Editorial

Replacement of laparoscopic total gastrectomy with laparoscopic proximal gastrectomy for upper early gastric cancer

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In accordance with the increased incidence of proximal early gastric cancer (EGC), particularly in Asian countries (1,2), the demand for proximal gastrectomy (PG) as a function-preserving surgery continues to escalate. Although PG offers numerous potential advantages in preserving the physiological function of the remnant stomach, a complicated reconstructive procedure is required to restructure the anti-reflux mechanism to prevent reflux esophagitis (3,4). Among the three main reconstruction methods, esophagogastrostomy (EG) is performed more often than double-tract reconstruction (DTR) and jejunal interposition (JI) (3,4); this is owing to its relative simplicity, although an optimal reconstructive procedure is yet to be established. With the recent advances in laparoscopic techniques and the expanded indications for laparoscopic gastrectomy for the treatment of proximal EGC, the number of reports of novel reconstructive procedures for laparoscopic PG (LPG) with EG has been rapidly increasing over the past few years (5-11). However, these reports have focused on technical aspects and surgical outcomes rather than on long-term quality of life (QOL), which remains unclear.

Recently, Nishigori *et al*. reported the institutional standardization of laparoscopic gastrectomy even for gastric cancer (GC) located in the upper third stomach; this is because of the advantages of LPG, unlike laparoscopic total gastrectomy (LTG), in preventing postoperative weight loss and in improving QOL in patients with stage I GC (12). In a single-institution retrospective comparative study, 42 patients with stage I GC underwent LTG followed by Roux-en-Y reconstruction with functional end-to-end esophagojejunal anastomosis (13), whereas to fix the distal esophagus to the gastric anterior wall, 20 GC patients underwent LPG followed by EG with a hand-sewn esophagogastric anastomosis and fundoplication using a knifeless endoscopic linear stapler (14). Although there was no significant difference in the incidence of early complications between these two groups, anastomotic stricture more frequently occurred in the LPG group (25%) than in the LTG group (0%). Although there was no significant difference in the incidence of grade ≥ B postoperative reflux gastritis based on the Los Angeles classification criteria between the two groups (5% and 2%, respectively), the percentage of weight loss at 12 months was lower in the LPG group than that in the LTG group (–10.7% *vs.* –16.3%, respectively). Furthermore, multivariate analysis revealed that LPG was associated with less body weight loss (12). Patient responses to a questionnaire survey using the Postgastrectomy Syndrome Assessment Scale (PGSAS)-45, which was distributed >1 year after operation, showed that the incidences of diarrhea and dissatisfaction with symptoms were better with LPG than those with LTG. However, this survey was limited to 17 patients who underwent TG and 11 who

underwent PG (12). There were three main limitations to this study: the retrospective design, small sample size, and only a single assessment time point in the questionnaire survey. Collectively, LPG for patients with proximal EGC offers several advantages over LTG, including less postoperative body weight loss, fewer diarrhea symptoms, and better QOL; however, anastomotic stricture occurred more frequently.

This study is of great value as the subjective symptoms were examined based on a patient-oriented survey using the PGSAS-45, which was designed to assess the severity of symptoms, living status, and QOL of the gastrectomized patients (15). Although many previous studies have mainly focused on body weight loss as an indicator of long-term nutritional status following LPG (3,4), Nishigori *et al*. successfully demonstrated that LPG is superior to LTG in terms of diarrhea and dissatisfaction with symptoms, and in maintaining body weight after operation. Overall, body weight loss after gastrectomy is induced by a reduction in gastric reservoir capacity and decrease in the number of various digestive hormones, including appetite hormone ghrelin, which lead to appetite loss, inadequate oral nutritional intake, alternation of intestinal flora, and increased peristalsis and diarrhea (3). Hence, further investigations with larger sample sizes using the study approach described by Nishigori *et al*. are warranted to clarify the association between postoperative body weight loss and QOL-related factors.

In contrast, the technical feasibility of LPG remains problematic. According to the results of a retrospective survey conducted by the Japan Society for Endoscopic Surgery, 19.7% of the patients developed LPG-associated postoperative complications with anastomotic stenosis being the most common at 6.5% (16). Particularly with LPG and EG reconstruction, anastomotic stricture is considered a major postoperative complication (range, 0–28.6%) (4-11). Nishigori *et al*. also reported that the anastomotic stricture occurred at a relatively high incidence of 25% although the rate of Clavien-Dindo grade III early complications was only 5% (12). The stricture itself directly induces dysphagia, chest discomfort, and eating disorders among other complications, resulting in deterioration in QOL. Additionally, our previous report demonstrated that anastomotic complications after laparoscopic gastrectomy, such as leakage and stricture, led to inferior long-term survival rates of patients with histologically proven T1 gastric adenocarcinoma (17). Hence, it may be necessary to overcome this high incidence of postoperative anastomotic stricture to further improve QOL and long-term survival.

Regarding the other essential issues directly related to QOL after LPG, Nishigori *et al*. reported that reflux esophagitis and grade ≥ B postoperative reflux esophagitis occurred in 5% of the patients in the LPG group (12). This result seems to be favorable as compared with a previous report on the incidence of these complications occurring at a rate of 12.5–30.8% after LPG and EG (4). This relatively low incidence may be due to restructuring of the artificial angle of His and fornix by fixation of the left side of the esophagus to the anterior gastric wall using a knifeless linear stapler (14). Conversely, grade A reflux esophagitis occurred in 20% of the patients. This finding suggests that this reconstruction method can potentially compromise QOL due to symptoms associated with reflux esophagitis. Recently, as an ideal reconstruction method to potentially reproduce the physiological anti-reflux mechanism, valvuloplastic EG (VEG) with a double flap technique (DFT) was developed (6-9). In this procedure, the distal esophagus and the site of anastomosis are implanted in the submucosal layer, and the anterior side of the anastomosis is completely covered by a seromuscular double flap. These structures and intragastric pressure generate a pressure gradient between the esophagus and stomach, substituting as a one-way valve (18). In fact, these studies demonstrated that the incidence of grade ≥ B reflux esophagitis was only 0–5% (6-9), although most included only small-scale, single-center experiences. However, this procedure requires complicated suturing and ligation. Additionally, the rate of anastomotic stricture reportedly is as high as 4.7–29.1%, particularly before attaining a learning plateau (6-9). Hence, the complexity and technical difficulty of VEG-DFT are obstacles to the standardization of this reconstructive procedure after LPG. Therefore, the technical difficulty and complexity of EG must be further improved.

LPG has great potential as a radical procedure for esophagogastric junction (EGJ) cancer. According to the Japanese gastric cancer guidelines 2014, PG, and not TG, is recommended considering the optimal extent of lymphadenectomy for junctional cancer of ≤4 cm in diameter centered within 2 cm of the EGJ (19). Several recent studies have demonstrated that low body mass index and sarcopenia were independent predictive factors of the short- and long-term outcomes of gastrectomized patients, particularly those with advanced cancer requiring multidisciplinary therapy (20-22). Therefore, avoiding TG can possibly prevent postoperative severe body weight loss of patients with advanced EGJ cancer, leading to improved

QOL and survival outcomes. However, no optimal reconstructive procedure following PG for EGJ cancer has yet been established as for upper EGC. Particularly in patients with EGJ cancer, the anastomotic procedure is often intra-mediastinally performed to secure an oral cancer-free margin. Therefore, JI or DTR is preferred considering the safety of an anastomotic procedure rather than EG, which is complicated with a high risk of reflux esophagitis and involves a larger surgical field. However, JI and DTR require a greater number of anastomoses; therefore, the anastomotic time is longer than with EG, and the long-term reservoir function of the remnant stomach after these reconstructive methods remains unclear. Therefore, the merits and demerits of EG, JI, and DTR should be cautiously considered on a case-by-case basis while selecting an optimal reconstruction method. The knowledge gained from further studies focused on the long-term function of the remnant stomach with each of these reconstructive procedures after PG would be indispensable.

Two points are particularly important to consider while selecting LPG as a replacement for LTG. First, the exact incidence of anastomotic complications in LPG must be surveyed in large-scaled prospective studies. In Japan, a nonrandomized confirmatory trial was commenced in April 2015 (Japan Clinical Oncology Group Study JCOG1401, UMIN000017155) to evaluate the safety of LTG and LPG for clinical stage I GC with the incidence of anastomotic leakage as the primary endpoints and other perioperative and long-term outcomes as the secondary endpoints (23). This study reveals the actual incidence of anastomotic complications and the safety and feasibility of LPG, although the reconstructive procedure is limited to JI or DTR. Moreover, the findings of this study are expected to help define the standards to examine the safety of EG reconstruction. Second, the application of robotic surgery can potentially relieve the technical complexity and difficulty of VEG-DFT because the use of a robotic system can facilitate precise performance in a confined surgical field with impressive dexterity through several technical properties, including stereoscopic vision, the use of wristed micro-surgical instruments and tremor filtration, and the ability to scale motion (24,25). In fact, we previously reported favorable short-term outcomes and an early learning curve with the use of robotic-assisted VEG-DFT (18). Additionally, an ideal reconstructive procedure after PG with fewer complications and a lower risk of reflux esophagitis is expected to be recognized with the full utilization of a robotic system.

In conclusion, LPG with EG reconstruction has great potential to become a remarkable, function-preserving, standard, surgical procedure for patients with upper EGC and EGJ cancer once the risks of anastomotic stricture and reflux gastritis are resolved.

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Footnote

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