Short-term outcomes and nutritional status after laparoscopic subtotal gastrectomy with a very small remnant stomach for cStage I proximal gastric carcinoma

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Abstract

Background Total or proximal gastrectomy is usually performed for early proximal gastric carcinoma, but the optimal type of gastrectomy is still unknown. We evaluated short-term outcomes and nutritional status after laparoscopic subtotal gastrectomy (LsTG) in comparison with laparoscopic total gastrectomy (LTG) and laparoscopic proximal gastrectomy (LPG).

Methods We analyzed 113 patients who underwent LsTG ($n = 38$), LTG ($n = 48$), or LPG ($n = 27$) for cStage I gastric cancer located in the upper third of the stomach. Postoperative morbidities, nutritional status including body weight, serum albumin, hemoglobin, the prognostic nutritional index (PNI), and endoscopic findings at 1 year after surgery were compared between LsTG and both LTG and LPG.

Results Operation time and intraoperative blood loss were similar among the three groups. The incidence of postoperative morbidities was lower in LsTG than in LTG. The degree of body weight loss was significantly smaller in LsTG than in LTG at 6 and 12 months. At 12 months, LsTG resulted in better serum albumin and PNI than LPG, and better hemoglobin than LTG. Endoscopic examination demonstrated that one LsTG patient and two LPG patients had reflux esophagitis. Remnant gastritis was observed more frequently in LPG than in LsTG. No LsTG patient had bile reflux, although it was observed in four LPG patients.

Conclusions LsTG with a very small remnant stomach had favorable short-term outcomes and nutritional status

compared with LTG and LPG, so it may be a better treatment option for cStage I proximal gastric carcinoma.

Keywords Early gastric cancer · Proximal gastric carcinoma · Laparoscopic subtotal gastrectomy · Small remnant stomach

Background

Gastric cancer is still a common malignancy worldwide, and its incidence in the upper third of the stomach has been increasing [1–3]. Early gastric cancer in the upper third of the stomach is usually treated with total or proximal gastrectomy. Total gastrectomy (TG) provides more complete lymphadenectomy, has no risk of remnant gastric cancer, and is associated with a lower incidence of reflux esophagitis than proximal gastrectomy (PG) [4–6]. However, TG has many disadvantages from the nutritional aspect, such as postoperative body weight loss and anemia [7]. On the other hand, PG has several benefits compared to TG in terms of maintaining gastric hormones and gastric acid production resulting from preservation of the gastric antrum. However, reflux esophagitis is common after PG, and although various reconstruction methods have been suggested to reduce this problem, no standard procedure has yet been established [5, 7–11].

A recently reported procedure, laparoscopic subtotal gastrectomy (LsTG) with a very small remnant stomach, has demonstrated advantages in postoperative morbidities and nutritional status compared with laparoscopic TG (LTG) [12, 13]. One of the most important roles of LsTG is to preserve ghrelin, which is mainly produced in the fundic gland of the stomach [14]. Therefore, the preservation of the fundus but not the antrum may preserve nutritional status after

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gastrectomy. However, no studies have compared LsTG with laparoscopic PG (LPG), so there is still no consensus about whether LsTG is a viable treatment option for gastric cancer located in the upper third of the stomach. In the present study, we evaluated the short-term outcomes and nutritional status after LsTG in comparison with LTG and LPG.

Patients and methods

Patients

Eligible patients were those who underwent LsTG, LTG, or LPG for clinically diagnosed stage I gastric cancer located in the upper third of the stomach at Osaka University Hospital between January 2010 and July 2016. Clinical stage was classified according to the Japanese Classification of Gastric Carcinoma [15]. Exclusion criteria were as follows: double cancer involving the stomach and another organ, esophagogastric junctional cancer, conversion laparotomy, and emergency surgery cases. Among the eligible 113 patients, LsTG, LTG, and LPG were performed for 38, 48, and 27 patients, respectively. All patients received either D1+ or D2 lymphadenectomy according to the Japanese Gastric Cancer Treatment Guidelines [16]. In principle, patients with pStage II/III underwent adjuvant S-1 therapy (80–120 mg/body) for 1 year. This study was approved by the institutional review board of the Osaka University Hospital.

Surgical procedure

The surgical procedure (LsTG, LTG, or LPG) was determined based on tumor location and the patient's wishes. When a tumor was located within 2 cm of the esophagogastric junction (EGJ), LsTG was contraindicated, and LPG was contraindicated for tumors spreading to the gastric angle.

In this study, LsTG was defined, according to the previous study, as follows: (1) laparoscopic distal gastrectomy with Roux-en-Y reconstruction; (2) tumors located in or spreading to the upper third of the stomach; (3) a certain distance from the tumor to the EGJ remained but the distance was <5 cm; and (4) the remnant gastric stump was 2–3 cm from the EGJ [12]. Almost all LsTG cases required total resection of the lesser curvature of the stomach. However, at least one of the short gastric vessels near the cardia was preserved as blood supply to the remnant stomach. The resection line of the stomach in the LsTG procedure varied according to the location of the tumor (Fig. 1). We usually put the marking clips approximately 1 cm proximal to the tumor with confirmation of negative biopsy. In addition, the tumor location and marking clips were confirmed by using intraoperative endoscopy before resection, and intraoperative frozen section diagnosis was performed in some cases. A gastrojejunal antecolic anastomosis was created using a linear stapler or a 25-mm circular stapler. A side-to-side jejunojejunostomy was performed 30 cm distal from the gastrojejunal anastomosis.

In the LTG procedure, the antecolic esophagojejunostomy was performed using a 25-mm circular stapler for the purse-string suture method or a linear stapler for the overlap method, as previously reported [17]. A side-to-side jejunojejunostomy was then performed 45 cm distal from the esophagojejunal anastomosis.

In the LPG procedure, esophagogastric anastomosis or double-tract reconstruction was performed. An esophagogastric anastomosis was performed by anastomosing the abdominal esophagus with the anterior wall of the remnant stomach using a 25-mm circular stapler. For esophagogastric anastomosis cases, Toupet-like partial fundoplication was performed according to a previous report [18]. For double-tract reconstruction cases, esophagojejunostomy was performed using a 25-mm circular stapler or linear stapler as in the LTG procedure. A jejunogastrostomy was performed

Fig. 1 Variation in resection lines in laparoscopic subtotal gastrectomy (LsTG) for tumors located in the lesser curvature (a), anterior or posterior wall (b), and greater curvature (c)

using a linear stapler, with interposition of 15–20 cm of jejunum between the esophagojejunostomy and jejunogastrostomy. A side-to-side jejunojejunostomy was performed 20 cm distal from the jejunogastric anastomosis.

Outcomes

The short-term outcomes evaluated in this study were operation time, blood loss, and postoperative morbidities within 30 days after surgery. Postoperative morbidities were classified according to the Clavien–Dindo classification of surgical complications, and those of grade II or higher were recorded [19, 20]. Nutritional parameters after gastrectomy were assessed on the basis of changes in body weight, serum albumin, hemoglobin, and the prognostic nutritional index (PNI) at 1, 6, and 12 months after surgery. PNI was calculated using the following formula: $10 \times \text{serum albumin value (g/dl)} + 0.005 \times \text{lymphocyte count in peripheral blood}$. Endoscopic examinations were performed 1 year after surgery for patients who underwent LsTG or LPG to evaluate reflux esophagitis, gastritis, bile reflux, and the presence of residual food in the remnant stomach according to the RGB (residue, gastritis, bile) classification [21].

Statistical analysis

Statistical differences between the LsTG and the LTG/LPG groups were calculated with the chi-square test and Fisher's

exact test for categorical variables and with the Mann–Whitney *U* test for continuous variables. Postoperative changes in body weight and nutritional parameters were compared between the two groups by Student's *t* test. Statistical significance was defined as $P < 0.05$. The statistical analysis was performed using the JMP (version 11.0) software program (SAS Institute, Cary, NC, USA).

Results

Patient characteristics

The clinicopathological characteristics of patients who underwent LsTG, LTG, or LPG are detailed in Table 1. There were no significant differences in patient background between the LsTG and the LTG and LPG groups except for lymph node dissection (LsTG vs. LPG) and the type of stapler used for anastomosis (LsTG vs. both LTG and LPG). Thirteen patients in the LsTG group and 16 in the LTG group underwent D2 lymphadenectomy, and all patients in the LPG group underwent D1+ lymphadenectomy. Clinical and pathological stages were similar among all groups. Although there was no significant difference in the proportion of patients who received adjuvant chemotherapy, slightly more patients underwent adjuvant chemotherapy in the LsTG group than in the LPG group (16% vs. 4%). In the LPG group, 21 patients (78%) underwent double-tract

Table 1 Patient characteristics

	LsTG (<i>n</i> = 38)	LTG (<i>n</i> = 48)	<i>P</i> value for LsTG vs. LTG	LPG (<i>n</i> = 27)	<i>P</i> value for LsTG vs. LPG
Age, median (range)	65 (44–86)	63.5 (29–82)	0.209	70 (59–84)	0.124
Sex, male/female	26/12	35/13	0.811	22/5	0.268
BMI (kg/m ²), median (range)	22.6 (16.6–32.5)	22.2 (13.9–26.5)	0.972	22.8 (19.3–26.8)	0.299
ASA-PS, 1/2/3	18/18/2	30/16/2	0.371	8/18/1	0.303
Tumor location, Ant/Post/Gre/Less	5/10/5/18	10/12/5/21	0.818	2/8/1/16	0.475
Tumor size (mm), median (range)	30 (10–70)	32 (10–100)	0.309	25 (12–50)	0.305
Histological type, differentiated/undifferentiated	19/19	24/24	1.000	15/12	0.802
cT, T1/T2	33/5	40/8	0.767	26/1	0.388
cN, N0/N1	37/1	48/0	0.432	27/0	1.000
cStage, IA/IB	32/6	40/8	1.000	26/1	0.224
Lymph node dissection, D1+/D2	25/13	32/16	1.000	27/0	< 0.001
Stapler used for anastomosis, circular/linear	18/20	38/10	0.003	23/4	0.002
pT, T1/T2/T3–4	31/3/4	32/9/7	0.258	24/0/3	0.327
pN, N0/N1/N2–3	33/3/2	41/3/4	0.830	26/0/1	0.306
pStage, I/II/III	31/6/1	39/4/5	0.239	24/2/1	0.589
Adjuvant chemotherapy, yes/no	6/32	6/42	0.758	1/26	0.224

LsTG laparoscopic subtotal gastrectomy, *LTG* laparoscopic total gastrectomy, *LPG* laparoscopic proximal gastrectomy, *BMI* body mass index, *ASA-PS* American Society of Anesthesiologists physical status, *Ant* anterior wall, *Post* posterior wall, *Gre* greater curvature, *Less* lesser curvature

reconstruction and only 6 patients (22%) underwent esophago-gastric anastomosis.

Postoperative morbidity

Surgical results and postoperative morbidities are shown in Table 2. Neither operation time nor intraoperative blood loss was significantly different between the LsTG group and the LTG and LPG groups. Regarding postoperative morbidities within 30 days after surgery, the overall incidence was lower in the LsTG group than in the LTG group (11% vs. 31%, $P = 0.035$). The incidences of anastomotic leakage and intraabdominal abscess were higher in the LTG group, but not significantly so. On the other hand, there were no significant differences in postoperative morbidities between the LsTG and LPG groups (11% vs. 19%, $P = 0.472$). There were no deaths consequent to surgery in all groups.

Postoperative nutritional status

We evaluated postoperative changes in body weight and nutritional parameters in 102 patients who were followed up for at least 1 year after surgery (Fig. 2). The degree of body weight loss was significantly smaller in the LsTG group than in the LTG group at both 6 months ($P < 0.001$) and 12 months ($P < 0.001$). On the other hand, there was a smaller decrease of body weight in the LsTG group as compared with the LPG group, although at no time point was it statistically significant. The serum albumin level recovered to the preoperative value at 12 months after surgery in the LsTG group but not in the LTG and LPG

groups. In particular, the decrease of serum albumin in the LPG group at 12 months after surgery was significantly higher than that in the LsTG group ($P = 0.020$). The decrease in serum hemoglobin was greater in the LTG group throughout the year than in the other two groups, but not significantly so, and the LTG group showed a significantly higher decrease of hemoglobin at 12 months after surgery than the LsTG group ($P = 0.043$). Regarding the PNI, there was no significant difference between the LsTG and LTG groups; however, the decrease of PNI was significantly greater in the LPG group than in the LsTG group at 12 months after surgery ($P = 0.007$).

Endoscopic findings

Patients who underwent LsTG or LPG were required to undergo endoscopic examination during the follow-up period. At 1 year after surgery, 27 of 31 patients (87%) in the LsTG group and 23 of 25 patients (92%) in the LPG group underwent endoscopic examination. The endoscopic findings are shown in Table 3. The endoscope could not reach the remnant stomach in 4 of 19 patients (21%) who underwent LPG with double-tract reconstruction. One patient (4%) in the LsTG group and 2 patients (9%) in the LPG group were confirmed to have reflux esophagitis. Remnant gastritis was observed more frequently in the LPG group than in the LsTG group (37% vs. 7%, $P = 0.022$). No patient in the LsTG group exhibited bile reflux, which was observed in 4 LPG patients (21%, $P = 0.024$).

Table 2 Surgical results and postoperative morbidities

	LsTG ($n = 38$)	LTG ($n = 48$)	P value for LsTG vs. LTG	LPG ($n = 27$)	P value for LsTG vs. LPG
Operation time (min), median (range)	274 (182–437)	256.5 (176–332)	0.122	286 (193–365)	0.837
Blood loss (ml) median (range)	75 (0–370)	60 (10–400)	0.973	90 (0–580)	0.215
Postoperative morbidity	4 (11%)	15 (31%)	0.035	5 (19%) ^a	0.472
Anastomotic leakage	1 (3%)	3 (6%)	0.627	3 (11%)	0.299
Anastomotic stricture	0 (0%)	1 (2%)	1.000	0 (0%)	–
Bleeding	1 (3%)	2 (4%)	1.000	1 (4%)	1.000
Pancreatic fistula	0 (0%)	2 (4%)	0.501	1 (4%)	0.415
Delayed gastric emptying	2 (5%)	0 (0%)	0.192	1 (4%)	1.000
Bowel obstruction	0 (0%)	1 (2%)	1.000	0 (0%)	–
Intraabdominal abscess	0 (0%)	4 (8%)	0.126	1 (4%)	0.415
Wound infection	0 (0%)	1 (2%)	1.000	0 (0%)	–
Pneumoniae	0 (0%)	1 (2%)	1.000	1 (4%)	0.415
Mortality, n (%)	0 (0%)	0 (0%)	–	0 (0%)	–

LsTG laparoscopic subtotal gastrectomy, LTG laparoscopic total gastrectomy, LPG laparoscopic proximal gastrectomy

^aData include duplicate cases

Fig. 2 Postoperative changes of body weight (a), serum albumin (b), serum hemoglobin (c), and prognostic nutritional index (PNI) (d) in the laparoscopic subtotal gastrectomy (LsTG) group, the laparoscopic

total gastrectomy (LTG) group, and the laparoscopic proximal gastrectomy (LPG) group. All postoperative data are represented as values (mean $\pm$ standard error) relative to preoperative data. * $P < 0.05$

Table 3 Endoscopic findings at 1 year after surgery

	LsTG (n = 27)	LPG (n = 23)	P value
Reflux esophagitis	1 (4%)	2 (9%)	0.588
RGB classification			
Residual foods (grade 0–1/2–4)	20/7	15/4	1.000
Gastritis (grade 0–1/2–4)	25/2	12/7	0.022
Bile reflux (grade 0/1)	27/0	15/4	0.024

LsTG laparoscopic subtotal gastrectomy, LPG laparoscopic proximal gastrectomy, RGB classification: residue, gastritis, bile classification

Oncological outcomes

The median follow-up periods for patients in the LsTG, LTG, and LPG groups were 31, 48.5, and 30 months, respectively. There was no recurrence in either the LsTG or LPG group, although two patients with pT3 gastric cancer in the LTG group developed recurrences and died of peritoneal

metastasis. The 2-year recurrence-free survival rates were 100% in the LsTG group, 96% in the LTG group, and 100% in the LPG group.

Discussion

In the present study, we assessed the short-term outcomes and nutritional status of patients who underwent LsTG with a very small remnant stomach for cStage I proximal gastric carcinoma, and compared these results with patients who underwent LTG and LPG. The morbidity rate was similar between the LsTG and LPG groups but was significantly higher in the LTG group than in the LsTG group. Regarding nutritional status, LsTG demonstrated an advantage over both LPG and LTG. Furthermore, remnant gastritis and bile reflux 1 year after surgery was observed more frequently in the LPG group than in the LsTG group. To the best of our knowledge, the present study is the first to compare

these three types of surgical procedures for proximal gastric carcinoma.

For early gastric cancer located in the upper third of the stomach, there are several surgical options, including reconstruction. Although LTG or LPG is usually performed for early gastric cancer in the upper third of the stomach, short-term outcomes and postoperative quality of life after LTG or LPG are unsatisfactory compared with those after laparoscopic distal gastrectomy (LDG) [5, 6, 22, 23]. LDG has been widely accepted as the standard surgery for cStage I gastric cancer since it was first reported in 1994, and its safety and favorable short-term outcomes have been already established [24–29]. Although LsTG is a technically more complicated and time-consuming procedure than conventional LDG, the incidence of postoperative morbidities was significantly lower after LsTG than that after LTG in the present study. Furthermore, the incidence of anastomotic leakage was a little less after LsTG than that after LPG, although the overall incidence of postoperative morbidities showed no statistical difference. In terms of postoperative morbidities, LsTG may result in favorable outcomes as compared with LTG and LPG.

Previous retrospective studies have documented that distal gastrectomy has advantages over TG in postoperative nutritional status and quality of life [30–32]. On the other hand, it has been reported that PG is better than TG in terms of body weight loss and postoperative symptoms such as diarrhea and dumping syndrome [7, 11, 33]. In the present study, however, nutritional status after LPG was poor or equal to that after LTG. We considered that the relatively poor nutritional status in the LPG group might be a result of older age (median, 70 years) as compared with the LsTG group (median, 65 years) and the LTG group (median, 63.5 years). The present study showed that LsTG had significant advantages in serum albumin and PNI compared with LPG, although patients in the LsTG group tended to have more advanced disease and to receive adjuvant chemotherapy more frequently than those in the LPG group. Furthermore, recovery of postoperative body weight and serum hemoglobin levels was significantly better after LsTG than LTG. We previously proposed that body weight loss after gastrectomy is caused not only by anatomical changes following gastric surgery, but also by a decrease of ghrelin, a gut hormone known to increase appetite [34–38]. The improved nutritional status after LsTG, despite a very small remnant stomach, might result from preservation of the gastric fundus, the primary location of ghrelin secretion [14].

Endoscopic findings at 1 year after surgery showed that significantly fewer patients had gastritis or bile reflux in the LsTG group than in the LPG group, although there was no significant difference in the proportion of patients with reflux esophagitis. Previous studies reported that the incidence of reflux symptoms after PG was significantly higher than that

after TG [5, 23]. In our cohort, about 80% of LPG patients underwent reconstruction by the double-tract method; however, the choice of reconstruction method after PG remains controversial. Although a novel double-flap esophagogastrostomy technique has been recently developed to prevent reflux after PG with esophagogastric anastomosis [39], LsTG could be a good option to prevent reflux esophagitis and remnant gastritis.

In the current version of the Japanese Gastric Cancer Treatment Guidelines, the extent of lymph node dissection differs depending on the type of gastrectomy [16]. Tumors located near the EGJ have a relatively high metastatic rate at lymph node station No. 2. LsTG was not performed in such cases because this procedure does not involve complete dissection of nodes in this station. As for station No. 4sa, it is possible to remove most of the lymph nodes along the short gastric vessels, but complete dissection, including the nodes around the superior pole of the spleen, should be avoided so as to preserve blood supply to the remnant stomach. We therefore consider that LsTG should be performed with complementary procedures such as sentinel node navigation methods for tumors in the greater curvature near the fundus. In addition, the proximal margin could be short in LsTG as compared with LTG or LPG. To ensure the proximal margin for the LsTG patients, we usually put the marking clips approximately 1 cm proximal to the tumor with confirmation of negative biopsy. The tumor location and marking clips were confirmed by using intraoperative endoscopy before resection, and intraoperative frozen section diagnosis was performed in some cases. Owing to these assistances, all cases in our series revealed negative margin in the final pathological diagnosis.

This study has several limitations. First, it was a retrospective study and therefore a certain degree of selection bias could not be avoided. The surgical procedure in each case was chosen based on a collaborative decision between surgeons and patients as well as on the tumor location. Second, the follow-up period was too short to assess oncological outcomes. Although there was no recurrence in the LsTG group during the follow-up period, the oncological outcomes of LsTG should be assessed in longer-term studies.

Our results suggest that LsTG is a safe procedure compared with LTG and LPG. Furthermore, LsTG may have an advantage over these procedures in terms of postoperative nutritional status and prevention of remnant gastritis. In conclusion, LsTG with a very small remnant stomach could be an alternative treatment option for cStage I proximal gastric carcinoma.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical standards Written informed consent was obtained from all patients before the procedure. The study was approved by the ethics committee of the Institutional Review Board.

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