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Laparoscopic proximal gastrectomy with jejunal interposition for gastric cancer in the proximal third of the stomach: a retrospective comparison with open surgery

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Abstract
Background The incidence of cancer in the proximal third of the stomach is increasing. Laparoscopic proximal gastrectomy (LPG) seems an attractive option for the treatment of early-stage proximal gastric cancer but has not gained wide acceptance because of technical difficulties, including the prevention of severe reflux. In this study, we describe our technique for LPG with jejunal interposition (LPG-IP) and evaluate its safety and feasibility.
Methods In this retrospective analysis, we reviewed the data of patients with proximal gastric cancer who underwent LPG-IP ($n = 22$) or the same procedure with open surgery (OPG-IP; $n = 68$) between January 2008 and September 2011. Short-term surgical variables and outcomes were compared between the groups. The reconstruction method was the same in both groups, with creation of a 15 cm, single-loop, jejunal interposition for anastomosis.
Results There were no differences in patient or tumor characteristics between the groups. Operation time was longer in the LGP-IP group (233 vs. 201 min, $p = 0.0002$) and estimated blood loss was significantly less (20 vs. 242 g, $p < 0.0001$). The average number of harvested lymph nodes did not differ between the two groups (17 vs. 20). There also were no differences in the incidence of leakage at the esophagojejunostomy anastomosis (9.1 vs. 7.4 %) or other postoperative complications (27 vs. 32 %). The number of times additional postoperative analgesia was required was significantly less in the LPG-IP group compared with the OPG-IP group (2 vs. 4, $p < 0.0001$).
Conclusions LPG-IP has equivalent safety and curability compared with OPG-IP. Our results imply that LPG-IP may lead to faster recovery, better cosmesis, and improved quality of life in the short-term compared with OPG-IP. Because of the limitations of retrospective analysis, a further study should be conducted to obtain definitive conclusions.

Keywords Proximal gastrectomy · Laparoscopic surgery · Jejunal interposition · Gastric cancer

The safety and efficacy of laparoscopic gastrectomy for the treatment of early gastric cancer have been demonstrated in many clinical studies [1–3]. An increasing number of laparoscopic gastrectomies are currently being performed, especially in eastern countries, which have high incidences of gastric cancer. Because gastric cancer has predominantly been located in the distal stomach in eastern countries, laparoscopic distal gastrectomy for cancer in the middle and distal stomach has been the more commonly performed surgical procedure. However, Japanese surgeons are confronted with an increasing number of gastric cancers involving the proximal third of the stomach, probably because of the aging population. For advanced cancer in the proximal third of the stomach, total gastrectomy with D2 lymph node dissection is standard in Japan [4]. For early-stage cancer in the proximal third, open proximal gastrectomy has been performed to preserve physiological function of the remaining stomach [5–7]. Early cancer is estimated to account for nearly 50 % of gastric cancer currently diagnosed in Japan [8]. In this context,

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laparoscopic proximal gastrectomy (LPG) is likely to be performed with increasing frequency in the near future, if the operative technique becomes well established.

The most difficult technical aspect of LPG may be the anastomosis and reconstruction method, which should prevent reflux esophagitis. Several authors have already reported novel techniques using various reconstruction methods, but an optimal method has not been established. Jejunal interposition acts as a substitute sphincter, which seems to be ideal for the prevention of postoperative reflux from the remnant stomach, but it is not widely used because of the difficulty of performing the complicated anastomotic procedures laparoscopically.

At our institution, open proximal gastrectomy with jejunal interposition (OPG-IP) has been performed since 1992, and LPG with jejunal interposition (LPG-IP) was introduced in 2010. In the present study, we describe our techniques and initial experiences with LPG-IP in the treatment of proximal gastric cancer and evaluate the safety of this approach through a retrospective data review comparing our results with the open procedure.

Methods

This retrospective study reviewed the records of gastric cancer surgery patients at the National Cancer Center Hospital East, Chiba, Japan. From August 1992 to September 2011, 298 proximal gastrectomies for gastric cancer were performed at our institution. OPG-IP was performed until August 2010, and from September 2010 LPG-IP was performed. We retrospectively compared surgical data of the patients who underwent LPG-IP until September 2011 ($n = 22$) with those who underwent OPG-IP with the same reconstruction procedures between January 2008 and August 2010 ($n = 68$; Fig. 1). The decision whether to perform OPG-IP or LPG-IP was based purely on the time period during which the operation was undertaken.

Patients were selected for proximal gastrectomy if they were diagnosed with T1N0M0 gastric cancer located in the proximal third of the stomach, and it was estimated that the distal half of the stomach could be preserved. Preoperative assessment was by gastroendoscopy, abdominal ultrasonography, barium swallow radiography, and computed tomography. After surgery, baseline analgesia was administered to all patients by continuous epidural infusion of ropivacaine plus fentanyl for 2 days, with additional analgesia administered if requested by the patient. Perioperative and postoperative management protocols (clinical pathways) were amended over time, and the length of hospital stay recommended by the protocol was progressively shortened. The latest clinical pathway was adopted in April 2009 and allows patients to start drinking on

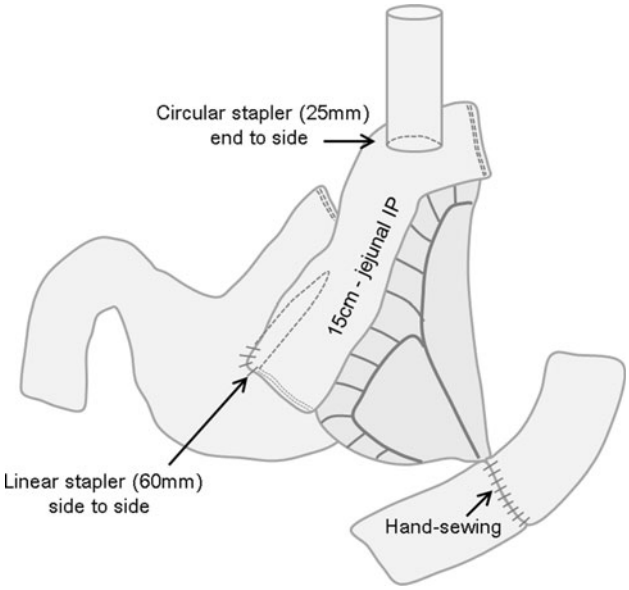

Fig. 1 Schematic of the completed reconstruction

postoperative day (POD) 1 and eating on POD 3 if there are no signs of major complications. Patients may be discharged from POD 8 if they are able to tolerate at least 50 % of a normal diet without fever, pain, or vomiting.

The following variables were recorded by retrospective review of the medical records: age, sex, body mass index (BMI), presence of comorbidity, tumor characteristics, operation time, estimated blood loss, number of times additional analgesia was administered, postoperative complications, number of harvested lymph nodes, and histological findings. To exclude differences due to changes in clinical pathways, parameters reflecting postoperative recovery, such as the time to first drinking or eating and time to hospital discharge, were compared only among patients who underwent surgery from April 2009 to September 2011: 22 patients in the LPG-IP group and 32 patients in the OPG-IP group. Postoperative complications were classified using the Dindo-Clavien classification [9], and complications were classified as grade II or higher were recorded. The extent of lymph node dissection followed the guidelines of the Japanese Gastric Cancer Association [10]. Staging was according to the 7th edition UICC TNM classification. Endoscopy was performed 6 months after surgery to evaluate reflux esophagitis and bile juice reflux into the interposed jejunum.

Surgical procedures for LPG-IP

The patient was placed in the supine position with legs apart. After placement of five trocars (Fig. 2), laparoscopic procedures were performed under a 10 mmHg CO_2 pneumoperitoneum. Mobilization of the stomach and *en bloc* systematic lymph node dissection were performed

laparoscopically. Esophagojejunostomy and jejunogastrostomy were performed laparoscopically, and creation of the jejunal interposition and jejunojejunostomy were performed via minilaparotomy. The distal half of the stomach, the greater omentum, and the spleen were preserved. The suprapancreatic lymph nodes (nos. 7, 8a, 9, and 11p) (Fig. 3A) and the lymph nodes around the cardia (nos. 1 and 2), the lesser curvature (no. 3), and the greater curvature (nos. 4sa and 4sb) were excised. The hepatic and pyloric branches of the vagal nerve were preserved on a case-by-case basis, and pyloroplasty was not performed. After mobilization of the proximal stomach, a detachable intestinal clip was placed on the abdominal esophagus as proximally as possible, and the esophagus was transected using an endoscopic linear stapler. A 5 cm transverse minilaparotomy incision was made in the upper left abdominal wall, and a wound retractor (Alexis Wound Retractor S; Applied Medical, Rancho Santa Margarita, CA) was inserted. The proximal-middle stomach was delivered via the minilaparotomy incision to determine the resection line by palpation of the marking clips placed during preoperative gastroendoscopy, and the stomach was then transected along the planned resection line using a linear stapler. The pneumoperitoneum was reestablished to find the ligament of Treitz, and the proximal jejunum was delivered via the minilaparotomy incision. A single-loop jejunal interposition (15 cm in length) was created approximately 20 cm from the proximal end of the jejunum (Fig. 3B). At the oral side of the jejunal interposition, the mesentery was divided vertically for approximately 7 cm, ligating the marginal artery. At the anal side of the jejunal interposition, the mesentery was divided along the intestine, sacrificing a 10 cm length of jejunum, similar to the procedure reported by Katai et al. [7]. Jejunojejunostomy was performed by hand via the minilaparotomy in an end-to-end fashion using the Gambee method. The mesenteric gap was sutured closed. The pneumoperitoneum was reestablished, and the anvil head of a 25 mm circular stapler (ECS; Ethicon Endosurgery, Cincinnati, OH) was fixed to the distal esophageal stump transabdominally after performing an intracorporeal handsewn pursestring suture via laparoscopy, as previously described by us for laparoscopic total gastrectomy [11]. The main body of the circular stapler was introduced into the jejunal interposition via its oral end and inserted into the abdomen through a surgical glove attached to the wound retractor to prevent the air leakage. The jejunal interposition was brought up in either antecolic or retrocolic fashion depending on the volume of adipose tissue in each case. Esophagojejunostomy was performed laparoscopically in an end-to-side fashion (Fig. 3C), and the oral stump of the interposed jejunum was closed by using an endoscopic linear stapler. A small opening was created on the anterior wall of the remnant stomach, and another small opening was created at the anal-side stump of the jejunal interposition. These openings were anastomosed in a side-to-side fashion using a 60 mm endoscopic linear stapler to form the jejunogastrostomy (Fig. 3D), and the entry hole for the stapler was closed by hand suturing. The esophagojejunostomy anastomosis was immersed in normal saline and tested for leaks by infusing air into the pouch lumen via a nasogastric tube and looking for escaping bubbles.

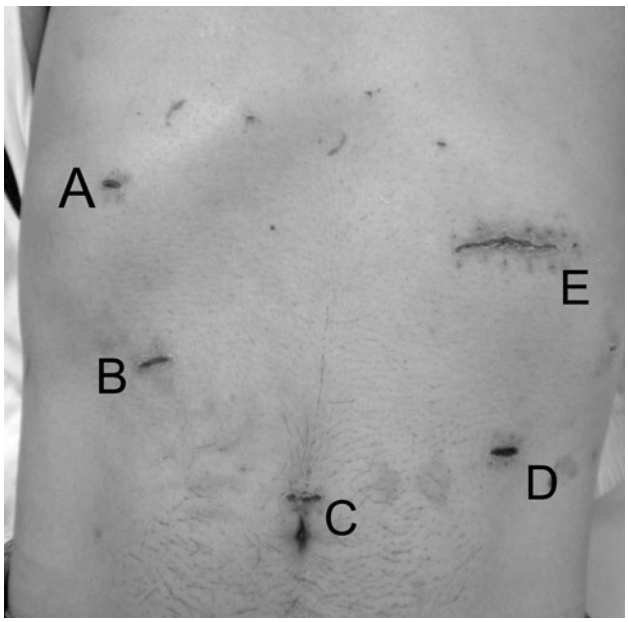

Fig. 2 Photo of the postoperative scars, indicating the placements of surgical ports. 5 mm ports were used at *A* and *D*, and 12 mm ports were used at *B*, *C*, and *E*. Port *E* was extended for the 50 mm minilaparotomy

Surgical procedures for OPG-IP

The same procedures as described above, including the same range of lymph node dissection and the same reconstruction method, were performed via an upper midline abdominal incision.

Statistical analysis

Statistical analyses were performed by using Student's *t* test, χ^2 test, or Fisher's exact probability test. A value of $p < 0.05$ was regarded as significant. All statistical analyses were performed by using Statistical Package for Social Science (SPSS) version 17.0 for Windows software (SPSS, Inc., Chicago, IL).

Results

A total of 90 proximal gastrectomies, including 22 LPG-IP procedures and 68 OPG-IP procedures, were included in

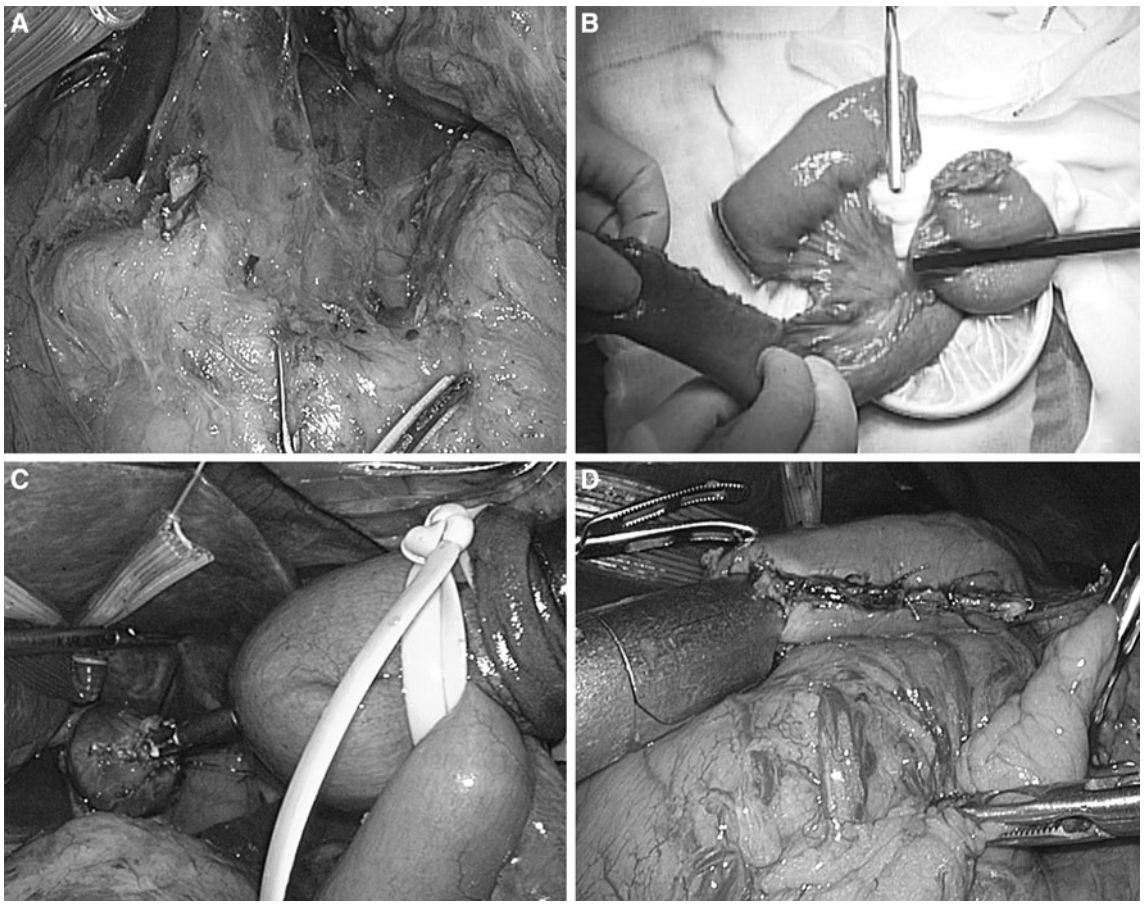

Fig. 3 **A** After lymph node dissection around the celiac artery. **B** Creation of the jejunal interposition via minilaparotomy. **C** Intracorporeal esophagojejunostomy using a *circular stapler*. **D** Intracorporeal jejunogastrostomy using a *linear stapler*

this study. No conversion to open surgery was recorded in the LPG-IP series. Patient characteristics are summarized in Table 1. There were no significant differences in age, sex, BMI, or presence of comorbidity between the two groups. Six patients (27 %) in the LPG-IP group and 15 patients (22 %) in the OPG-IP group underwent endoscopic submucosal resection before surgery and proceeded because pathological examination of specimens showed submucosal invasion or vessel infiltration, indicating the need for radical surgery with lymph node dissection. In the LPG-IP group, the jejunal interposition was brought up in antecolic fashion in 10 patients and in retrocolic fashion in 12 patients, and in the OPG-IP group the jejunal interposition was brought up in antecolic fashion in 21 patients and in retrocolic fashion in 47 patients, according to the surgeons' preferences and decisions. These proportions were not significantly different between groups.

Operation details are shown in Table 2. The operation time was significantly longer in the LPG-IP group (233 (range, 190–321) min) compared with the OPG-IP group (201 (range, 125–272) min; $p = 0.0002$), and the estimated blood loss was significantly less in the LPG-IP group (20 (range, 0–174) g) compared with the OPG-IP group (242 (range, 75–776) g; $p < 0.0001$). There was no difference in the number of harvested lymph nodes between the two groups. Pathological findings are shown in Table 2. There were no differences in the T factor, N factor, or TNM staging between the two groups. A negative surgical margin was achieved in all cases. The rate of accurate preoperative diagnosis in this study was 78.9 %.

Parameters for postoperative recovery are shown in Table 3. First drinking was on POD 1 and first eating was on POD 3 in both groups. Hospital discharge was on POD 11 in the LPG-IP group and on POD 10 in the OPG-IP group, which was not a significant difference. This indicates that most patients followed the planned clinical pathway. However, the number of times that additional analgesia was administered was significantly less in the LPG-IP group (2, range 0–5) compared with the OPG-IP group (4, range 0–9; $p < 0.0001$).

Postoperative complications in the two groups are listed in Table 4. The incidence rate of postoperative complications was not significantly different between the two groups (27 % in the LPG-IP group vs. 32 % in the OPG-IP group).

Table 1 Summary of patients with gastric cancer treated by laparoscopic and open proximal gastrectomy

	LPG-IP ($n = 22$)	OPG-IP ($n = 68$)	p value
Age (years)	64.3 ± 11.6	65.5 ± 9.0	NS
Sex (male/female)	18/4	52/16	NS
BMI	22.8 ± 3.3	22.4 ± 3.2	NS
ESD before surgery (yes/no)	6/16	15/53	NS
Comorbidity			
Absent/present	13/9	34/34	NS
Hypertension	5	20	
Diabetes mellitus	4	13	
COPD	1	1	
Arrhythmia	0	3	
Cardiac angina	2	1	
Other	0	2	

LPG-IP laparoscopic proximal gastrectomy with jejunal interposition, *OPG-IP* open proximal gastrectomy with jejunal interposition, *ESD* endoscopic submucosal dissection, *NS* not significant

Values are mean ± standard deviation

Table 2 Surgical and pathological findings in laparoscopic and open proximal gastrectomy

	LPG-IP ($n = 22$)	OPG-IP ($n = 68$)	p value
Operation time (min)	233 (190–321)	201 (125–272)	0.0002
Blood loss (g)	20 (0–174)	242 (75–776)	<0.0001
No. of dissected lymph nodes	17 (10–32)	20 (10–44)	NS
pT stage			NS
pT1a (M)	5	22	
pT1b (SM)	11	32	
pT2	4	5	
pT3	1	7	
pT4	1	2	
pN stage			NS
pN0	18	58	
pN1	2	8	
pN2	2	2	
TNM stage			NS
IA	16	50	
IB	1	9	
IIA	1	3	
IIB	2	2	
IIIA	2	4	

NS not significant

Values are median (range)

Table 3 Postoperative recovery after laparoscopic and open proximal gastrectomy using the current clinical pathway

	LPG-IP ($n = 22$)	OPG-IP ($n = 32$)	p value
Time to first drinking (POD)	1 (1–7)	1 (1–20)	NS
Time to first eating (POD)	3 (3–10)	3 (3–27)	NS
Time to hospital discharge (POD)	11 (7–32)	10 (7–34)	NS
Additional analgesia (number of times)	2 (0–5)	4 (0–9)	<0.0001

POD postoperative day, *NS* not significant

Values are median (range)

Anastomotic leakage occurred in two patients (9.1 %) in the LPG-IP group and five patients (7.4 %) in the OPG-IP group, all of which occurred at the esophagojejunostomy anastomosis. Among them, one patient in the LPG-IP group developed a grade II pancreatic fistula followed by secondary anastomotic leakage. One patient in the OPG-IP group with a major leakage required emergency reoperation via a thoracoabdominal approach for drainage (grade IIIb), but other patients were treated conservatively. Intra-abdominal hemorrhage requiring reoperation occurred in two patients in the OPG-IP group, and one patient required reoperation (grade IIIb). Anastomotic stricture at the esophagojejunostomy anastomosis occurred in two patients (9.1 %) in the LPG-IP group and four patients (5.9 %) in the OPG-IP group. All of these patients were successfully treated by outpatient endoscopic balloon dilatation. No

Table 4 Postoperative complications after laparoscopic and open proximal gastrectomy

	LPG-IP ($n = 22$)	OPG-IP ($n = 68$)	p value
Absent/present	16/6 (27 %)	46/22 (32 %)	NS
Wound infection, n	2 (9.1 %) grade II	6 (8.8 %) grade II	
Anastomotic leakage, n (%)	2 (9.1 %) grade II	5 (7.4 %) 4 grade II, 1 grade IIIb	
Intra-abdominal hemorrhage, n (%)	0	2 (2.9 %) 1 grade II, 1 grade IIIb	
Pancreatic fistula, n (%)	1 (4.5 %) grade II	1 (1.5 %) grade II	
Intra-abdominal abscess, n (%)	1 (4.5 %) grade II	2 (2.9 %) grade II	
Anastomotic stenosis, n (%)	2 (9.1 %) grade II	4 (5.9 %) grade II	
Cholecystitis, n (%)	0	2 (2.9 %) grade II	

NS not significant

Grade: according to Dindo-Clavien classification

patient complained of reflux symptoms after surgery, and there was no operation-related death. Follow-up endoscopy could be performed 20 of 22 patients (90.9 %) in the LPG-IP group and 61 of 68 patients (89.7 %) in the OPG-IP group. A small amount of bile juice reflux to the remnant stomach or interposed jejunum was observed in 25 % of patients, but esophagitis was recorded in only in one patient (1.1 %) in the OPG-IP group. Endoscopic survey of the remnant stomach was possible in all of the patients.

Discussion

The choice of reconstruction method following LPG remains controversial. Because the optimal method has not been established, a number of techniques are currently used. Most past reports describe direct esophagogastric anastomosis, probably because it is very simple and requires only one anastomosis [12–16]. In these reports, direct esophagogastrostomy was performed by using a linear or circular stapler, with the addition of antireflux measures, similar to Toupet fundoplication. However, it may be impossible to completely prevent reflux in direct esophagogastrostomy. Jejunal interposition has been recognized as a favorable method for preventing severe postoperative reflux and is widely performed in open surgery, but LPG-IP has not gained wide acceptance because of its technical complexities. These complexities include the creation of a pedicled jejunal limb and the requirement for three anastomoses. Until recently, very few reports have described the outcomes of LPG-IP. The first report was by Uyama et al. [17] and described their entirely laparoscopic LPG-IP technique, which they had performed in four cases. Their technique was excellent, but the mean operative time (614 min) was long. In 2002, Ikeda et al. [18] reported three cases of hand-assisted LPG-IP, which shortened operation time. However, no study has evaluated the feasibility and safety of these techniques in a larger series. As far as we know, this is the largest study to report the outcomes of LPG-IP to date and the first to compare the results with open surgery.

At our institution, OPG-IP has long been a standard procedure for the treatment of early-stage gastric cancer in the proximal third of the stomach, and it was therefore natural for us to adopt jejunal interposition to laparoscopic surgery. Our results show that LPG-IP can be performed safely with an equivalent complication rate compared to open surgery. We did not experience any case with symptomatic postoperative reflux. Operation time was longer in laparoscopic surgery than in open surgery, but this difference was approximately 30 min and seems acceptable for a routine surgical procedure. In our procedure, transection of the stomach, creation of the jejunal interposition, and subsequent jejunojejunostomy were performed via minilaparotomy under direct vision, which might have contributed to time-saving. The proximal jejunum was easily delivered via the upper left abdominal incision, and the subsequent creation of the jejunal limb and jejunojejunostomy anastomosis also were easy. The other anastomoses (esophagojejunostomy and jejunogastrostomy) and systematic lymphadenectomy were performed laparoscopically, because laparoscopy provides better vision for these procedures than open surgery regardless of the size of the patient or the thickness of the abdominal wall. The shortened operation time also might be partly due to advancements in instrumentation and skills, because laparoscopic distal gastrectomy is frequently performed in our institution.

Postoperatively, leakage of the esophagojejunostomy anastomosis occurred in two patients (9.1 %) in the LPG-IP group and five patients (7.4 %) in the OPG-IP group. These incidences seem relatively high compared with other reports, which cannot be ignored. In one patient in the LPG-IP group, the pancreatic fistula caused the secondary anastomotic leakage. However, we were not able to determine the reasons for anastomotic leakage in the other patients. The high incidence may reflect the complexity of the jejunal interposition rather than the technical complexity of laparoscopic surgery, because the incidence was relatively high in both groups. This procedure has several different points from a Roux-en-Y anastomosis in total gastrectomy, which may be causes of tension to the interposed jejunum. We speculate that these tensions may influence the esophagojejunostomy. One possible cause of tension is a large feeding artery in a pedicle of the interposed jejunum, because we always make a large artery remain in the pedicle expecting sufficient blood supply. It seems that the retrocolic route may cause less tension when using a pedicled jejunum, but we experienced anastomotic leakage in four patients using the antecolic route and three using the retrocolic route, so the route did not appear to make a difference in this series. Another possible cause of tension to the interposed jejunum may be the remnant stomach, which is also a different point from Roux-en-Y. This tension is likely to be caused if the length of the interposed jejunum is short. We have believed that the 15 cm length interposed jejunum is ideal for the prevention of reflux esophagitis and for postoperative endoscopic survey, but there is not sufficient evidence to determine this definitively. Evaluation of a larger number of cases is required before the reasons for anastomotic leakage can be concluded. Our LPG-IP sample size was small, and it is possible that the incidence rate may be improved following an increase in patient numbers and surgical experience.

The incidence of stenosis at the esophagojejunostomy anastomosis was 9.1 % in the LPG-IP group and 5.9 % in

the OPG-IP group. The tendency for stenosis in open proximal gastrectomy has been reported; Katai et al. [19] reported an incidence of 6.3 %. The incidences recorded in this study seem higher than for total gastrectomy, in which esophagojejunal anastomosis is performed in the same manner [20]. The reason for this is unclear, but it is speculated that the small amount of reflux after partial gastrectomy causes stenosis [14]. We observed a small amount of bile reflux to the interposed jejunum in 25 % of patients on postoperative endoscopy. Stenosis also may be caused by tension to the interposed jejunum as mentioned above. The patients with stenosis were successfully treated by outpatient endoscopic balloon dilatation.

Pancreas-related complications are sometimes experienced in gastric cancer surgery, even when the pancreas is not obviously injured during lymph node dissection. This is probably due to thermal injury by surgical devices or retraction of the pancreas to obtain a better view around the celiac artery. One patient in the LPG-IP group developed a grade II pancreatic fistula, even though no pancreatic injury was recognized intraoperatively. As a result, this patient developed secondary anastomotic leakage. It is important to be conscious of handling the pancreas gently during lymph node dissection.

The relative invasiveness of the procedures is difficult to determine based only on our retrospective study with limited case numbers. Blood loss was significantly less in the LPG-IP group, with the difference being in excess of 200 g. This might be associated with more meticulous laparoscopic techniques due to the magnified view. Time to first drinking, time to first eating, and time to hospital discharge did not differ between the two groups, because the management protocol was same in both groups. However, the requirement for additional analgesia was significantly less in the LPG-IP group. Finally, the cosmetic result is unquestionably better in the LPG-IP group. These results suggest that LPG-IP may have a number of benefits, including a better postoperative quality of life.

Several oncological parameters were evaluated, although they were limited to short-term outcomes. The number of harvested lymph nodes was similar between the two groups, and the median number for both groups was more than 15, which is the number suggested for adequate resection in the American Joint Committee on Cancer guidelines. A negative surgical margin was achieved in all cases. These data suggest that LPG-IP is at least equivalent to OPG-IP in short-term oncological outcomes. The preoperative diagnosis of invasion depth is sometimes underestimated, and in our series some patients were finally diagnosed as T2 or T3, even though their preoperative diagnosis was T1. The rate of accurate preoperative diagnosis in this study was 78.9 %. This suggests that lymph node dissection in proximal gastrectomy should be performed to the level of the celiac trunk (nos. 7, 8a, 9, 11p), which we were able to achieve laparoscopically. Ideally, a more accurate preoperative diagnostic method for depth of invasion should be established.

In conclusion, our initial case series demonstrated that our technique for LPG-IP is technically feasible and safe, and provides similar curability and outcomes to open surgery in the short-term. Our study is limited by its retrospective nature, small number of patients, and short-term follow-up. In this kind of function-preserving surgery, long-term outcomes should be evaluated, including the patients' quality of life. Another large-scale study evaluating long-term outcomes is necessary to confirm these findings.

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