Similar hematologic and nutritional outcomes after proximal gastrectomy with double-tract reconstruction in comparison to total gastrectomy for early upper gastric cancer

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Abstract

Background Proximal gastrectomy offers theoretical benefits over total gastrectomy in terms of hematologic and nutritional outcomes. However, little evidence confirming these benefits has been reported. The aim of this study was to assess the hematologic and nutritional outcomes of proximal gastrectomy with double-tract reconstruction in comparison to those of total gastrectomy.

Methods We retrospectively analyzed data from 80 patients with stage I gastric cancer who underwent proximal gastrectomy with double-tract reconstruction ($n = 38$) or total gastrectomy ($n = 42$) from September 2014 to December 2015. We compared hematologic (including hemoglobin, ferritin, vitamin B_{12}, etc.) and nutritional outcomes [including body mass index (BMI), serum total protein, albumin, total cholesterol, and total lymphocyte count] between the two groups.

Results We found no significant differences in changes in hemoglobin ($P = 0.250$) or cumulative incidence of iron deficiency anemia ($P = 0.971$) during a median follow-up period of 24 months (range 18–30 months) after surgery. Cumulative incidence of vitamin B_{12} deficiency also did not differ significantly between the proximal and total gastrectomy groups ($P = 0.087$). BMI changes from baseline were not significantly different between the two groups ($P = 0.591$). Likewise, there were no statistically significant differences in nutritional outcomes.

Conclusions Proximal gastrectomy with double-tract reconstruction exhibited similar outcomes in terms of hematologic and nutritional features in comparison to total gastrectomy.

Keywords Proximal gastrectomy · Double-tract reconstruction · Total gastrectomy · Anemia · Iron deficiency · Vitamin B_{12}

Although the overall incidence of gastric cancer has decreased in recent years, the incidence of adenocarcinoma of the proximal stomach is rising [1–3]. The current standard treatment for proximal early gastric cancer is total gastrectomy. Meanwhile, however, proximal gastrectomy has been used as a function-preserving surgery to improve quality of life [4–7]. By preserving the distal stomach, proximal gastrectomy conserves gastric reservoir function for improved oral intake after surgery and maintains volumes of parietal cells important for vitamin B_{12} absorption [8]. Furthermore, proximal gastrectomy provides a route for iron absorption by allowing food to pass into the duodenum [9, 10]. These theoretical benefits over total gastrectomy are expected to improve hematologic, nutritional, and metabolic outcomes in patients undergoing surgery for early gastric cancer [7, 11–14].

Despite the aforementioned theoretical advantages, surgeons are often reluctant to perform proximal gastrectomy because of the risk of reflux esophagitis after esophago-gastrostomy or gastric stasis after jejunal interposition [15, 16]. To overcome these drawbacks, double-tract reconstruction after proximal gastrectomy was developed [17]. With demonstration of the surgical feasibility of double-tract

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reconstruction after proximal gastrectomy, accompanied by resolution of these drawbacks [18, 19], this new procedure has become the major reconstruction method after proximal gastrectomy in Korea [3]. However, only a few studies have compared hematologic and nutritional outcomes after proximal gastrectomy with double-tract reconstruction with those after total gastrectomy [20]. Therefore, in the present study, we aimed to investigate the effects of proximal gastrectomy with double-tract reconstruction on hematologic and nutritional outcomes in comparison to those after total gastrectomy.

Materials and methods

Patients

At our institution, we began performing proximal gastrectomy with double-tract reconstruction in September 2014 for proximal early gastric cancer. We retrospectively reviewed a prospective database of patients with gastric cancer who underwent curative gastrectomy from September 2014 to December 2015. This study was approved by the Institutional Review Board of Severance Hospital, Yonsei University Health System (4-2016-0427), who waived the need for informed consent for the use of patient data due to the retrospective nature of the study.

A total of 135 consecutive patients underwent minimally invasive (laparoscopic or robotic) proximal or total gastrectomy for gastric cancer during the study period. We excluded patients from analysis to eliminate confounding factors, such as chemotherapy or medical conditions, related to hematologic or nutritional abnormalities. We excluded 26 patients who received neoadjuvant ($n = 1$) or adjuvant ($n = 24$) chemotherapy, and a single patient who underwent nephrectomy for renal cell carcinoma within 6 months after gastrectomy ($n = 1$). Of the 109 patients diagnosed with stage I gastric cancer, we excluded 29 because they exhibited vitamin B_{12} deficiency preoperatively ($n = 1$), underwent insufficient vitamin B_{12} or iron profile evaluation ($n = 25$), were lost to follow-up ($n = 2$), or experienced postoperative mortality ($n = 1$). Finally, 80 patients were included in this study: 38 patients in the proximal gastrectomy group, who underwent minimally invasive proximal gastrectomy with double-tract reconstruction, and 42 patients in the total gastrectomy group, who underwent minimally invasive total gastrectomy with Roux-en-Y esophagojejunostomy. The indications for proximal gastrectomy comprised a diagnosis of clinical early gastric cancer located in the upper-third of the stomach, without evidence of lymph node metastasis. Proximal gastrectomy was not indicated if there were any deformities or ulcer scars of the distal stomach or duodenum.

Surgical procedures

Robotic/laparoscopic total gastrectomy

Detailed procedures for minimally invasive total gastrectomy at our institution have been described previously [21, 22]. For reconstruction, the abdominal esophagus was fully mobilized and rotated 90 degrees in a counter-clockwise direction. After transection of the esophagus using an articulating 45-mm linear stapler with a blue cartridge, the proximal jejunum was brought to the esophageal stump. Then, the posterior wall of the esophagus and the antimesenteric side of the jejunum were anastomosed intracorporeally using the overlap method with a linear stapler. The common entry hole was generally closed using the stapler, although we occasionally performed hand-sewn closure when the anastomosis level was high. The jejunal loop located 2–3 cm proximal to the anastomosis was then divided without mesenteric division and anastomosed to the Roux-limb 50 cm below the esophagojejunostomy. All anastomoses were performed intracorporeally using a 45-mm linear stapler (Fig. 1A).

Robotic/laparoscopic proximal gastrectomy with double-tract reconstruction.

Detailed procedures for laparoscopic proximal gastrectomy with double-tract reconstruction have also been described elsewhere [23]. The robotic procedures did not differ from laparoscopic procedures, except for the devices used within the peritoneal cavity. The stomach was transected above the gastric angle using a 45-mm linear stapler with blue cartridges. Anastomoses, including esophagojejunostomy, jejunogastrostomy, and jejunojejunostomy, were performed as follows: the esophagojejunostomy was performed in the same manner as that during minimally invasive total gastrectomy; the jejunogastrostomy was created with blue cartridges 15–20 cm below the esophagojejunostomy, and the jejunojejunostomy was done with white cartridges 20 cm below the jejunogastrostomy (Fig. 1B).

Data collection

Patient demographics, tumor pathologic characteristics, operative data, and clinical outcomes were collected. Patient physical status was assessed using the American Society of Anesthesiologists Physical Status classification system [24]. The number and types of comorbidities were also recorded. Pathologic data were based on the 7th edition of the American Joint Committee on Cancer staging system [25], and histologic data were based on the Lauren classification [26].
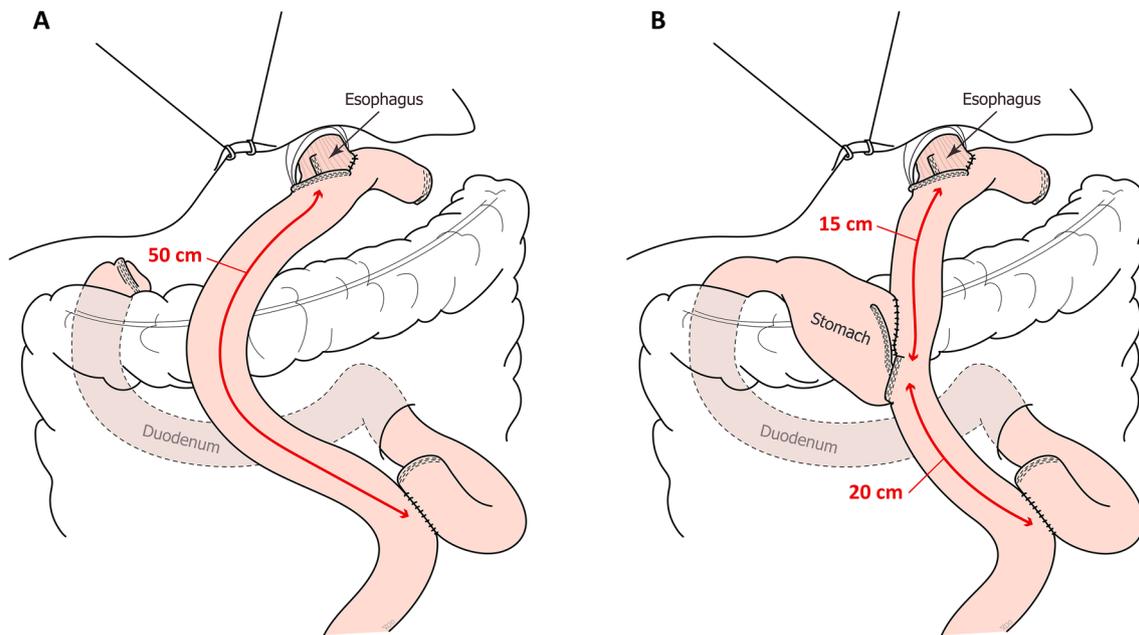
Fig. 1 Schema of reconstruction after **A** total gastrectomy with Roux-en-Y esophagojejunostomy and **B** proximal gastrectomy with double-tract reconstruction

Table 1 Patient characteristics

Variable	Proximal gastrectomy (n=38)	Total gastrectomy (n=42)	P-value
Sex			0.256
Male	32 (84.2%)	31 (73.8%)	
Female	6 (15.8%)	11 (26.2%)	
Age (year)	55.8 ± 11.6	59.3 ± 11.8	0.184
ASA-PS classification			0.422
1	5 (13.2%)	9 (21.4%)	
2	27 (71.1%)	24 (57.1%)	
3	6 (15.8%)	9 (21.4%)	
Weight (kg)	69.1 ± 12.2	66.1 ± 12.6	0.289
BMI (kg/m^2)	24.2 ± 3.1	23.5 ± 3.0	0.316
Number of comorbidities			0.647
0	18 (47.4%)	21 (50.0%)	
1	18 (47.4%)	16 (38.1%)	
2	1 (2.6%)	4 (9.5%)	
3	1 (2.6%)	1 (2.4%)	
Comorbidities*			
Hypertension	12 (31.6%)	11 (26.2%)	0.595
Cardiac disease	0 (0.0%)	1 (2.4%)	>0.999
Diabetes	4 (10.5%)	5 (11.9%)	>0.999
Hepatic disease	1 (2.6%)	0 (0.0%)	0.475
Cerebrovascular disease	2 (5.3%)	1 (2.4%)	0.602
History of pulmonary tuberculosis	3 (7.9%)	6 (14.3%)	0.487
Asthma	0 (0.0%)	1 (2.4%)	>0.999

Values represent means ± standard deviations or numbers (%)

ASA-PS American Society of Anesthesiologists Physical Status, *BMI* body mass index

*Comorbidities include all comorbidities in patients with multiple diseases

Table 2 Operative characteristics

Variable	Proximal gastrectomy (n = 38)	Total gastrectomy (n = 42)	*P*-value
Operation method			0.133
Laparoscopic	27 (71.1%)	23 (54.8%)	
Robotic	11 (28.9%)	19 (45.2%)	
Lymph node dissection			0.001
D1+	38 (100%)	31 (73.8%)	
D2	0 (0.0%)	11 (26.2%)	
Combined resection			
Gallbladder	1 (2.6%)	2 (4.8%)	> 0.999
Adrenal	1 (2.6%)	0 (0.0%)	0.475
Operation time (min)	217.7 ± 53.0	226.9 ± 66.2	0.498
Estimated blood loss (mL)	100.2 ± 92.0	118.8 ± 157.2	0.528
Intraoperative transfusion			0.495
No	38 (100%)	40 (95.2%)	
Yes	0 (0.0%)	2 (4.8%)	
Length of hospital stay (d)	8.18 ± 5.72	8.44 ± 9.55	0.882

Values represent means ± standard deviations or numbers (%)

Table 3 Postoperative morbidity within 30 postoperative days

Variable	Proximal gastrectomy (n = 38)	Total gastrectomy (n = 42)	*P*-value
Complications			0.077
No	22 (57.9%)	16 (38.1%)	
Yes	16 (42.1%)	26 (61.9%)	
Clavien–Dindo grade			0.102
Grade I	4 (25.0%)	9 (34.6%)	
Grade II	10 (62.5%)	7 (26.9%)	
Grade III	2 (12.5%)	9 (34.6%)	
Grade IV	0 (0.0%)	1 (3.8%)	
Intra-abdominal complications			
Fluid collection/abscess	3 (7.9%)	0 (0.0%)	0.103
Anastomotic leakage	1 (2.6%)	4 (9.5%)	0.362
Anastomotic stenosis	0 (0.0%)	2 (4.8%)	0.495
Duodenal stump leakage	0 (0.0%)	1 (2.4%)	> 0.999
Cholecystitis	1 (2.6%)	0 (0.0%)	0.475
Pancreatitis	2 (5.2%)	1 (2.4%)	0.602
Chylous ascites	2 (5.2%)	0 (0.0%)	0.222
Profuse drainage	1 (2.6%)	0 (0.0%)	0.475
Wound complications	1 (2.6%)	4 (9.5%)	0.362
Medical complications			
Respiratory	1 (2.6%)	2 (4.8%)	> 0.999
Cardiovascular	0 (0.0%)	1 (2.4%)	> 0.999
Urinary	1 (2.6%)	3 (7.1%)	0.617

Values are expressed in terms of number (%)

Hematologic and nutritional outcome measures

For comparison of hematologic parameters, hemoglobin, hematocrit, and iron profiles (serum iron, ferritin, transferrin, transferrin saturation, and total iron-binding capacity [TIBC]), were measured. Serum ferritin levels were measured with a competitive immunoassay using direct chemiluminescence (ADVIA Centaur; Bayer Diagnostics,

Table 4 Histopathologic characteristics

Variable	Proximal gastrectomy (n = 38)	Total gastrectomy (n = 42)	P-value
Tumor location (Tubular)			0.067
EG junction	2 (5.3%)	1 (2.4%)	
Cardia	5 (13.2%)	10 (23.8%)	
Fundus	0 (0.0%)	0 (0.0%)	
Upper body	24 (63.2%)	15 (35.7%)	
Mid body	7 (18.4%)	11 (26.2%)	
Lower body	0 (0.0%)	2 (4.8%)	
Tumor size (mm)	21.4 ± 17.1	32.5 ± 27.1	0.034
Proximal margin (mm)	28.0 ± 22.8	37.6 ± 34.2	0.143
Distal margin (mm)	62.3 ± 26.0	130.7 ± 45.2	< 0.001
Histology (Lauren classification)			> 0.999
Intestinal	19 (51.4%)	21 (50.0%)	
Diffuse	17 (45.9%)	18 (42.9%)	
Mixed	0 (0.0%)	1 (2.4%)	
Indeterminate	1 (2.7%)	2 (4.8%)	
T stage			0.112
T1a (m)	17 (44.7%)	17 (40.5%)	
T1b (sm)	20 (52.6%)	17 (40.5%)	
T2 (mp)	1 (2.6%)	8 (19.0%)	
N stage			> 0.999
N0	37 (97.4%)	40 (95.2%)	
N1	1 (2.6%)	2 (4.8%)	
Stage			0.045
Stage IA	36 (94.7%)	32 (76.2%)	
Stage IB	2 (5.3%)	10 (23.8%)	
Retrieved lymph nodes	43.9 ± 15.7	56.2 ± 21.7	0.005

Values represent means ± standard deviations or numbers (%)

EG esophagogastric, *N* node, *T* tumor

Tarrytown, NY), and serum transferrin levels were measured using a nephelometer (Dade Behring, Siemens Healthcare Diagnostics, Liederbach, Germany). Transferrin saturation was calculated as the ratio of serum iron to TIBC, multiplied by 100. Anemia was defined as a hemoglobin level < 13 g/dL in men and < 12 g/dL in women, according to World Health Organization criteria [27]. Iron deficiency was defined as a serum ferritin level < 30 ng/mL [28, 29]. Serum vitamin B_{12} levels were measured using an electrochemilumines-cence immunoassay kit (Roche Diagnostics GmbH, Mannheim, Germany), and vitamin B_{12} deficiency was defined as a serum level < 200 pg/mL [8]. We also evaluated neutrophil counts, total lymphocyte counts, and serum protein, serum albumin, and total cholesterol levels as a reflection of immune and nutritional status.

Follow-up

We followed all patients every 3 months for 1 year after surgery, and then every 6 months thereafter. Body mass index (BMI) and blood samples for assessing hematologic and nutritional parameters were evaluated at each visit. We examined abdomino-pelvic computed tomography scans every 6 months for the first 2 years after surgery, and then yearly thereafter. We performed upper endoscopy every year. We followed patients for a median of 24 months (range 18–30 months) in both groups.

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics software for Windows, version 23.0 program (Armonk, NY: IBM Corp.). Independent variables were compared using the Chi-square test for categorical variables and the Mann–Whitney U test or Kruskal–Wallis test for continuous
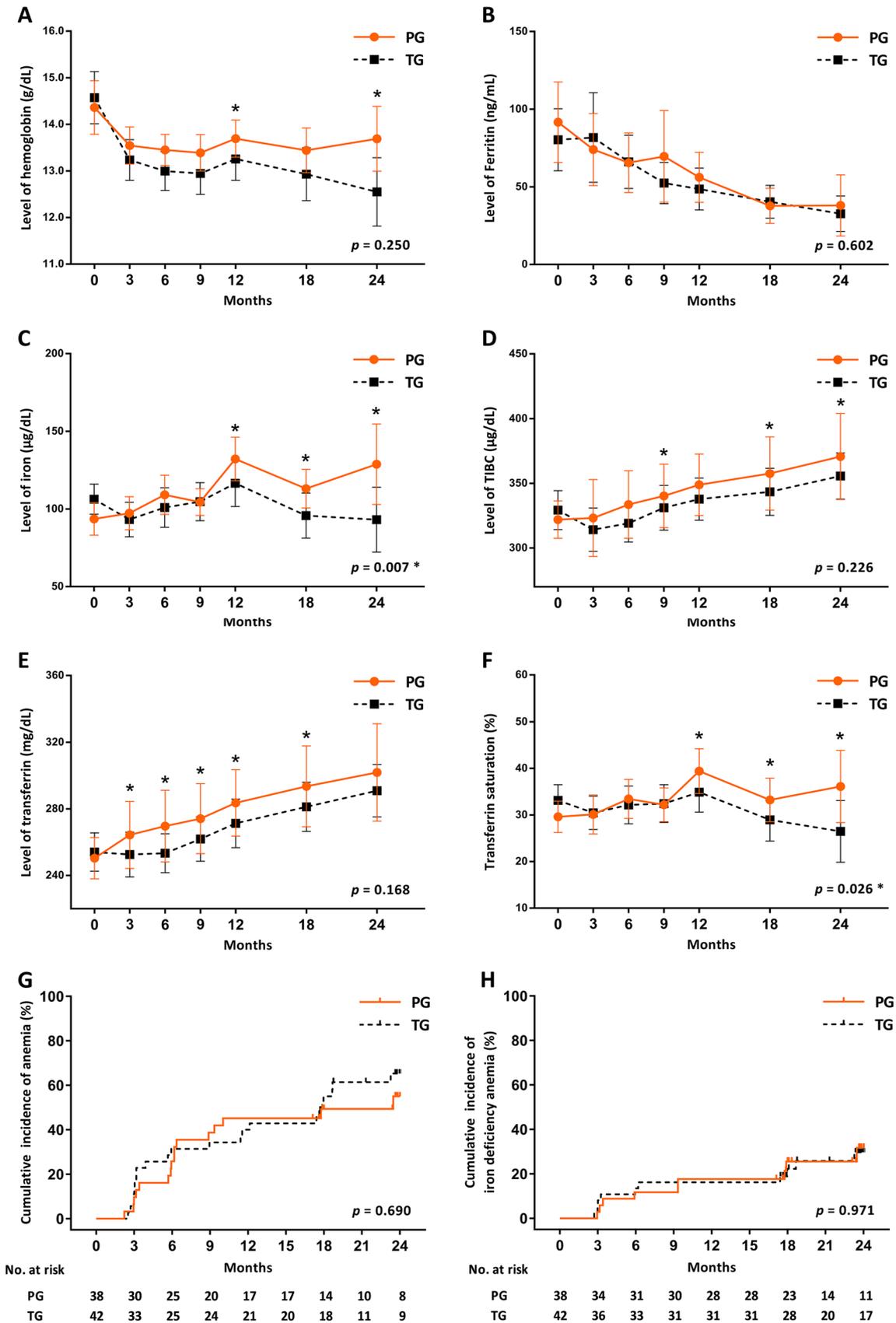
◄**Fig. 2** Comparison of changes in hematologic parameters between proximal gastrectomy with double-tract reconstruction and total gastrectomy. Levels of **A** hemoglobin, **B** ferritin, **C** iron, **D** total iron-binding capacity, **E** transferrin, and **F** transferrin saturation. Cumulative incidences of **G** anemia and **H** iron deficiency anemia. Asterisk (*) represents a *P* value < 0.05 for between-group comparison. *PG* proximal gastrectomy with double-tract reconstruction, *TG* total gastrectomy with Roux-en-Y esophagojejunostomy, *TIBC* total iron-binding capacity

variables. The Kaplan–Meier method with log-rank tests was used to analyze the cumulative occurrences of anemia, vitamin B_{12} deficiency, and iron deficiency. Mixed model analysis with post-hoc tests was utilized to analyze changes in continuous variables between the two groups. All *P* values < 0.05 were considered statistically significant.

Results

Patient characteristics and surgical outcomes

Patient demographics showed no statistically significant differences between the two groups (Table 1). Operation time, estimated blood loss, and length of hospital stay were also comparable between the two (Table 2). In terms of postoperative morbidity within the first 30 days after surgery (Table 3), the overall complication rate was lower in the proximal gastrectomy group (42.1%) than in the total gastrectomy group (61.9%), although it was not statistically different ($P = 0.077$). In patients with complications, the rate of major complications (grade III or IV) was also lower in the proximal gastrectomy group (12.5%) than in the total gastrectomy group (38.5%); however, the difference was not statistically significant ($P = 0.102$). Of the histopathologic characteristics (Table 4), only tumor size, distal margin, and number of retrieved lymph nodes exhibited significant differences between groups ($P = 0.034$, < 0.001, and 0.005, respectively), as expected because of differences in the extents of resection and lymph node dissection. Although the proximal gastrectomy group overall comprised patients of lower pathologic tumor stage than the total gastrectomy group ($P = 0.045$), T and N stages did not differ between the two groups ($P = 0.112$ and > 0.999, respectively).

Hematologic outcomes

Concentrations of hemoglobin, ferritin, TIBC, and transferrin were not significantly different between the two groups ($P = 0.250$, 0.602, 0.226, and 0.168, respectively), whereas serum iron and transferrin saturation were significantly higher in the proximal gastrectomy group ($P = 0.007$ and 0.026, respectively, Fig. 2A–F). The proportion of patients who required iron supplements was lower in the proximal

gastrectomy group (3/38, 7.9%) than in the total gastrectomy group (6/42, 14.3%, $P = 0.487$). The cumulative incidence of anemia was lower after proximal gastrectomy than after total gastrectomy, although the difference was not statistically significant ($P = 0.690$, Fig. 2G). Patients in both groups experienced a similar cumulative incidence of iron deficiency anemia, which was almost identical after 18 months postoperatively ($P = 0.971$, Fig. 2H).

Vitamin B_{12} metabolism

For accurate analysis, patients were excluded when they began treatment with vitamin B_{12} supplements and thereafter. In both groups, vitamin B_{12} levels were > 600 pg/mL preoperatively. After surgery, these levels decreased markedly to < 300 pg/mL at 3 months and approximately 200 pg/mL at 9 months. In the total gastrectomy group, most patients were receiving vitamin B_{12} supplements within 12 months after surgery, and all were taking supplements after 18 months. Mean changes in vitamin B_{12} levels did not differ between two groups, although the number of patients still included in the analysis by 12 months was low ($P = 0.095$, Fig. 3A).

Figure 3B shows the cumulative incidences of vitamin B_{12} deficiency after surgery. The proximal gastrectomy group had a lower cumulative incidence of vitamin B_{12} deficiency than the total gastrectomy group. Approximately 90% of the patients in the proximal gastrectomy group exhibited vitamin B_{12} deficiency at 24 months after surgery, whereas 100% of patients in the total gastrectomy group had vitamin B_{12} deficiency by 21 months. Nevertheless, the difference in the cumulative incidences of vitamin B_{12} deficiency between the groups was not statistically significant ($P = 0.087$). However, the proportion of patients who required vitamin B_{12} supplements was lower in the proximal gastrectomy group (34/38, 89.5%) than in the total gastrectomy group (42/42, 100%, $P = 0.047$).

Body mass index and nutritional parameters

Mean changes in BMI from baseline are shown in Fig. 4A. In both groups, BMI decreased by more than 2.5 kg/m^2 from baseline within 12 months after surgery. Afterwards, BMI in the proximal gastrectomy group tended to recover, whereas BMI in the total gastrectomy group remained constant. Nevertheless, the differences in BMI between the groups were not statistically significant ($P = 0.591$). Regarding nutritional outcomes, the proximal gastrectomy group exhibited similar total protein, albumin, and cholesterol levels, as well as total lymphocyte counts, with the total gastrectomy group ($P = 0.678$, 0.743, 0.144, and 0.938, respectively, Fig. 4B–E).
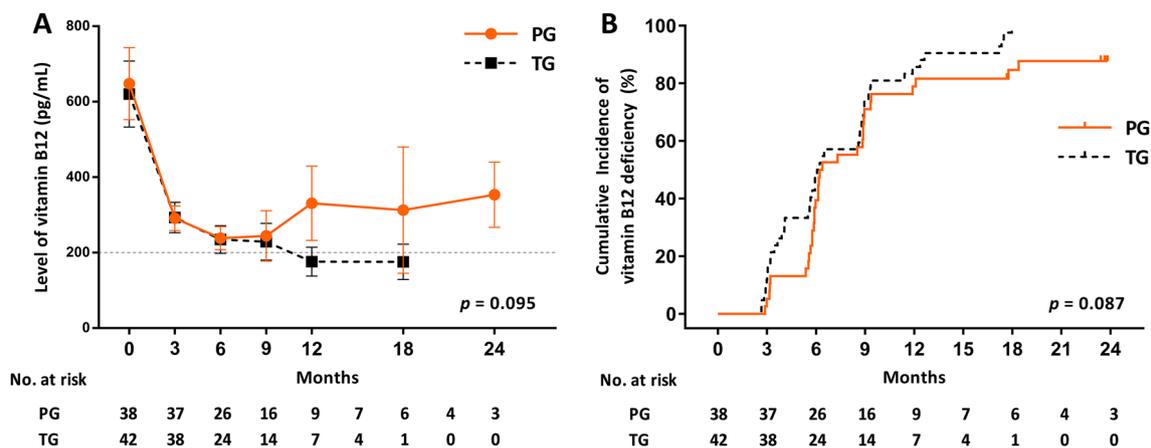
Fig. 3 A Vitamin B_{12} levels without supplementation and **B** cumulative incidence of vitamin B_{12} deficiency. Asterisk (*) represents a P value < 0.05 for between-group comparison. *PG* proximal gastrec-tomy with double-tract reconstruction, *TG* total gastrectomy with Roux-en-Y esophagojejunostomy, *TIBC* total iron-binding capacity

Long-term outcomes

During the 24-month median follow-up period (range 18–30 months), no recurrence or mortality was recorded in either group. Four patients in the proximal gastrectomy group (10.5%) and one patient in the total gastrectomy group (2.4%) developed reflux symptoms and/or endoscopically proven reflux esophagitis ($P = 0.185$).

Discussion

In this study, minimally invasive proximal gastrectomy with double-tract reconstruction was associated with hematologic and nutritional outcomes similar to those for minimally invasive total gastrectomy with Roux-en-Y esophagojejunostomy. Postoperative hematologic parameters, including hemoglobin, ferritin, and transferrin saturation, did not differ significantly between the two types of gastrectomy. Although the cumulative incidence of anemia was lower in the proximal gastrectomy group than in total gastrectomy group, the difference was not statistically significant. Furthermore, the two groups exhibited a similar cumulative incidence of iron deficiency anemia. Likewise, there were no significant differences in postoperative vitamin B_{12} levels or the cumulative incidence of B_{12} deficiency between the proximal gastrectomy with double-tract reconstruction and total gastrectomy groups, although the proportion of patients who needed vitamin B_{12} supplementation was smaller in the proximal gastrectomy group. Nutritional parameters, including serum protein, albumin, and cholesterol, were also comparable between the two groups after surgery.

Proximal gastrectomy followed by reconstruction with various methods, except double-tract reconstruction, completely preserves food passage into the duodenum and has been reported to facilitate better iron metabolism outcomes than total gastrectomy [11–14, 30–33]. Double-tract reconstruction, wherein two food passages are created, only allows for partial preservation of duodenal food passage. Nonetheless, this reconstruction method is thought to be beneficial to iron metabolism. Indeed, when compared with total gastrectomy, proximal gastrectomy with double-tract reconstruction has been shown to produce favorable or comparable outcomes in regards to iron metabolism [10, 34]. In the present study, mean hemoglobin and ferritin were higher in the proximal gastrectomy group than in the total gastrectomy group; however, the values in both groups remained within the normal range and the difference between groups was not statistically significant. Moreover, the cumulative incidences of anemia and iron deficiency anemia did not differ between groups. This suggests that partial preservation of duodenal food passage by diversion in double-tract reconstruction reduces iron absorption amounts relative to other reconstruction methods. While accurate determination of the proportion of food passing through the duodenum in proximal gastrectomy with double-tract reconstruction has not been reported, one study found only 60% of ingested food in the remnant stomach after double-tract reconstruction, with the rest having passed into the jejunum [18]. This partial passage of ingested food into the duodenum after double-tract reconstruction would be insufficient to prevent iron deficiency.

In addition to the reconstruction method, the gastrectomy itself may also affect iron deficiency, since less oral intake as the result of a smaller stomach volume can reduce iron intake as well. Moreover, decreased chief cell mass in the stomach and vagotomy decreases gastric acidity, resulting
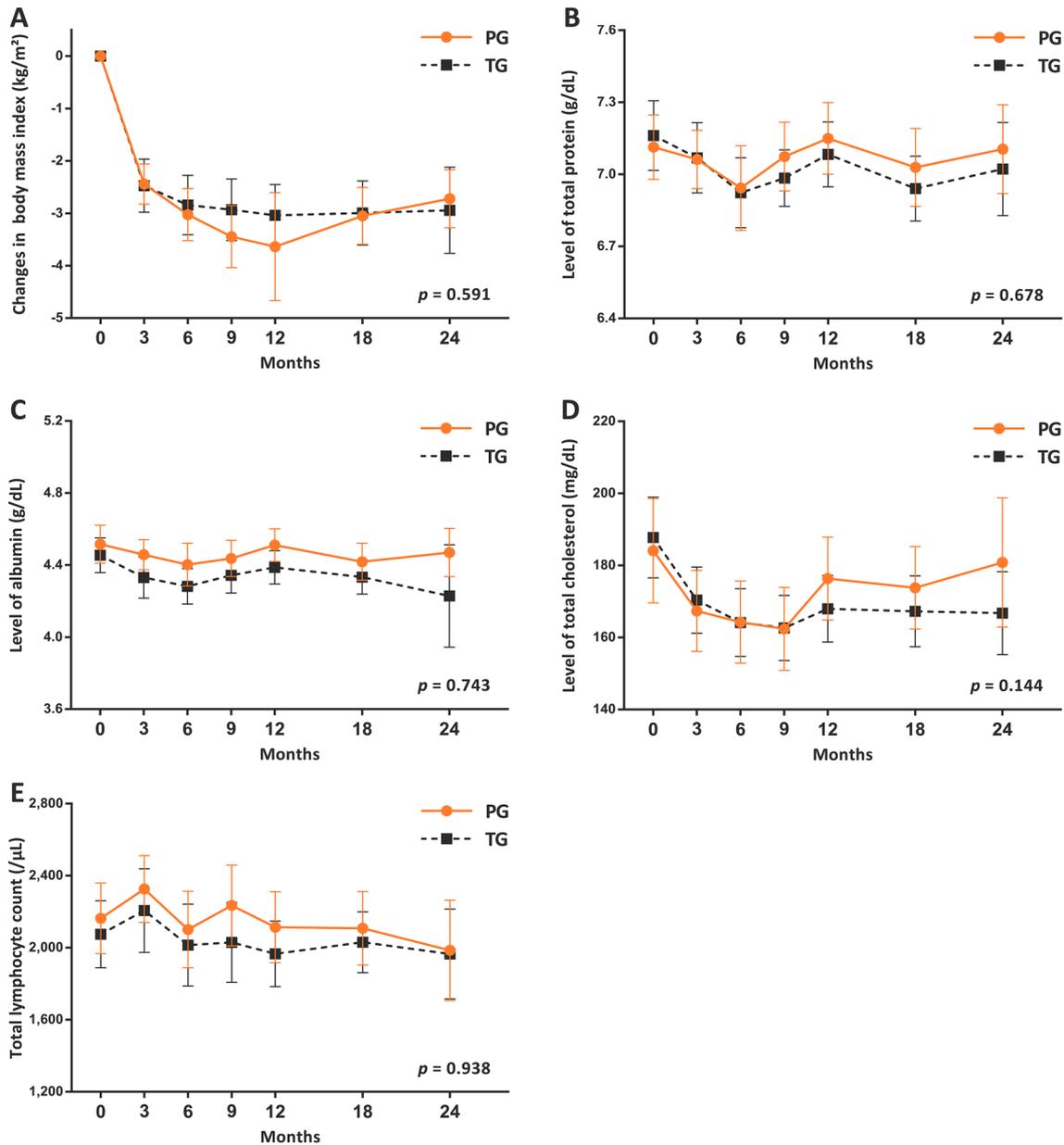
Fig. 4 **A** Mean changes in body mass index from baseline and changes in nutritional parameters, including **B** total protein, **C** albumin, **D** total cholesterol, and **E** total lymphocyte count. *PG* proximal gastrectomy with double-tract reconstruction, *TG* total gastrectomy with Roux-en-Y esophagojejunostomy

in decreased efficacy of iron absorption [35, 36]. This phenomenon has been observed for distal subtotal gastrectomy with gastroduodenostomy (Billroth I anastomosis), which completely preserves food passage into the duodenum. In a previous study applying the aforementioned procedure, iron deficiency was reported in more than half of patients at 3 years after surgery [9]. Thus, preservation of the distal stomach alone after proximal gastrectomy would not be sufficient to prevent iron deficiency.

As with iron metabolism, preservation of the distal stomach during proximal gastrectomy has been reported to have beneficial effects on vitamin B_{12} metabolism [10, 30, 34]. Nevertheless, most studies on proximal gastrectomy with double-tract reconstruction have only reported mean levels of vitamin B_{12} after surgery, not the exact incidences of vitamin B_{12} deficiency. In our study, the cumulative incidence of vitamin B_{12} deficiency after proximal gastrectomy with double-tract reconstruction was similar to that after total gastrectomy, although the proportion of patients who needed

vitamin B_{12} supplementation was smaller in the proximal gastrectomy group. Nevertheless, vitamin B_{12} levels of the 4 patients that did not need supplementation in the proximal gastrectomy group markedly dropped below the preoperative levels during follow-up. Therefore, there might be a high probability of supplementation in those 4 patients in the proximal gastrectomy group with long-term follow-up.

Gastric parietal cells are the most important factor affecting vitamin B_{12} metabolism, as absorption of vitamin B_{12} is mediated by intrinsic factor released from gastric parietal cells. Since parietal cells are mainly located in the body of the stomach, with very few being found in the gastric antrum and pylorus [37], patients who undergo proximal gastrectomy may be left with too few parietal cells with which to maintain sufficient vitamin B_{12} metabolism. In addition, parietal cell mass can also be influenced by pathologic changes, such as atrophic gastritis or intestinal metaplasia, in the remnant gastric mucosa after proximal gastrectomy with double-tract reconstruction [38, 39]. Therefore, vitamin B_{12} deficiency after proximal gastrectomy with double-tract reconstruction is also generally inevitable.

In our institution, we transect the stomach above the angle during proximal gastrectomy and preserve only two or three branches of the right gastric and gastroepiploic arteries. This leaves a remnant stomach that is approximately half the volume of the entire stomach. This small remnant stomach might have affected our results. In contrast to a study reporting superior clinical and nutritional outcomes after proximal gastrectomy with double-tract reconstruction in comparison to total gastrectomy [34], the distal resection margin for proximal gastrectomy in our study (6.2 cm) was much greater than that in the previous study (2.8 cm). Thus, while mean tumor size and proximal resection margin were similar, the volume of gastric remnant in our study was smaller than that reported in the aforementioned study. We speculate that disparities in gastric remnant volume contributed to the differences in results compared with the previous study in terms of hematologic and nutritional outcomes.

In addition to the above, gastric remnant volume can also affect recovery of food intake and gastrointestinal symptoms after surgery. A previous study reported that patients with a larger remnant stomach (resection of 1/2 of the stomach) exhibited higher postoperative/preoperative body weight ratios than patients with a small remnant stomach (resection of 2/3 of the stomach) or no remnant stomach (total gastrectomy) [20]. In the current study, changes in BMI from baseline were not significantly different between the proximal gastrectomy with double-tract reconstruction and total gastrectomy groups. As food intake has a significant impact on body weight, the relatively small volume of remnant stomach with which to act as a reservoir for food could lead to insufficient food intake. Of note, a nationwide questionnaire survey in Japan reported that surgeons at approximately 30% of institutions indicated that they preserve less than half of the entire stomach or make decisions about the remnant volume on a case-by-case basis while performing proximal gastrectomy [40]. Thus, further research is required to define appropriate volume of gastric remnant.

As the number of patients included in this study was relatively small, we were unable to show more statistically significant differences. However, our study population was larger than that in other studies comparing proximal gastrectomy with double-tract reconstruction to total gastrectomy. The short duration of follow-up was another limitation. Accordingly, we could not evaluate oncologic outcomes, such as survival rates or recurrence. Moreover, because of the small number of patients after 18 months of follow-up, owing to its short duration, statistical power dropped lower than 50%. This might obscure possible differences in hematologic or nutritional outcomes between groups. A well-designed, large-scale study is required to further outline the outcomes of proximal gastrectomy. Indeed, a multicenter prospective randomized controlled trial comparing laparoscopic proximal gastrectomy with double-tract reconstruction to total gastrectomy for upper third early gastric cancer (KLASS-05, NCT02892643) [41] is in progress in Korea. The KLASS-05 trial should provide definitive results regarding the efficacy of proximal gastrectomy with double-tract reconstruction with respect to clinical, surgical, and functional outcomes. Despite the study's limitations, our results showed similar short-term outcomes for proximal gastrectomy with double-tract reconstruction in comparison to total gastrectomy. Additional research on iron metabolism in relation to duodenal food passage and on vitamin B_{12} metabolism in relation to parietal cell volume in remnant stomach would be necessary to further understand the consequences of proximal gastrectomy with double-tract reconstruction.

Conclusions

In the present study, proximal gastrectomy with double-tract reconstruction and total gastrectomy were found to be associated with similar hematologic and nutritional outcomes, including incidences of iron-deficiency anemia and vitamin B_{12} deficiency, although the proportion of patients who required vitamin B_{12} supplementation was smaller in the proximal gastrectomy group. For patients with gastric cancer located in the upper third of the stomach, proximal gastrectomy with double-tract reconstruction can be considered a reasonable alternative to total gastrectomy, if oncological safety is assured. Clinicians, however, should be aware that proximal gastrectomy with double-tract reconstruction does not avert the risk of iron and/or vitamin B_{12} deficiency associated with total gastrectomy.

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