

Postoperative Functional Evaluation of Gastric Tube After Laparoscopic Proximal Gastrectomy for Gastric Cancer

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Abstract. *Background:* The primary aim of this study was to examine the motor activity (motility) of a gastric tube after laparoscopic-assisted proximal gastrectomy (LPG). A secondary objective was to ascertain whether a correlation exists between gastric tube motor activity and reflux esophagitis. *Patients and Methods:* A total of 41 patients who underwent LPG for early gastric cancer were studied. The motility of the gastric tube and the status of reflux esophagitis were evaluated. Manometric recording was performed 2 weeks and 1 year after surgery. *Results:* In a fasting state, the motilities of the distal gastric tube and duodenum recovered within 1 year after surgery but that of the proximal gastric tube did not recover. Improvement of the motility of the gastric tube was associated with a decreased number of patients with reflux esophagitis 1 year after surgery. In patients with reflux esophagitis, the motility of the distal gastric tube was significantly lower than that in patients without reflux esophagitis. *Conclusion:* After LPG, the motility of the gastric tube recovered, and the incidence of reflux esophagitis decreased with time, in parallel to recovery of gastrointestinal motility.

Advances in screening mechanisms and diagnostic techniques have increased the detection rate of early-stage gastric carcinoma arising in the upper third of the stomach (1, 2). Treatment considerations, such as gastrectomy type, extent of resection, reconstruction methods, surgical curability, and outcomes, have become important issues.

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Some authors have reported that proximal gastrectomy for early gastric cancer arising in the upper third of the stomach is an appropriate operation in terms of curability and safety. Their findings support the notion that proximal gastrectomy achieves survival rates equivalent to those of total gastrectomy, while preserving the physiologic functions of the gastric remnant (2). However, other authors remain skeptical about whether the advantages of proximal gastrectomy outweigh the functional drawbacks of esophageal reflux, which can substantially compromise the patients' quality of life (3). Proximal gastrectomy destroys anatomic anti-reflux barriers, including the lower esophageal sphincter, diaphragmatic angle, and diaphragmatic esophageal ligament.

Several methods can be used for reconstruction after proximal gastrectomy. A high incidence of reflux esophagitis after simple esophago-gastrostomy has prompted the development of several novel techniques for reconstruction (jejunal pouch interposition and jejunal interposition) that are designed to prevent reflux (2, 4). However, proximal gastrectomy with jejunal interposition is complicated, time-consuming, and sometimes unsatisfactory.

Laparoscopic gastrectomy for gastric cancer has become a more common procedure owing to advances in surgical techniques (5-7). Previous studies have shown that laparoscopic distal gastrectomy (LDG) with lymph node dissection can be performed safely and radically in patients with gastric cancer arising in the middle and lower thirds of the stomach (5, 8). LPG is associated with technical difficulties with potential effects on curability and safety, as compared with LDG or laparoscopic total gastrectomy (9). LPG was developed to preserve the physiologic function of the gastric remnant in patients with gastric cancer located in the upper or middle third of the stomach.

The development of reflux esophagitis may greatly compromise the postoperative quality of life of patients who undergo proximal gastrectomy. To prevent this complication, anti-reflux procedures such as fundoplication and interposition of a jejunal segment have been applied.

However, performing these procedures laparoscopically is sometimes difficult and time consuming. Kitano *et al.* introduced a technique for performing gastric tube reconstruction with a circular stapling device after LPG (10), and Adachi *et al.* evaluated the usefulness of gastric tube reconstruction for preventing reflux esophagitis after open proximal gastrectomy (11). In 2010 we reported that LPG with gastric tube reconstruction was a simple and safe technique for the treatment of proximal early gastric cancer (9). From June 2007 to June 2011, we performed LPG with gastric tube reconstruction in 41 patients with cancer located in the upper third of the stomach. To our knowledge, gastric tube motor activity after proximal gastrectomy has never been investigated previously, in contrast to that after esophagectomy (12).

The aim of this study was to evaluate gastric tube motor activity after LPG. A secondary objective was to ascertain whether gastric tube motor activity correlates with reflux esophagitis.

Patients and Methods

Patients. Between September 2006 and June 2011, 41 patients underwent LPG with gastric tube reconstruction at the Department of General Surgical Science, Gunma University Hospital. The indications for LPG were determined according to the Guidelines for Gastric Cancer of the Japan Gastric Cancer Society (13). All tumors were located in the upper third of the stomach, and the depth of tumor invasion was assessed to be less than submucosal invasion preoperatively. The stage of gastric cancer was evaluated on preoperative examinations, including gastrointestinal endoscopy and endoscopic ultrasonography (EUS). All patients underwent computed tomography (CT), and none had evidence of distant metastasis in any organ, including the liver and lymph nodes. Patients who had severe systemic disease, incapacitating general condition, other synchronous or metachronous cancers, or a history of gastric or esophageal surgery were excluded from the study. No patient received preoperative neoadjuvant chemotherapy or radiotherapy. The patients were informed of the study objectives, the nature of surgery, possible postoperative complications, and the availability of other treatment options.

Surgical technique. All operations were performed with curative intent. Gastric tube reconstruction was performed as described previously (9).

Initially, five ports were introduced into the right upper quadrant (5 mm), right middle quadrant (12 mm), umbilical region (12 mm), left middle quadrant (5 mm), and left upper quadrant (12 mm). Before reconstruction, proximal gastrectomy was completed, with dissection of the perigastric lymph nodes and some second-tier lymph nodes according to the Japanese Classification of Gastric Carcinoma. Reconstruction was done using a gastric tube. Esophagogastrostomy was performed using an Orvil package (Covidien; Dublin, Ireland) consisting of a 25-mm anvil with the head pretilted and the tip attached to an 18-Fr orogastric tube. In preparation for transoral placement of the anvil head, the esophagus was transected using an Endo-GIA 60-3.5 stapler (Covidien). A median incision (about 4 cm long) was performed in the upper abdomen, and the peritoneal cavity was entered. The stomach was exteriorized through the median incision in the abdomen. After the

vessels of the greater and lesser curvatures were ligated, the gastric body was divided with the Endo-GIA 60-3.5 stapler to create a gastric tube (20 cm long, 3-4 cm wide). The posterior wall of gastric tube and the esophagus were anastomosed with the use of a circular stapler introduced through the stump of the gastric tube. A pyloroplasty was carefully performed by the finger fracture method.

Manometric recording. After surgery, an epidural tube was used to control pain and was left in place for 48 h. On the third day after surgery, each patient received a soft meal. From the fifth day after surgery, each patient was allowed to gradually resume a normal diet. Manometric recording was done two weeks except for the patients with anastomotic leakage and 1 year after surgery. Manometric recording for two patients with leakage was done after verifying cure.

A 6-mm-diameter flexible probe containing four strain gauge pressure transducers was used to monitor intestinal motor activity (GMMS-600; Star Medical, Tokyo, Japan). All subjects were required to stop taking medications known to affect gastrointestinal motility for at least 48 h before the study. After the subjects had fasted for at least 12 h overnight, the manometry assembly was inserted through a nostril, and all pressure transducers were positioned in the reconstructed tract under fluoroscopic control as described below. The pressure transducers were positioned to measure intraluminal pressure in the esophagus, gastric tube, and duodenum. The most proximal pressure transducer was positioned in the esophagus. The second and third pressure transducers were positioned 15 cm and 25 cm distal to the first pressure transducer in the gastric tube. The fourth transducer was located in the proximal duodenum 15 cm distal to the third transducer. Recording was started at 9:00 a.m. in all patients and continued for 4 h, the first 2 h with the subject fasting and the remaining 2 h after a 400-kcal meal (carbohydrates, 62.4 g; proteins, 17.52 g; lipids, 8.9 g/400 ml). All patients ingested the entire meal.

Analysis of motor activity. Analysis was visual and computerized. Visual analysis was performed for both the fasting and fed states. Each phase of contractile activity was defined according to the following criteria. Phase I was defined as the quiescent period. Phase II consisted of clusters of irregular contractions that followed phase I and preceded phase III. Phase III was a period of strong contractions lasting more than 5 min. Phase IV was a very short period of subsiding contractions that immediately followed phase III. Data were recorded on a computer (Adif1412. DII; Star Medical, Tokyo, Japan) for analysis. To quantitatively measure motor activity, the motility index (MI) was determined. Signals from the manometric assembly, which were stored on a data recorder (GMMS-TB; Star Medical), were digitized at a sampling frequency of 500 ms and analyzed with the same system, which was controlled by a computer (Adif1412. DII; Star Medical). The MI obtained by the processing system corresponded to measurements of the area surrounded by the contraction wave and baseline, *i.e.*, to the product of amplitude and time in minutes during a certain fixed period. The MIs of the gastric tube and the duodenum were calculated for each sequential 30 min of spontaneous motility and after the meal.

Endoscopic examination. At the 1 and 12-month visits, the patients underwent endoscopic examination in addition to the conventional outpatient follow-up procedures. The severity of reflux esophagitis was assessed according to the Los Angeles Classification of Esophagitis (14).

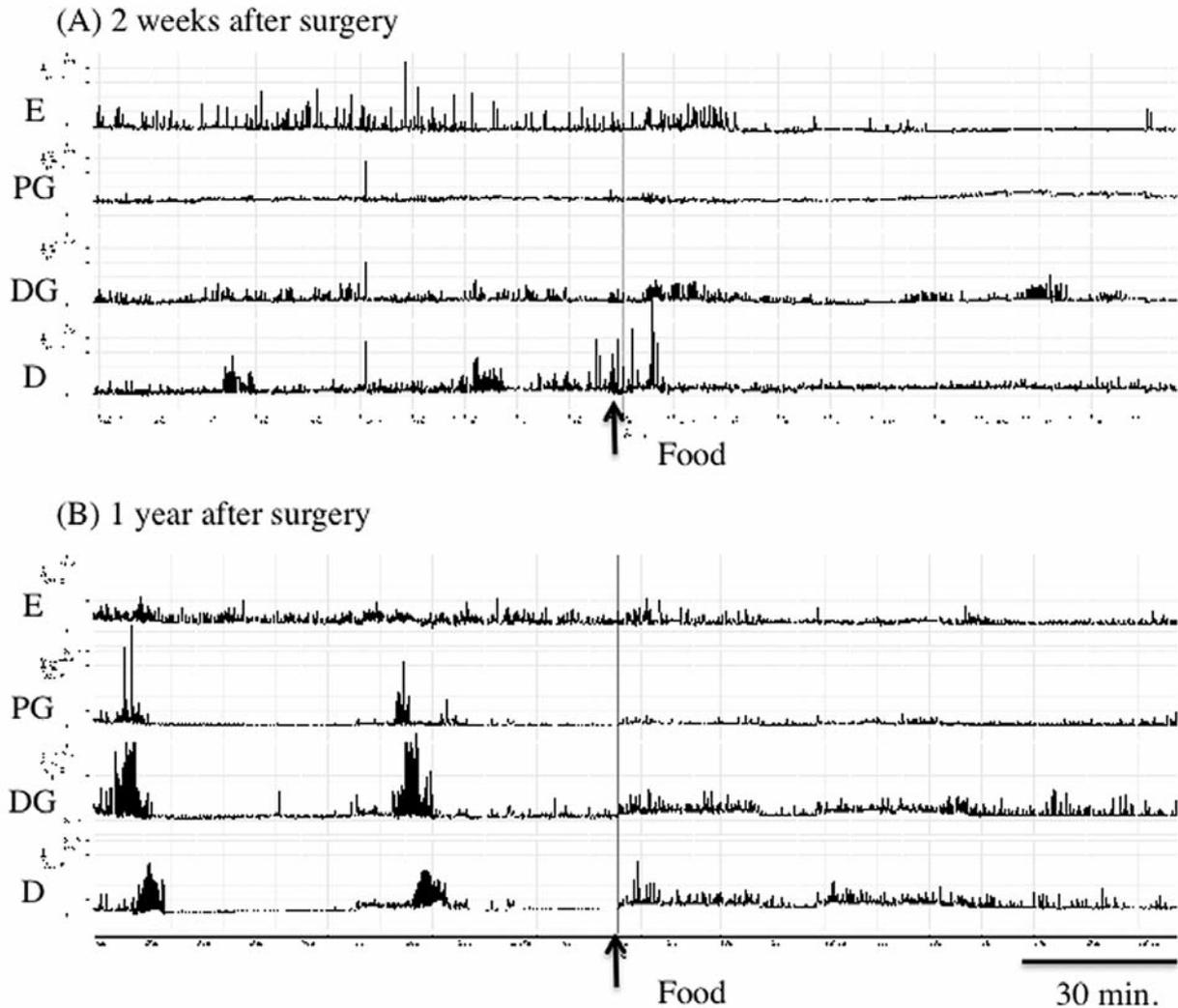


Figure 1. Gastrointestinal motor activity 2 weeks after surgery (A) and 1 year after surgery (B). E, Esophagus; PG, proximal gastric tube; DG, distal gastric tube; D, duodenum.

Statistical analysis. Data were collected and analyzed with the use of a commercially available computer program (JMP 9, SAS Institute Inc., Cary, NC) and are expressed as means±standard errors. The quantitative data were subjected to further statistical analysis, which involved repeated measures of analysis of variance (ANOVA). When significant differences were detected, differences between means were checked for significance by the Fisher's protected least significant difference test. The paired data were compared with the use of Student's *t*-test. Differences with *p*-values of less than 0.05 were considered significant.

Results

Forty-one patients (28 men and 13 women) underwent LPG. The mean age was 64.8 years (range=38-82). The mean operating time and blood loss were 202±6.3 min and

158±17.8 ml, respectively. The depth of invasion on postoperative examination was T1 (mucosa, submucosa) in 33 patients, the muscularis propria in 6, the subserosa in 1, and penetration of the serosa in 1. All procedures were curative, and all resected margins were free of invasion. Laparoscopic surgery was not converted to laparotomy in any patient. The main complication after LPG was anastomotic-site stenosis, occurring in 6 patients (14.6%), among whom 2 patients (4.8%) had anastomotic-site leakage. The mean postoperative hospital stay was 17 days (range=11-62). After a median follow-up of 31 months, the overall 5-year survival rate after LPG was 90.0%. One patient died of peritoneal recurrence 44 months after surgery.

Phase III of the gastric tube was not observed 2 weeks after surgery, but phase III of the duodenum was noted in

Table I. Postoperative phase III contractions 2 weeks after and 1 year after surgery

	Phase III (+)	Phase III (-)	p-Value
2 weeks after surgery	10 (24%)	31 (76%)	<0.05
1 year after surgery	26 (63%)	15 (37%)	

this patient (Figure 1). Phase III, in which contractions originated from the proximal site of the gastric tube and then migrated to the distal site and followed by the duodenum, was evident in patients 1 year after surgery (Figure 1). Phase III of the gastric tube was observed in 10 patients 2 weeks after surgery and in 26 patients 1 year after surgery (Table I). The incidence of phase III was significantly higher 1 year after surgery than 2 weeks after surgery ($p < 0.05$). The recovery course of gastroduodenal motor activity is shown as the MI value in Figure 2. The motor activity of the proximal gastric tube did not recover within 1 year after surgery in either the fasting or fed states (Figure 2A, B). The motor activities of the distal gastric tube and duodenum recovered within 1 year after surgery in the fasted state (MI of distal gastric tube; from 62 ± 8 to 179 ± 28 , $p < 0.05$, MI of duodenum; from 54 ± 6 to 109 ± 8 , $p < 0.05$) (Figure 2A). In the fed state, however, the motor activities of none of the sites recovered (Figure 2B).

The findings of endoscopic examinations performed 1 month and 1 year after surgery are shown in Figure 3. Eight patients (19.5%) were confirmed to have reflux esophagitis on endoscopy 1 month after surgery. The severity of esophagitis in these eight patients was grade A in two patients, grade B in four, and grade C in two according to the Los Angeles Classification of Esophagitis. Five patients (12.1%) were confirmed to have reflux esophagitis on endoscopy 1 year after surgery. The severity of esophagitis was in grade A in one patient, grade B in three, and grade C in one. In these 13 patients with reflux esophagitis, the motor activity of the distal gastric tube was significantly lower than that in patients without reflux esophagitis (MI, 87 ± 11 vs. 134 ± 23 , $p < 0.05$) (Figure 4).

Discussion

Proximal gastrectomy was introduced to improve performance status by preserving half of the stomach. Gastroesophageal reconstruction has frequently been performed since the direct anastomosis is very simple. However, the high incidence of reflux esophagitis after simple esophagogastrostomy has prompted the development of several reconstruction techniques to prevent reflux (2, 15). Katai *et al.* reported a very low incidence of reflux symptoms after proximal gastrectomy with

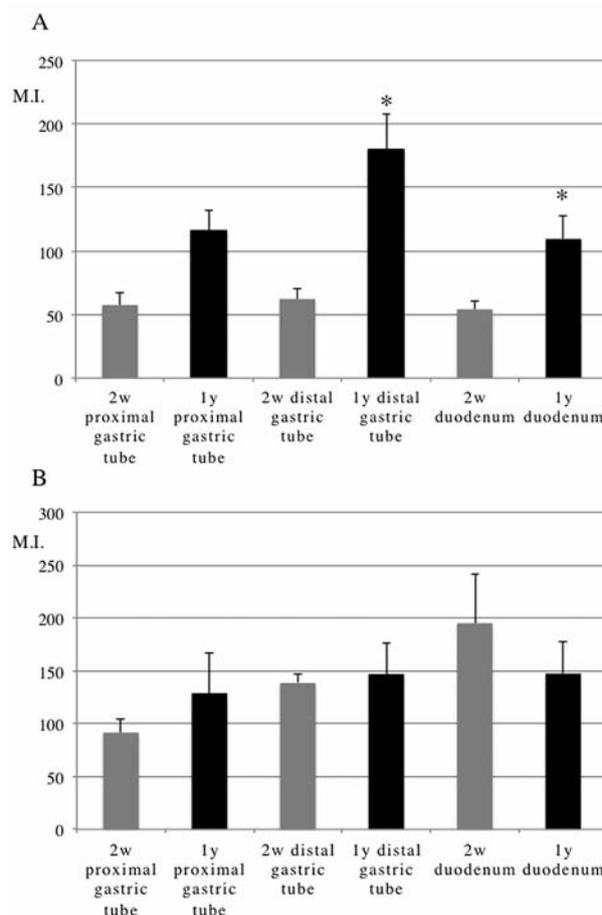


Figure 2. Recovery course of gastroduodenal motor activity in (A) fasting state and (B) fed state. * $p < 0.05$ vs. 2 weeks after surgery. MI, Motility index.

jejunal interposition (16). However, jejunum interposition is complex and time-consuming because it requires at least three anastomoses. Since laparoscopic proximal gastrectomy for cancer arising in the upper third of the stomach requires a very complex technique, simple and less complicated reconstruction methods are needed. The use of a gastric tube made from the greater curvature of the stomach provides a simple and safe anastomosis for proximal gastrectomy because it is a single anastomosis. A technique for gastric tube reconstruction by open surgery that was designed to prevent esophageal reflux was first reported by Adachi *et al.* (17). They demonstrated that gastric tube reconstruction is superior to jejunal interposition because it is simple, safe, and less complex. We also reported that LPG with gastric tube reconstruction is a simple and safe technique for the treatment of proximal early gastric cancer (9). However, the physiological function of the residual stomach after proximal gastrectomy has not been clearly evaluated in humans.

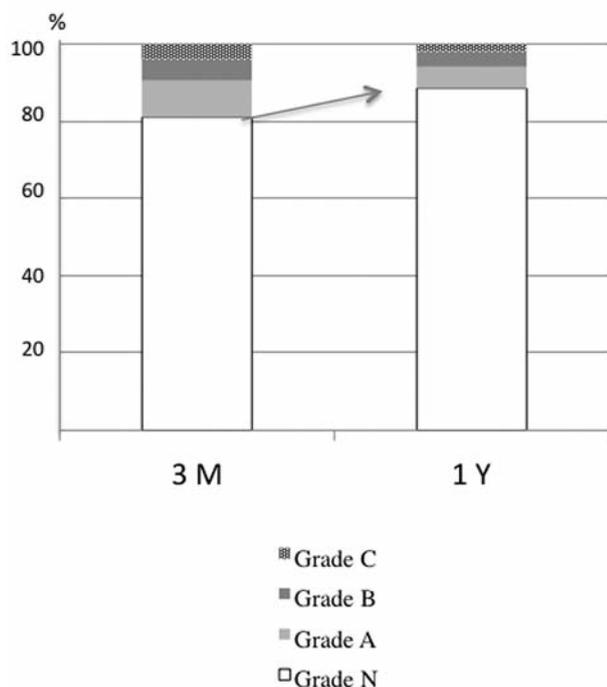


Figure 3. Findings of endoscopic examination. Reflux esophagitis was classified according to the Los Angeles classification.

Previous studies have shown that proximal gastrectomy is more likely to produce complications such as heartburn and reflux esophagitis and to worsen nutritional status compared to other types of gastrectomy (18). Katsoulis *et al.* reported that 100% of patients experienced reflux symptoms after proximal gastrectomy(3), and Kim *et al.* reported that the rate of reflux esophagitis was 48% (19). The removal of anti-reflux barriers by proximal gastrectomy facilitates the backward flow of gastric contents, subsequently leading to regurgitation or reflux esophagitis. Manometric investigations showed that interdigestive gastrointestinal motility gradually recovered with time after proximal gastrectomy. The number of patients with reflux esophagitis decreased 1 year after surgery compared to that after 1 month. The grade of reflux esophagitis 1 year after surgery was also milder than that 1 month after surgery. Furthermore, the motor activity of the gastric tube was significantly lower in patients with reflux esophagitis than in those without reflux esophagitis. These results suggest that good intestinal motility after proximal gastrectomy has an important role in decreasing reflux into the esophagus. Abnormal gastric-tube motility can lead to post-gastrectomy disorders such as esophageal reflux. We believe that the risk of reflux esophagitis might decrease with time due to the recovery of gastrointestinal motility after proximal

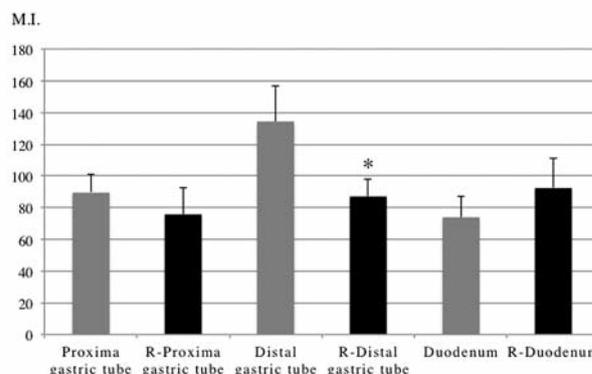


Figure 4. Gastroduodenal motor activity of patients with (■) or without (▒) reflux esophagitis. R-, reflux esophagitis. * $p < 0.05$ vs. distal gastric tube. MI, Motility index.

gastrectomy. In the fasting state, phase III seems to be the most important motor activity because indigestible food particles and gastric juice are emptied from the gastric tube into the small intestine during this phase. A paucity of phase III seems to result in stasis in the gastric tube. Phase III is the period during which the most important contractions occur in the interdigestive state. The gastric contents must be emptied to prevent esophageal reflux. In the present study, the incidence of phase III 1 year after surgery was significantly higher than that 2 weeks after surgery. Furthermore, the number of patients with reflux esophagitis decreased 1 year after surgery. These findings suggest that phase III plays an important role in preventing reflux esophagitis.

Pyloric function involves a complex mechanism for clearance of gastric contents, coordinated with the peristaltic movement of the stomach and prevention of bile reflux into the stomach. Whether pyloroplasty is required after proximal gastrectomy to prevent postoperative symptoms such as reflux esophagitis remains a matter of debate. Although the motility of the pylorus was not measured in this study, several reports have suggested that pyloroplasty is required to prevent postoperative symptoms. Zhan *et al.* reported that pyloroplasty improves gastric emptying and decreases gastric stasis (20). Other studies have suggested that pyloroplasty relieves gastric distention and speeds up gastric emptying (21). As a draining procedure, pyloroplasty contributes to a lower incidence of complications such as gastric distention, nausea, and vomiting, and promotes faster gastric emptying. We performed pyloroplasty by the finger fracture method to partially maintain pyloric function. Our findings suggest that clearance of gastric contents from the gastric tube can decrease the risk of esophageal reflux, although further detailed evaluations are needed.

Conclusion

In patients who underwent proximal gastrectomy followed by reconstruction with a tube created from the denervated remnant stomach, the gastric tube was found to be a contractile organ. With time, the motor activity of the gastric tube recovered, and the incidence of reflux esophagitis decreased. The motor activity of the gastric tube was low in patients with reflux esophagitis.

Conflicts of Interest

Erito Mochiki, Minoru Fukuchi, Kyouichi Ogata, Tetsuro Ohno, Hideyuki Ishida, and Hiroyuki Kuwano have no conflicts of interest or financial ties to disclose.

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