracer passed evenly through both tracts, namely, the stomach and the jejunum, in all patients (Fig. 3B). However, the estimated half-time of solid food emptying through the remnant stomach was significantly prolonged, which was observed in all patients, despite a wide range of variation among them (median, 105.1 minutes;

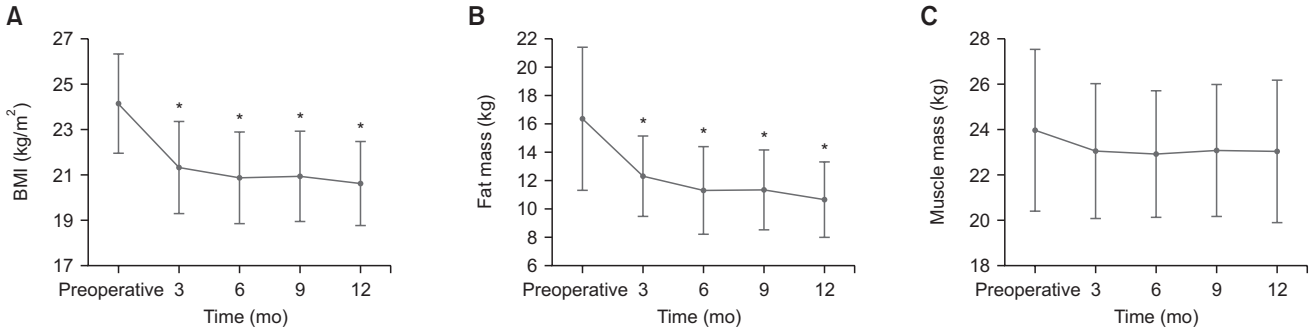

Fig. 2. Changes in body compositions assessed by bioelectric impedance test. (A) Body mass index (BMI), (B) fat mass, and (C) muscle mass. Data are plotted as means with 95% confidence intervals. *P < 0.05 compared with the preoperative level.

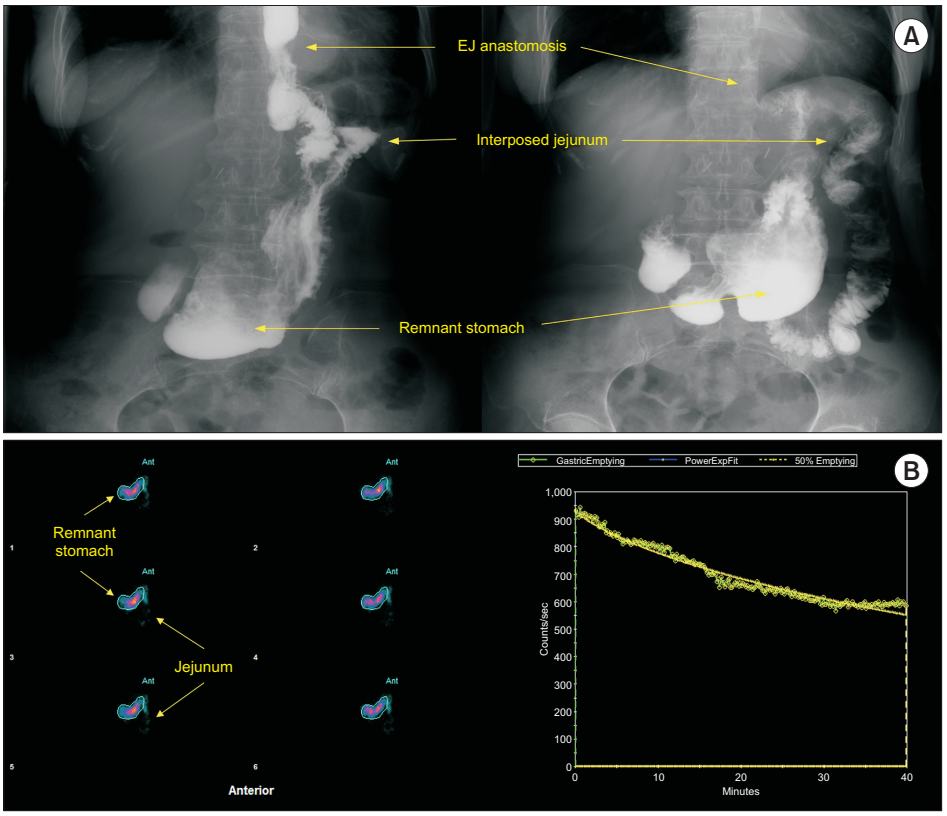

Fig. 3. Evaluation of the food passage after surgery (findings from case 5 in Table 2). (A) Liquid passage assessed by the upper gastrointestinal contrast study. (B) Solid passage assessed by gastric emptying radionuclide scintigraphy. The regions of interest corresponding to the remnant distal stomach were outlined in the frame images. EJ, esophagojejunal.

range, 50.8–2,194.2 minutes). The solid food passage into the duodenum via the remnant distal stomach was observed in all patients; however, the amount was extremely small in 1 patient, and the rest of the tracers migrated back through the interposed jejunum (case 7 in Table 2). In 1 patient (case 6 in Table 2), proper measurement of GET was impeded due to esophagogastric stenosis and, consequently, this patient was excluded from further analysis utilizing GET.

Correlation between nutritional status and food passage

No significant correlation was found between the presence of contrast passage into the duodenum in the upper gastrointestinal series and nutritional indices in the laboratory results at 6 months. Similarly, no linear correlation was noted between the GET in scintigraphy and the changes in the nutritional indices or amount of weight loss. However, when patients were divided into 2 subgroups based on their GET, those with GET exceeding 3 hours (n = 3) exhibited a notably higher percentage of weight loss at 12 months compared to those with GET ≤3 hours (n = 6; 19.5 ± 1.4 % *vs.* 12.5 ± 1.1 %, P = 0.024). Additionally, this subgroup of GET >3 hours experienced a more pronounced reduction in serum albumin levels from preoperative measures both at 6 months (–0.3 ± 0.1 g/dL *vs.* 0.2 ± 0.3 g/dL, P = 0.024) and at 12 months (–0.5 ± 0.3 g/dL *vs.* 0.0 ± 0.2 g/dL, P = 0.024) after surgery. Conversely, serum vitamin

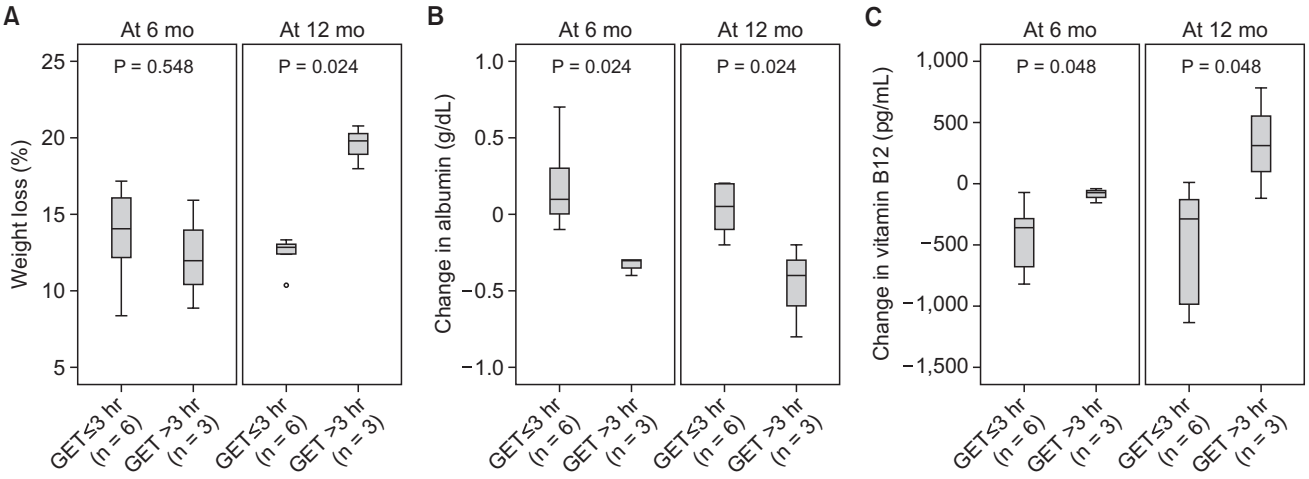

Fig. 4. Comparison of the changes in body weight and nutritional indices from baseline between patients with solid gastric emptying half-time (GET) exceeding 3 hours and those with less than 3 hours. (A) Percentage of weight loss, (B) changes in serum albumin levels, and (C) changes in serum vitamin B12 levels

B12 levels either decreased to a lesser extent or unexpectedly increased in the patients with GET >3 hours (Fig. 4).

Endoscopic surveillance of the remnant stomach

None of the patients demonstrated reflux esophagitis 12 months after surgery. Endoscopists failed to intubate into the distal remnant stomach in 2 of 10 patients (20.0%) despite knowledge of the type of reconstruction. One patient required a colonoscope to evaluate the remnant stomach.

DISCUSSION

This study demonstrated a difference in the main passage route between liquid and solid foods following LPG-DTR, which was mainly via the interposed jejunum in liquid contents whereas via both tracts after solid food intake. Solid food emptying from the residual stomach was significantly delayed. However, this delayed gastric emptying was not significantly associated with nutritional status or amount of postoperative weight loss. To the best of our knowledge, this is the first study to evaluate the passage of both liquid and solid contents following LPG-DTR.

TG has long been the standard procedure in patients with gastric cancer located in the upper third of the stomach. However, TG results in prolonged deterioration of the QOL beyond 5 postoperative years, particularly in terms of eating restriction [16]. TG can also cause malabsorption of some macro- and micronutrients, such as iron and vitamin B12, which develop within a few years after surgery in most patients who underwent TG unless prophylactic supplementations are given [12,17]. As the proportion of EGC has gradually increased over the last decade as well as upper-third gastric cancer, preserving the QOL by reducing the surgical extent with PG in these patients has become one of the main interests of gastric cancer surgeons in Korea [1].

There has been a controversy over whether PG truly benefits patients with gastric cancer in the upper third of the stomach compared with conventional TG. The optimal reconstruction method following PG also has been debated. Restoring the gastrointestinal continuity with esophagogastrostomy incurred critical problems related to anastomosis, such as anastomotic stricture or intolerable gastroesophageal reflux [18-20]. The DTR method has been considered an alternative by some surgeons to avoid refractory reflux following PG. Several studies have shown that the incidence of reflux esophagitis following PG-DTR was negligible compared with the esophagogastrostomy [12,21].

Theoretically, the ingested food would travel through both tracts via the residual stomach and then the duodenum and via the interposed jejunum following PG-DTR. Compared with TG, this food passage will allow better absorption of the nutrients that are mainly absorbed in the duodenum and proximal jejunum. Furthermore, the residual stomach may serve as a food reservoir and subsequently help maintain body weight postoperatively. Previous studies have demonstrated that PG-DTR led to favorable outcomes in terms of micronutrient deficiencies. Vitamin B12 and iron supplementation were required much less frequently following PG-DTR compared with that following conventional TG [11,12,22]. The present study also demonstrated that the levels of hemoglobin, vitamin B12, and iron were well preserved or recovered from the initial drop during the first year after surgery. It was an expected result because patients who underwent PG were not deprived of intrinsic factors and gastric acid, which is critical in the absorption of vitamin B12 and iron, thanks to the remnant distal stomach. It appears that the main route of food did not

significantly influence micronutrient absorption as far as the remnant stomach is present.

However, surgical outcomes following PG-DTR were not as good as expected in terms of weight preservation and improvement in subjective symptoms. In this study, patients who underwent PG-DTR lost 14.5% of their body weight, which was comparable with that following TG in previous studies, and it was mainly from fat mass loss [12,23]. This finding is in line with those of previous studies showing similar weight loss following PG and TG, and the reasons were indirectly reflected in the prolonged eating restriction in the QOL assessment [12,14,22]. Yamashita et al. [24] suggested that the lack of physiologic passage of the contrast through the remnant stomach following PG-DTR was related to malnutrition, which was defined as weight loss >10% or BMI <20 kg/m^2.

Previous studies have shown that patients typically reach a plateau in their body weight and nutritional indices within 6 months following LPG-DTR, with no significant further changes thereafter [12,21]. Therefore, it was hypothesized that food intake and the remnant gastric function would sufficiently recover by 6 months postoperatively, allowing for the evaluation of gastric emptying at 6 months in the current study. The present study revealed a significant delay in solid food emptying from the residual stomach following LPG-DTR, which is up to 30 times longer than the normal gastric emptying time of 68.7 min suggested by Vasavid et al. [25]. Park et al. [22] reported similar findings, i.e., the mean half-lives of gastric emptying following LPG-DTR were prolonged to 204 and 295 min at 12 and 24 months, respectively. Nakajima et al. [26], however, presented contrary findings showing that gastric emptying half-time was significantly reduced after PG-DTR compared to the preoperative baseline (from 36.2 to 20.7 minutes), notably shorter than the outcomes observed in the current study. Their study demonstrated that 70% of the patients exhibited rapid food transit either through the jejunum or accelerated gastric emptying, suggesting that preserving a larger gastric volume might be advantageous in slowing down the initial emptying and in optimizing the mixture of food with bile. It is important to note that Nakajima et al. [26] utilized a semi-liquid enteral nutrition, unlike the solid food regimen employed in the present study, which could contribute to the conflicting observations in gastric emptying between the studies. This is also demonstrated in our study revealing distinct food passage patterns contingent upon food content, with liquid predominantly traversing the interposed jejunum while solids utilize both pathways. The strength of this study resides in offering insights into the physiologic digestive processes after actual meals following LPG-DTR.

While this study did not show a direct linear correlation between the emptying time and amount of weight loss, there appeared to be a discernable inclination toward poorer nutritional status after surgery among patients experiencing substantially prolonged GET, which was evident in their greater weight loss and more pronounced reduction in serum albumin levels. According to the consensus recommendation on gastric emptying scintigraphy, delayed gastric emptying is defined as gastric retention of >60 % at 2 hours, >30% at 3 hours, or >10% at 4 hours [27]. Therefore, it would be reasonable to consider 50% retention at 3 hours as indicative of delayed gastric emptying when utilizing GET, particularly in gastrectomized patients in the current study. Although it is difficult to draw a concrete conclusion from this limited number of patients, these results suggest that delayed gastric emptying of solid food from the distal residual stomach can negatively influence eating behavior, which might prolong abdominal fullness or impair hunger sensation postoperatively. Therefore, the preservation of the physiologic function of the remnant antrum and the pyloric ring to enhance food passage via the duodenum would be the key factor in improving nutritional parameters as well as QOL related to eating behaviors following PG-DTR. In a previous study, it was observed that preserving more than half of the distal stomach, particularly longer than 20 cm of the length of the greater curvature, effectively maintained the motility and contractility of the distal remnant stomach after PG, even in cases involving truncal vagotomy [28]. Additionally, this might also be carried out by preserving the hepatic branch of the vagal nerve as much as possible and manual dilatation of the pyloric ring intraoperatively or pyloroplasty might be another option, although the actual effect of this additional procedure should be investigated in further studies.

One of the concerns is the regular surveillance of the distal remnant stomach. Iwata et al. [29] reported that the incidence of metachronous cancer was significantly higher following PG (6.6%) than following distal gastrectomy (1.8%) during the median follow-up of 52.8 months in patients with EGC; therefore, regular endoscopic surveillance is important for early detection and treatment of metachronous cancer in the remnant stomach following PG. In this study, endoscopists failed to evaluate the remnant stomach in 2 of 10 patients (20.0%), although the information on the anatomic changes was given in advance; this failure rate is not negligible. In addition, regular cancer screening is usually conducted at the primary care clinics near home in Korea, and patients who underwent LPG-DTR are highly likely to be referred back to these clinics after their intensive follow-up period, which usually is 5 years in Korea. Endoscopists at primary clinics might not be familiar with the anatomic changes following gastric cancer surgery, especially if the procedure has been recently introduced or is rarely performed; they might terminate examination when they encounter esophagojejunostomy without further exploration. Failure to intubate the distal remnant stomach can be caused by endoscopists' unawareness of the anatomic

changes and difficulty in advancing the endoscope through the interposed jejunum. Tokunaga et al. [20] reported that the interposed jejunum >10 cm was associated with a higher failure in endoscopic evaluation following LPG-DTR. Therefore, the interposed jejunum should not be too long to facilitate easy endoscopic evaluation, and the endoscopists must be informed about the type of surgical procedure and subsequent changes in anatomy to not miss metachronous cancer lesions in the remnant stomach following LPG-DTR.

This study has several limitations. The small number of enrolled patients cannot clearly demonstrate the true effect of the changes in food passage or gastric emptying following DTR on clinically relevant nutritional outcomes. Food passage can be influenced by the patient's position; however, the effect of postural changes on the difference in the food passage was not considered in this study. The learning curve of the surgical procedure has not been considered, and 3 surgeons participated in this study. The procedure was not fully standardized, and there could have been procedural differences in terms of the method of bowel length measurement, anastomosis, extent of mobilization of the distal stomach, etc., which might have resulted in variations in the study results.

In conclusion, LPG-DTR exhibited varying food passage patterns depending on the food contents. Liquid contents were primarily emptied through the jejunal tract, whereas solid contents passed through both the tracts of the remnant stomach and jejunum. Solid food emptying from the remnant distal stomach through the pyloric ring was considerably delayed, and this delay appears to be associated with ineffective weight maintenance and subjective symptoms of eating restriction.

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Conflict of Interest

Ji Yeon Park, serving as an Editorial Board member of *Annals of Surgical Treatment and Research*, did not participate in the review process of this article. No other potential conflicts of interest pertinent to this article were reported.

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