5-cm skin incision [14]. Patients who underwent RPLDG were particularly satisfied with the cosmetic appearance of the surgical wounds. Therefore, assessing the feasibility of using reduced-port laparoscopic total gastrectomy (RPLTG) in gastric cancer patients is a rational next step for those who have the skills and willingness to exploit further the potential of this approach. In this study, we have therefore retrospectively compared the short-term outcomes for conventional LATG (CLATG; five ports with a 5-cm skin incision) and RPLTG (a multiaccess port at the umbilicus plus one other port).

Patients and methods

Patients

Between April 2002 and February 2014, a total of 645 patients with gastric cancer underwent laparoscopy-assisted gastrectomy with regional lymph node dissection at the Department of Surgery, Gastroenterological Center, Yokohama City University, Japan. Between June 2009 and February 2014, 90 of these patients underwent pancreas- and spleen-preserving LATGs, performed by the same surgeon who had previously performed 207 laparoscopic distal gastrectomies, including 34 RPLDGs, 26 laparoscopy-assisted proximal gastrectomies, and 93 CLATGs, before performing the first RPLTG in June 2012. Preoperative diagnosis had established that these were all cases of early gastric cancer. Half of these patients underwent RPLTG and half underwent CLATG and, as this was a retrospective, historical study, it was the former 44 patients who underwent CLATG. Of the latter 46 patients, 45 patients underwent RPLTG and one patient selected CLATG after sufficient explanation of the advantages and disadvantages of CLATG and RPLTG. Surgery was performed only after all possible alternative procedures or treatments had been explained to the patient and informed consent had been obtained. Data for these patients were collected by reviewing their medical records.

The 90 consecutive patients (59 men and 31 women) in this study were aged 35.6–85.4 years (mean 67.6 years), and in all of them gastric adenocarcinoma had been diagnosed before surgery with the use of imaging techniques, after the analysis of endoscopic biopsy specimens. All patients had also undergone a barium swallow test and computed tomography scans. Ultrasonography of the abdomen had been performed in 42 patients (46.7 %).

The staging and definition of lymph nodes were principally based on the Japanese Classification of Gastric Carcinoma [15] and the lymph node dissection protocol was based on the Japanese Gastric Cancer Guidelines [16]. Splenectomy was performed in patients with early gastric cancer, diagnosed preoperatively as stages I and II. Experienced pathologists in our institution provided high-quality pathological diagnosis service records. Our institutional review board had approved both the use of laparoscopic gastrectomy for tretament of gastric cancer and the retrospective review of patients' records. A range of surgical parameters (such as operation time, volume of blood loss, and number of dissected lymph nodes) and postoperative parameters (such as incidence of morbidity and length of hospital stay) were evaluated.

Surgical procedures

CLATG with regional lymph node dissection was performed as previously reported [12]. Reconstruction after laparoscopic total gastrectomy used a Roux-en-Y anastomosis, using a transorally inserted anastomotic anvil, OrVil™ (Covidien), in 45 patients in the CLATG group and 14 patients in the RPLTG group. In the remaining 31 patients in the RPLTG group, the Roux-en-Y anastomosis was formed by hand-sewing a purse-string suture at the esophageal stump followed by the intracorporeal insertion of the anvil head into the esophagus.

In the RPLATG group, a small 40-mm skin incision was made at the umbilicus to insert the OCTO™ Port V2 (DalimSurgNet, Seoul, Korea), and a 12-mm port was inserted into the right lateral abdomen to support laparoscopic manipulation. The operator stood mainly on the right side of the patient. The OCTO™ port had four ports, allowing the simultaneous insertion of a 10-mm flexible simple endoscope, an energy device such as a LigaSure™, and a Roticulator™ Endograsp™ II (Covidien). In addition, a DST Series™ EEA™ shaft could be introduced through the upper port with a detachable blue cap into the abdominal cavity at the esophagojejunostomy. This port had three functions: a 5-mm port, a 12-mm port, and a 21–28-mm port. The endoscope was routinely inserted through the lower portion of the square, the energy device through the upper portion, and the endograsp through the right side of the port (Fig. 1). Throughout laparoscopic manipulations, the energy device was usually held in the right hand. However, sometimes it was held in the left hand and inserted through the 12-mm port in the right lateral abdomen, when it was necessary to dissect tissue in a tangential direction and subsequently necessary to avoid injuring organs. For example, suprapancreatic lymph nodes could be most easily dissected using left-hand manipulations. In addition, sometimes when the energy device was held in the right hand and the forceps in the left hand, the operator was forced to cross the instruments and this could interfere with the surgeon's manipulations. In such situations, changing the hand holding the energy device allowed us to perform the procedure comfortably.

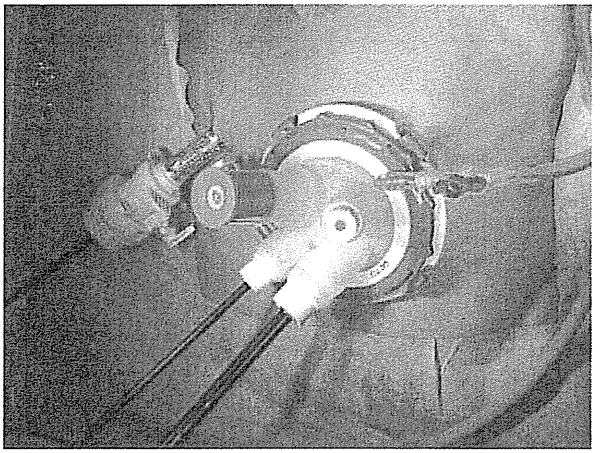

Fig. 1 Photograph showing the position of the ports and devices used for reduced-port laparoscopic total gastrectomy. The OCTO™ port was inserted in a 4-cm incision at the umbilicus and had 5-, 12-, and 21–28-mm ports. An additional 12-mm port was inserted in the right lateral abdomen

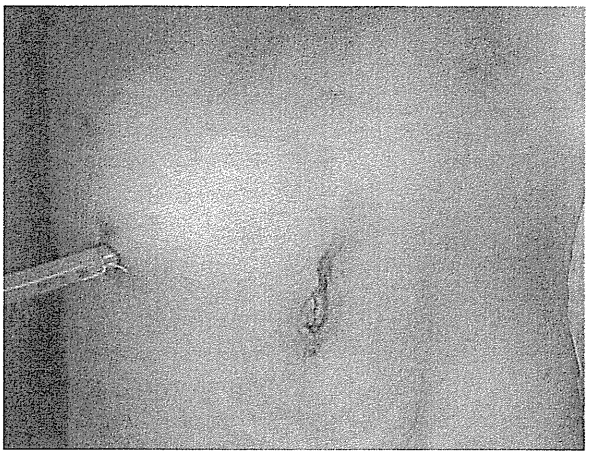

Fig. 2 Photograph showing a patient's abdomen on completion of reduced-port laparoscopic total gastrectomy. A silicon drain was inserted at the site of the port in the right lateral abdomen and the 4-cm skin incision was closed meticulously

In CLATG, the so-called triangle formation achieved by retracting the tissues with three forceps with appropriate strengths has been considered essential for safe and effective dissection. However, in RPLTG, a surgical team is equipped with a maximum of two forceps to retract tissues. Thus, it is important to use the Roticulator™ grasper to retract tissue in the optimal direction with sufficient force, and sometimes to make use of tissue adhesion or gravity.

After lymph node dissection, the stomach was resected within the abdomen using an Endo GIA™ Ultra universal stapler, a straight cut at the junction with the abdominal esophagus, and extraction through the umbilical incision. After a purse-string suture had been had sewn at the abdominal esophageal stump within the abdomen, an anvil head was inserted intracorporeally and securely attached. A jejunal loop was made extracorporeally through the OCTO™ port and brought up behind the colon and through the transverse mesocolon intracorporeally. A DST Series™ EEA™ shaft was inserted into the jejunal loop extracorporeally, and the jejunum was secured to the shaft with a rubber band. A DST Series™ EEA™ shaft was introduced into the abdominal cavity through the upper side port of the OCTO™ port to maintain a pneumoperitoneum. The esophagojejunostomy could be completed without making the small skin incision at the upper abdomen used in the CLATG group. The jejunal stump was sutured intracorporeally using an Endo GIA™ universal stapler (60–2.5). To create a 40 -m Roux-en-Y limb, the transected jejunum was used extracorporeally to form a side-to-side jejunojejunostomy using a DSTSeries™ EEA™ stapler (25–3.5; Covidien). The jejunal stump was also sutured extracorporeally using an Endo - GIA™ universal stapler (60–2.5). After the abdomen had been irrigated with 3,000 mL irrigation fluid, one silicon drain was placed behind the esophagojejunal anastomosis (Fig. 2).

Postoperative care

All patients in both groups received epidural analgesia for 3 days after the operation. However, if a patient required additional pain control during or after administration of the epidural, nonsteroidal anti-inflammatory drugs were administered. Before March 2010, patients resumed an oral diet on day 6 after surgery and were discharged on day 14, in accordance with the clinical pathway used at our institution, provided there was no morbidity and their food intake was sufficient. The clinical pathway then changed and an oral diet commenced on day 4 after surgery,and patients were discharged on day 12.

After discharge, all 90 patients were asked by the surgeon to grade their satisfaction with the cosmetic appearance of their scars as low, moderate, or high.

Statistical analysis

Data were analyzed using the SPSS statistical software program (SPSS, Chicago, IL, USA). Patient characteristics were compared using the two-tailed Fisher exact test or the chi square test with the Yates correction. Quantitative variables were compared using Student's t test and were expressed as the mean ± standard deviation. Probability (p) values of less than 0.05 were considered to be statistically significant.

Table 1 Comparison of the characteristics of patients in the reduced-port laparoscopic total gastrectomy (*RPLTG*) and conventional laparoscopy-associated total gastrectomy (*CLATG*) groups

	RPLTG ($n = 45$)	CLATG ($n = 45$)	p value
Age (years)	67.1 ± 10.9	67.4 ± 10.9	0.911
Median (range)	68.4 (36–84)	67.0 (36–85)	
Gender (male/female)	28/17	31/14	0.658
Body mass index (kg/m^2)	22.7 ± 3.5	22.3 ± 2.5	0.582
Median (range)	23.6 (14.7–32.4)	22.9 (17.0–27.5)	
ASA classification			0.666
1	17	21	
2	25	22	
3	3	2	
Prognostic nutritional index	54.5 ± 5.2	54.5 ± 5.5	0.997
Past history of laparotomy			
Present	7	9	0.784
Cholecystectomy	1	2	
Appendectomy	4	5	
Gynecological	4	2	
Comorbid disease			
Present	28	24	0.522
Cardiovascular	21	16	
Hyperlipidemia	12	6	
Diabetes mellitus	3	2	
Respiratory	2	2	
Cerebrovascular	2	2	
Other cancer	1	6	
Others	1	1	
Location of tumor			0.011
Middle third	11	25	
Upper third	31	18	
Entire stomach	3	2	
Macroscopic appearance			0.393
Superficial[a]	38	42	
Well defined	3	1	
Ill defined	4	2	
Tumor diameter (mm)	42.1 ± 27.6	36.9 ± 18.5	0.297
Histological type			0.382
Differentiated	26	31	
Undifferentiated	19	14	
Depth of invasion			0.858
Mucosa, submucosa	35	37	
Proper muscle, subserosa	9	7	
Serosa exposed	1	1	
Lymph node metastasis present	7	7	1.000
Stage			0.010
IA	30	35	
IB	7	4	
IIA	7	0	
IIB	1	1	
IIIA	0	5	

Ranges are given in *parentheses*

ASA American Society of Anesthesiologists

[a] Slightly depressed, elevated type, and elevated plus depressed type

Table 2 Comparison of the surgical outcomes of patients in the reduced-port laparoscopic total gastrectomy (*RPLTG*) and the conventional laparoscopy-associated total gastrectomy (*CLATG*) groups

	RPLTG ($n = 45$)	CLATG ($n = 45$)	p value
Lymph node dissection			0.090
D1 plus no. 8a, 9, 11p	16	25	
D1 plus no. 8a, 9, 11p, 11d, 12a	29	20	
Total operation time (min)	319.0 ± 45.3	259.0 ± 34.1	<0.001
Total blood loss (mL)	93.7 ± 75.1	118.9 ± 83.5	0.137
No. of lymph nodes dissected	46.3 ± 23.2	46.6 ± 22.0	0.752

Results

Patient characteristics

The characteristics of the 90 patients enrolled in this study are shown in Table 1. There were no significant differences between the CLATG and RPLTG groups in age, sex, body mass index, the American Society of Anesthesiologists physical status classification, the prognostic nutritional index, the presence of comorbidities, or prior abdominal surgery. Pathologically, we found that tumors mainly located in the upper third of the stomach and more advanced tumors were significantly more frequent in the RPLTG group than in the CLATG group. By contrast, the macroscopic appearance, tumor diameter, histological type, depth of invasion, and the extent of lymph node metastasis did not show significant differences between the two groups.

Surgical characteristics

There were significant differences in the total operation time. However, the total blood loss, the extent of lymph node dissection, and the number of lymph nodes retrieved did not differ between the two groups (Table 2).

Postoperative recovery

As shown in Table 3, the time to resumption of an oral diet and the length of stay in hospital postoperatively were shorter in the RPLTG group although the clinical pathway was different between the two groups. The peak value of C-reactive protein was significantly higher in the CLATG group owing to the high incidence of anastomotic and duodenal leakage. However, cosmetic satisfaction was significantly greater in the RPLTG group than in the CLATG group ($p = 0.021$). No significant differences were observed between the two groups in the peak value of the white blood cell (WBC) count, the presence of liver dysfunction, the time to first flatus, the time for which nonsteroidal anti-inflammatory drugs were used, and postoperative morbidity. Death was not observed in the two groups.

Discussion

Reduced-port gastrectomy can sometimes create conflicts between different surgical devices and may make precise manipulations more difficult to perform. Therefore, the application of this technique to such a technically complex surgery as laparoscopic gastrectomy may be considered inappropriate. However, we have shown in this retrospective study that our RPLTG technique for treatment of gastric cancer resulted in acceptable and satisfactory short-term patient outcomes compared with those achieved using a conventional laparoscopic technique.

The application of CLATG for treatment of gastric cancer has also been reported [11–13]. The surgical procedure for CLATG is more complex and challenging than that for laparoscopic distal gastrectomy, even for an experienced gastric surgeon. In particular, the reconstruction technique has not yet been well established in CLATG [9, 10].

In all laparoscopic surgery, adequate retraction and counter-retraction are essential to control the orientation of organs during surgery and prevent intraoperative complications. In reduced-port gastrectomy, it is sometimes difficult to manipulate organs in the appropriate direction with appropriate force. It is therefore essential that surgeons have sufficient education, training, and experience in performing gastrectomies, including laparoscopic procedures, to be able to perform complex reduced-port gastrectomy safely. Optimal organ retraction provides surgeons with good visibility within the abdomen and enables them to dissect lymph nodes safely and create intracorporeal anastomoses within an acceptable time and with acceptable blood loss, and so subsequently reduces the incidence of postoperative complications. In CLATG, adequate retraction in the required direction can be performed by an assistant surgeon using two forceps in addition to the single forceps manipulated by the operator. In RPLTG, the Roticulator™ grasper used throughout the operation by the assistant surgeon and the forceps used by the operator, and using adhesion between tissues or organs, provide us with an acceptable intra-abdominal view. The organs and tissues were retracted ventrally using a Roticulator™ grasper, and this manipulation allowed meticulous dissection of lymph nodes and tissues, by avoiding conflicts between different devices. It was also important to change the hand holding the energy device if it was thought necessary and useful.

Table 3 Comparison of the postoperative recovery of patients in the reduced-port laparoscopic total gastrectomy (*RPLTG*) and the conventional laparoscopy-associated total gastrectomy (*CLATG*) groups

	RPLTG ($n = 45$)	CLATG ($n = 45$)	p value
Peak C-reactive protein (mg/dL)	11.9 ± 5.6	16.5 ± 6.8	0.001
Peak WBC (/m^3)	12,385 ± 4,080	12,760 ± 4,530	0.682
Peak ALT (U/L)	120.9 ± 115.7	144.2 ± 201.9	0.505
Peak AST (U/L)	122.2 ± 106.9	161.6 ± 170.7	0.366
Time to first flatus (days)	2.6 ± 1.9	2.9 ± 1.2	0.432
Median time to first flatus (days)	3.0 (2–5)	3.0 (2–4)	
No. of doses of NSAIDs used	5.7 ± 2.0	6.0 ± 5.3	0.258
Median no. of doses of NSAIDs used	5.0 (2–7)	6.0 (4–8)	
Time to resumption of oral diet (days)	4.8 ± 2.4	7.5 ± 4.9	0.001
Median (range)	4 (4–16)	5 (4–29)	
Morbidity	6	13	0.120
Anastomotic leakage	2	5	
Duodenal stump leakage	1	2	
Surgical site infection	2	2	
Pneumonia	0	3	
Cholecystitis	0	1	
Anastomotic stenosis	1	1	
Mortality	0	0	1.000
Postoperative hospital stay (days)	16.3 ± 8.9	27.0 ± 19.1	0.008
Median postoperative hospital stay (days)	13.0 (11–41)	19.0 (12–114)	
Cosmetic satisfaction			0.021
Low	0	3	
Moderate	7	15	
High	38	27	

Ranges are given in *parentheses*

ALT alanine aminotransferase, *AST* aspartate aminotransferase, *NSAIDs* nonsteroidal anti-inflammatory drugs, *WBC* white blood cell

When dissecting the infrapyloric lymph nodes, we usually revealed and dissected the right gastroepiploic vein using the right hand, and similarly dissected the lymph nodes around the right gastroepiploic artery using the left hand, to prevent injury to the pancreas. This procedure is difficult and sometimes lengthened the operation. When dissecting lymph nodes along the suprapancreatic arteries, we found that using the left hand was safe and smooth while retracting the pancreas to the dorsal side using the right hand.

Successful results using single-port or reduced-port laparoscopic surgery for distal gastrectomies in patients with early gastric cancer have been reported previously [17–19]. An experienced and skillful surgeon can perform such complex laparoscopic gastrectomies after gaining sufficient experience of conventional laparoscopic gastrectomies. In our previous study [14], we also reported satisfactory outcomes for reduced-port (SILS Port^{TM} plus one port) LADG.

In this study, we found that the technical difficulty of this operation resulted in a longer overall operation time, with more time spent on lymph node dissection, compared with CLATG although the time taken for reconstruction did not differ significantly between the two groups. We used an OCTO^{TM} port and added a 12-mm port in the lateral abdomen, which could be used as a drain after surgery. The addition of this one extra port enabled us to perform lymph node dissection laparoscopically to a satisfactory and sufficient degree, although this took longer to complete than in CLATGs. It may be difficult to shorten the operation time for RPLTG even for an experienced laparoscopic surgeon.

During this study, we encountered seven cases of anastomotic leakage after using the OrVil^{TM} device and we therefore changed the method used to a hand-sewn, purse-string suture technique. Since then, we have had no further cases of leakage. However, there is an urgent need to develop a reliable technique using an innovative device for performing esophagojejunostomy.

Both the time to the resumption of an oral diet and the length of stay in hospital postoperatively were significantly longer in the CLATG groups. Postoperative morbidity and our institution's current clinical pathway affected these results, and so it may be difficult to emphasize the advantage of RPLTG.

The observation that the number of lymph nodes dissected was the same in both patient groups suggested that lymph node dissection in the RPLTG group was done to an

acceptable standard. This also suggested that the long-term survival for these patients may be expected to be equivalent in the two groups, although follow-up studies are needed to confirm this.

Some previous studies have shown that totally laparoscopic total gastrectomy (TLTG) using either functional end-to-end esophagojejunostommy or OrVil™ reconstructions is an acceptable surgical procedure [20, 21]. Blood losses and postoperative morbidities in these studies were similar to those in our study, although our operation times were longer than those in the TLTG studies. Although RPLTG does not need additional three-port sites compared with the TLTG procedure, this technique does need great laparoscopic skills and longer operation times. The fundamental difference between TLTG and RPLTG is the number of very small incisions for ports although the resected specimen is similarly retrieved through the umbilical wound in both methods. By contrast, satisfaction of patients in the RPLTG group may depend on the small umbilical wound instead of the minilaparotomy in the upper abdomen in the CLATG group rather than the number of ports. Therefore, this study looked at a mixture of the CLATG versus TLTG comparison and CLATG versus RPLTG comparison. This is a clear weakness and limitation of this retrospective study. In our institution, we initially made the Roux-en-Y anastomosis through a 10-cm skin incision made after LATG. We then used an OrVil™ device for the esophagojejunostomy through a small, 4–5-cm skin incision, and more recently we have used an OrVil™ device for an intracorporeal esophagojejunostomy using the reduced-port technique. Most recently, we have inserted an anvil head after creating a hand-sewn, purse-string suture of the esophageal stump, which was secured intracorporeally, and subsequently we were able to complete the esophagojejunostomy as quickly as an open esophagojejunostomy. Introducing these complex surgical procedures step by step would be ideal to achieve a steady and safe surgical learning curve. However, it is difficult to conclude that RPLTG reduced the incidence of anastomotic leakage and subsequently shortened the hospital stay because the anastomotic methods were changed with time in this retrospective study.

As we have shown in this study, cosmetic satisfaction was obtained in a subset of patients receiving RPLTG. Therefore, it is important to explain the advantages and disadvantages of this technique to patients before surgery.

Conclusion

Our results suggest that RPLTG for treatment of gastric cancer may be an acceptable and satisfactory technique although this retrospective study has some limitations. This method may be one of the operative methods for treatment of gastric cancer requiring or indicating laparoscopic total gastrectomy by some experienced laparoscopic surgeons.

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ORIGINAL ARTICLE

Early phase II study of robot-assisted distal gastrectomy with nodal dissection for clinical stage IA gastric cancer

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Abstract
Background Robot-assisted distal gastrectomy (RADG) is increasingly performed in Japan and Korea and is thought to have many advantages over laparoscopic gastrectomy. However, a prospective study investigating the safety of RADG has never been reported. The present study evaluated the safety of RADG with nodal dissection for clinical stage IA gastric cancer.
Methods This single-center, prospective phase II study included patients with clinical stage IA gastric cancer located within the lower two-thirds of the stomach. The primary endpoint was the incidence of postoperative intraabdominal infectious complications including anastomotic leakage, pancreas-related infection, and intraabdominal abscess. The secondary endpoints included all in-hospital adverse events, RADG completion rate, and survival outcome.
Results From May 2012 to November 2012, 18 eligible patients were enrolled for this study. The incidence of intraabdominal infectious complication was 0 % (90 % CI, 0–12.0 %). The overall incidence of in-hospital adverse events was 22.2 % (90 % CI, 8.0–43.9 %). No patient required conversion to laparoscopic or open gastrectomy; thus, the RADG completion rate was 100 %.
Conclusions This early phase II study suggested that RADG might be a safe and feasible procedure for stage IA gastric cancer, providing experienced surgeons perform the surgery. This conclusion should be clarified in subsequent late phase II studies with a larger sample size.

Keywords da Vinci · Gastric cancer · Gastrectomy · Clinical trial · Safety

Introduction

Laparoscopy-assisted distal gastrectomy (LADG) is performed increasingly often, particularly in East Asian countries where the incidence of early gastric cancer is higher than in Western countries. The safety of LADG was clarified by prospective studies [1, 2], and survival outcome of LADG compared with open gastrectomy was under investigation in two large, nationwide, randomized controlled trials in Japan and Korea [1, 3]. However, current laparoscopic procedures have several drawbacks, including a limitation in range of forceps movement and the two-dimensional surgical view available to the operating surgeons.

Robot-assisted distal gastrectomy (RADG) may enable us to overcome these drawbacks. Using the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA), surgeons were able to attain a three-dimensional surgical view, instrument flexibility, tremor suppression, and improved ergonomics, although RADG still has disadvantages such as high cost and lack of tactile sensation [4–8]. In addition, a shorter learning curve has been reported for robotic surgery compared to laparoscopic surgery [9–11].

Reported studies rate RADG as a feasible procedure, although most such studies involved a retrospective or prospective study cohort [4, 5, 8–10, 12–22]. So far, no prospective clinical trials have focused on the feasibility of RADG, a step that is necessary before RADG could be

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explored further with greater number of patients. To this end, the current prospective study evaluated the safety of RADG with nodal dissection for clinical stage IA gastric cancer.

Methods

The present study was designed as a single-center, prospective phase II trial. The institutional review board of Shizuoka Cancer Center approved the study protocol, which had the following inclusion criteria: histologically confirmed adenocarcinoma of the stomach, clinical stage IA early gastric cancer according to the International Union Against Cancer classification system (UICC) [23], no indication for endoscopic submucosal dissection (ESD), a tumor located in the lower two-thirds of the stomach, no involvement of the duodenum, patient age of 20–80 years, an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1, a body mass index (BMI) less than 30 kg/m^2, no prior upper abdominal surgery or intestinal resection other than appendectomy, no prior chemotherapy or radiotherapy for any malignancy, adequate organ function, and written informed consent. The study was registered with clinical trials.gov (clinical trials.gov identifier: NCT 1504997).

In this study period, medical cost for hospital admission, including surgical fee, was funded by the Shizuoka Cancer Center because the national insurance system in Japan did not reimburse patients for RADG.

Surgical procedure

All RADG operations were performed using the da Vinci Surgical System with four robotic arms; a central arm for a dual-channel endoscope, and the other three for a Cadiere forceps, fenestrated bipolar forceps, and bipolar Maryland forceps or monopolar electrocautery, respectively. One assistant port was placed in the right umbilical level. The surgical procedures were similar to that used in LADG, with a standardized surgical field to achieve omentum preservation, D1+ lymph node dissection according to the Japanese gastric cancer treatment guidelines [24–27], and vagal nerve preservation [28, 29]. Removal of resected specimens and reconstruction were performed by a 4- to 5-cm upper midline incision. In the case of distal gastrectomy, a Billroth I reconstruction with circular stapler was selected in general. In the case of pylorus-preserving gastrectomy, reconstruction was performed by hand-sewn sutures.

In this study, the operations were separated into three parts. The docking time was defined as the time from skin incision to completion of docking. The console time was the time that the da Vinci system was used by the surgeon at the console. The anastomosis time was the time spent from the creation of the mini-laparotomy to the completion of the surgery.

Training for RADG

A team of two gastric surgeons who were board certified by the Japanese Society of Endoscopic Surgery (JSES) as experts in laparoscopic surgery performed RADG in all cases. To be board certified by the JSES as an expert laparoscopic surgeon, an applicant is required to perform more than 20 laparoscopic gastrectomies or alternative advanced laparoscopic surgeries within 3 years and to submit a non-edited video of one of the surgeries for a review by at least two board-qualified referees. The strict review process, which takes place once a year, allows only one-third of the applicants to be certified. Before introducing RADG at Shizuoka Cancer Center, the two surgeons completed a fixed training program for RADG as recommended by the JSES. The program consisted of e-learning, training sessions at an animal laboratory, and site visits to a specified high-volume center to observe actual RADG. In addition, surgeons with sufficient experience in RADG were invited as instructors in the initial two cases of RADG at our institution.

Endpoints

The primary endpoint in this study was the incidence of postoperative intraabdominal infectious complications, which included anastomotic leakage, pancreas-related infection, and intraabdominal abscess. Patients who developed Clavien–Dindo classification grade II or more complications by discharge were regarded as having complications [30, 31]. The secondary endpoints were overall survival (OS), relapse-free survival (RFS), RADG completion rate, and the incidence of all surgical morbidities.

Anastomotic leakage was diagnosed by radiologic examination using orally administered contrast media. Pancreas-related infection was defined as amylase-rich purulent discharge. Intraabdominal abscess was defined as an abscess not associated with anastomotic leakage or pancreas-related infection. The completion of RADG was defined as the proportion of patients without conversion from RADG to LADG or open distal gastrectomy (ODG).

Study design and statistical methods

In this phase II trial, the sample size was 18 cases, providing 70 % power under the hypothesis of a primary endpoint with an expected value of 4 % and a threshold

value of 15 %, using one-sided testing at a 10 % significance level. The expected value was decided according to the postoperative outcome of 265 patients who had undergone an ODG or LADG for early gastric cancer in the lower two-thirds of the stomach at the Shizuoka Cancer Center; the incidence of intraabdominal infectious complication among these patients was 4.5 % [32]. All statistical analyses were conducted using R Statistics version 2.13.1.

Results

A total of 18 patients were recruited in this phase II study from May 2012 to November 2012. Table 1 summarizes the patient characteristics. The male-to-female ratio was 1.57, median body mass index was 21.1 kg/m^2, and all patients had stage IA gastric cancer located within the lower two-thirds of the stomach. Undifferentiated histology was more frequently observed than differentiated histology.

Table 2 shows details of the surgical procedure. The median duration of the surgery was 311.5 min; median docking, console, and anastomosis times were 22, 212.5, and 63 min, respectively. Distal gastrectomy and pylorus-preserving gastrectomy were performed in nine patients each, and all patients underwent D1 + lymph node dissection. No patient required conversion to laparoscopic or open surgery; thus, the RADG completion rate was 100 %. Median blood loss was 32.5 ml; blood transfusion was not required in any of the patients.

Postoperative clinical course is shown in Table 3. The median duration of postoperative hospital stay was 8 days. Incidence of intraabdominal infectious complication was 0 % [0/18; 90 % confidence interval (CI), 0–12.0 %]. The overall proportion of in-hospital adverse events was 22.2 % (90 % CI, 8.0–43.9 %), with all rated as grade II, from which all patients recovered well with medical treatment only and no surgical interventions.

Table 1 Patient characteristics

Number of patients	18
Sex (cases)	
Male	11
Female	7
Age (years)	
Median	65.5
Range	53–80
Body mass index (kg/m^2)	
Median	21.1
Range	16.2–25.8
Tumor location (cases)	
Upper third	0
Middle third	11
Lower third	7
Histological type (cases)	
Differentiated	6
Undifferentiated	12
Tumor size (cm)	
Median	
Range	
Clinical stage (cases)	
IA	18
IB	0

Table 2 Details of surgical procedures

Operation time (min)	
Median	311.5
Range	225–375
Docking time (min)	
Median	22
Range	11–41
Console time (min)	
Median	212.5
Range	161–291
Anastomosis time (min)	
Median	63
Range	41–111
Blood loss (ml)	
Median	32.5
Range	0–160
Perioperative blood transfusion (cases)	
Yes	0
No	18
Type of gastrectomy (cases)	
PPG	9
DG	9
Reconstruction method	
Roux-en-Y	1
Billroth I	8
Gastro-gastrostomy	9
Extent of lymph node dissection (cases)	
D1+	18
D2	0
Number of retrieved lymph nodes (cases)	
Median	40
Range	26–89
Completion of RADG (cases)	
Yes	0
No	18

PPG pylorus-preserving gastrectomy

DG distal gastrectomy

Table 3 Postoperative clinical course

Postoperative hospital stay (days)	
Median	8
Range	7–10
Postoperative morbidities (cases)	
Intraabdominal infectious complications	0
Anastomotic leakage	0
Pancreas-related infection	0
Intraabdominal abscess	0
Other complications	
Wound infection	2
Delayed gastric emptying	1
Liver dysfunction	1

Discussion

The present study showed RADG is feasible in terms of safety if experienced laparoscopic surgeons perform the surgery, with a zero incidence of intraabdominal infectious complications recorded (90 % CI, 0–12.0 %).

Before May 2012, we had performed five RADGs as an institute, and based on this experience, we assessed RADG as technically feasible. In addition, none of these five patients developed any postoperative complications. We therefore decided to more thoroughly assess the safety of RADG in the present prospective study.

Previous retrospective studies demonstrated that RADG was a feasible treatment for gastric cancer [4, 5, 10, 12, 14, 18, 19]. Surgeons generally believed that much more meticulous surgery could be performed with the da Vinci Surgical System because of the three-dimensional surgical view provided and the flexibility of instrumentation. However, RADG required longer operation times [5, 14, 17–19, 21] and was more expensive than laparoscopic or open gastrectomy [14, 16, 21, 33]. In addition, the advantages of RADG compared to conventional procedures were not clear from these previous studies, and no prospective study investigating the safety of RADG was reported.

The incidence of postoperative intraabdominal infectious complication in the present study was 0 % (90 % CI, 0–12.2 %) with a 22.2 % overall proportion of in-hospital adverse events (90 % CI, 8.0–43.9 %) in this study. A similar complication rate (0–47.3 %) has been reported in previous retrospective studies, although none had focused on the incidence of intraabdominal infectious complication [4, 5, 8–10, 12, 17, 18, 22, 33]. With the three-dimensional magnified view available with RADG, surgeons were able to recognize anatomical structures much more precisely than with the standard two-dimensional view. In addition, the flexibility of instruments used helped surgeons perform meticulous surgery. We propose that these advantages of RADG resulted in the low complication rate.

Other possible reasons for the low complication rate recorded in this study were involving only experienced laparoscopic surgeons to perform the procedures and the relatively lower BMI of the patients compared with that reported in Western series. High BMI is a possible risk factor for postoperative complications after open and laparoscopic gastrectomy, although this association remains controversial [34–38]. The present study included only one overweight patient (BMI, 25.8). The feasibility of RADG in overweight or obese patients is still unclear and must be clarified in a future trial.

RADG procedures required longer surgical times than LADG. Indeed, there was a difference of 86.5 min in our institute between RADG and LADG [31]. We considered that the meticulousness of the procedure was inversely proportional to operation time to some degree. With the magnified and three-dimensional magnified view and instrument flexibility, surgeons were able to perform much more meticulous surgery at the expense of increased operation time.

There were other possible reasons for the longer operation times. First, RADG was performed during our learning curve period whereas LADG was not. Second, we did not use ultrasonic shears provided for RADG because such usage is not allowed in Japan with the da Vinci Surgical System. Thus, if we achieve our learning curve with RADG and the usage of ultrasonic devices is permitted in the future, we will be able to reduce the operation time.

We believe that the advantages of the da Vinci Surgical System would be enhanced when we use it for more complicated surgery such as gastrectomy with extended (D2) lymph node dissection or mediastinal lymph node dissection. During extended lymph node dissection, we were able to recognized layers precisely as well as small vessels because of the three-dimensional magnified view. In addition, the flexibility of instruments and tremor suppression enabled us to do each procedure meticulously, resulting in high-quality lymph node dissection. Similar advantages would be obtained when we perform lower mediastinal lymph node dissection for adenocarcinoma of esophagogastric junction in which the surgical field is narrow and linear instruments used in laparoscopic surgery frequently interfere. Thus, our next step is to indicate the da Vinci Surgical System for these complicated surgeries.

In the present study, early surgical outcomes of RADG were not compared with conventional open or laparoscopic surgery; thus, it is still unclear if RADG is superior to conventional surgeries in this regard. Although previous retrospective studies compared surgical outcomes of RADG with LADG or ODG, there is no prospective randomized trial comparing RADG and other procedures [5, 17, 18, 20, 22]. In addition, survival outcomes of RADG

remain unclear. Future trials are needed to clarify the superiority of RADG over other procedures, including both short- and long-term outcomes, before it can be accepted as a standard treatment for gastric cancer.

The present study had limitations including the relatively small sample size. The Japanese national insurance system does not reimburse patients for RADG; thus, either the patient or the hospital has to pay the entire admission fee in addition to the surgical fee (around USD $20,000). It was therefore challenging to recruit sufficient patient numbers even for a small phase II trial, and so long as this situation persists, the cost of such surgeries will be an issue and the forthcoming surgeries will be paid by the hospital or the patient in our hospital. We consider that the future practical use of RADG in Japan as an advanced medical technology will require a well-planned prospective trial involving sufficient patient numbers to provide important information about issues such as reimbursement. However, we also believe that accumulated evidence from smaller prospective studies such as ours will help future, larger-scale trials for RADG.

In conclusion, this early phase II study suggested that RADG might be a safe and feasible procedure for stage IA gastric cancer, providing experienced surgeons perform the surgery. This conclusion should be clarified in subsequent late phase II studies with a larger sample size.

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ORIGINAL ARTICLE

Characteristics and clinical relevance of postgastrectomy syndrome assessment scale (PGSAS)-45: newly developed integrated questionnaires for assessment of living status and quality of life in postgastrectomy patients

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Abstract
Background Lack of a suitable instrument to comprehensively assess symptoms, living status, and quality of life in postgastrectomy patients prompted the authors to develop postgastrectomy syndrome assessment scale (PGSAS)-45.
Methods PGSAS-45 consists of 45 items in total: 8 items from SF-8, 15 items from GSRS, and an additional 22 items selected by 47 gastric surgeons. Using the PGSAS-45, a multi-institutional survey was conducted to determine the prevalence of postgastrectomy syndrome and its impact on everyday life among patients who underwent various types of gastrectomy. Eligible data were obtained from 2,368 patients operated and followed at 52 institutions in Japan. Of these, data from 1,777 patients were used in the current study in which symptom subscales of the PGSAS-45 were determined. We also considered the characteristics of the postgastrectomy syndrome and to what extent these symptoms influence patients' living status and quality of life (QOL).
Results By factor analysis, 23 symptom-related items of PGSAS-45 were successfully clustered into seven symptom subscales that represent esophageal reflux, abdominal pain, meal-related distress, indigestion, diarrhea, constipation, and dumping. These seven symptom subscales and two other subscales measuring quality of ingestion and dissatisfaction for daily life, respectively, had good internal consistency in terms of Cronbach's α (0.65–0.88).

For the Japan Postgastrectomy Syndrome Working Party.

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Conclusion PGSAS-45 provides a valid and reliable integrated index for evaluation of symptoms, living status, and QOL in gastrectomized patients.

Keywords Postgastrectomy syndrome · Questionnaires · Quality of life · Gastrectomy

Introduction

Postgastrectomy syndrome (PGS) remains a serious drawback for gastric cancer survivors after gastrectomy [1–6]. PGS includes numerous symptoms related to the loss of the stomach, leading to impairments in living status and quality of life (QOL). Several surgical procedures have been sought to maintain or even to reconstruct the gastric functions through preservation of nerves and other anatomical structures and through sophistication in the method of reconstruction [7, 8]. Hard data showing benefits of various considerations in surgical procedure have been scarce, however, partly because of the lack of adequate endpoints when these procedures are evaluated in clinical trials. It is important, therefore, to be able to weigh the intensity of the various symptoms that emerge after gastrectomy and elucidate to what extent they affect the patients. If an appropriate instrument is available, we shall be able to identify which surgical procedure can be helpful in preventing or ameliorating PGS. Evidence-based knowledge in this area of interest is mandatory for adequate selection of surgical procedure, especially at reconstruction.

To establish an adequate instrument to measure the incidence and relevance of the PGS in terms of patient-reported outcome, the Japanese Postgastrectomy Syndrome Working Party led by the authors designed and constructed a new integrated questionnaire, the Postgastrectomy Syndrome Assessment Scale (PGSAS)-45, to specifically assess symptoms, living status, and QOL of the patients who underwent gastrectomy. A nationwide multi-institutional study was then undertaken to validate the PGSAS-45 and to survey the incidence and intensity of the PGS observed after various surgical procedures.

Standard procedures for scale development in medical research and practice were used to construct a valid, reliable, and clinically useful scale for the assessment of PGS. In the current article, this challenging process is described with particular emphasis on the selection and aggregation of the list of symptoms. The structure and characteristics of the final version of PGSAS-45 were then disclosed. Through findings from a clinical study to validate the PGSAS-45, characteristics of PGS among postgastrectomy patients were summarized, and the influence of the symptoms on the QOL and living status of the patients was identified.

Patients and methods

The Japanese Postgastrectomy Syndrome Working Party

The Japanese Postgastrectomy Syndrome Working Party (JPGSWP), established in 2006, is a voluntary organization of surgeons whose aims were (1) to construct a standardized instrument to evaluate PGS and (2) to use the instrument to identify the optimal surgical procedure that minimizes impairment of QOL among patients who undergo gastrectomy. The JPGSWP has grown during the process and currently consists of 212 surgeons and 52 other medical staff persons (pharmacologists, nurses, and nutritionists) from various Japanese institutions. The first task undertaken by the JPGSWP, thus, was to construct the PGSAS-45.

Development of a new questionnaire, PGSAS-45

PGSAS-45 was designed to comprehensively characterize and evaluate symptoms, living status, and QOL of patients who underwent gastrectomy (Table 1). It was expected to provide a realistic image of the status of the patients and to be regarded as a gold standard in surveillance of the PGS and evaluation of various types of gastrectomy and reconstruction.

First, a comprehensive item pool or list of items representing symptoms and functions was generated. For this purpose, data on PGS were collected from a variety of sources such as published articles and abstracts of domestic surgical meetings. In addition, symptoms that were actually claimed to have been the cause of annoyance for the patients or considered to have affected their everyday lives were retrieved through scrutiny of an earlier questionnaire survey from 252 patients who underwent gastrectomy and by direct interview with 117 patients. This comprehensive and potentially over-inclusive list of items and symptoms was then reviewed to determine which items should be retained. To do so, the list was dispatched by mail to 51 members of the JPGSWP who were asked to arrange the items in the order of clinical importance. Although the items related to issues of significant clinical importance were not to be deleted (all items that were considered by more than 50 % of the surgeons as clinically relevant were to be retained), the total number of items was expected to be within 50. Forty-seven of the 51 surgeons (92 %) eventually responded and met at a consensus meeting in March 2007 to discuss which items should eventually be retained to construct the PGSAS-45.

Further discussion among the JPGSWP members and interviews with the experts in QOL evaluation (Y.S.) were carried out and, through empirical verification, items that

Table 1 Structure of postgastrectomy syndrome assessment scale (PGSAS)-45 (domains/subdomains/items/subscales)

Domains	Subdomains	Items			Subscales
QOL	SF-8	1	Physical functioning*	Five- or six-point Likert scale	Physical component summary*
		2	Role physical*		Mental component summary*
		3	Bodily pain*		
		4	General health*		
		5	Vitality*		
		6	Social functioning*		
		7	Role emotional*		
		8	Mental health*		
Symptoms	Gastrointestinal Symptom Rating Scale (GSRS) items	9	Abdominal pains	Seven-point Likert scale except items 29 and 32	Esophageal reflux subscale (items 10, 11, 13, 24)
		10	Heartburn		Abdominal pain subscale (items 9, 12, 28)
		11	Acid regurgitation		Meal-related distress subscale (items 25–27)
		12	Sucking sensations in the epigastrium		Indigestion subscale (items 14–17)
		13	Nausea and vomiting		Diarrhea subscale (items 19, 20, 22)
		14	Borborygmus		Constipation subscale (items 18, 21, 23)
		15	Abdominal distension		Dumping subscale (items 30, 31, 33)
		16	Nausea and vomiting		
		17	Increased flatus		Total symptom scale (above seven subscales)
		18	Decreased passage of stools		
		19	Increased passage of stools		
		20	Loose stools		
		21	Hard stools		
		22	Urgent need for defecation		
		23	Feeling of incomplete evacuation		
	PGSAS-specific items	24	Bile regurgitation		
		25	Sense of foods sticking		
		26	Postprandial fullness		
		27	Early satiation		
		28	Lower abdominal pains		
		29	Number and type of early dumping symptoms		
		30	Early dumping, general symptoms		
		31	Early dumping, abdominal symptoms		
		32	Number and type of late dumping symptoms		
		33	Late dumping symptoms		
Living status	Meals (amount) 1	34	Ingested amount of food per meal*		–
		35	Ingested amount of food per day*		
		36	Frequency of main meals		
		37	Frequency of additional meals		
	Meals (quality)	38	Appetite*	Five-point Likert scale	Quality of ingestion subscale* (items 38–40)
		39	Hunger feeling*		
		40	Satiety feeling*		
	Meals (amount) 2	41	Necessity for additional meals		–
	Social activity	42	Ability for working		–
Quality of life (QOL)	Dissatisfaction	43	Dissatisfaction with symptoms		Dissatisfaction for daily life subscale (items 43–45)
		44	Dissatisfaction at the meal		
		45	Dissatisfaction at working		

In items or subscales with *, higher score indicates better condition

In items or subscales without *, higher score indicates worse condition

Each subscale is calculated as the mean of composed items or subscales except physical component summary and mental component summary of SF-8

Items 29 and 32 do not have a score. Thus, they were analyzed separately

Table 2 Outcome measures in PGSAS (patients after conventional gastrectomy: $N = 1,777$)

Domain	Item number (#)	Main outcome measures	Mean	SD
Symptoms	10, 11, 13, 24	Esophageal reflux subscale	1.71	0.85
	9, 12, 28	Abdominal pain subscale	1.70	0.77
	25–27	Meal-related distress subscale	2.19	0.96
	14–17	Indigestion subscale	2.07	0.87
	19, 20, 22	Diarrhea subscale	2.14	1.11
	18, 21, 23	Constipation subscale	2.17	1.01
	30, 31, 33	Dumping subscale	2.04	1.04
	9–28, 30, 31, 33	Total symptom score	2.00	0.70
Living status	–	Change in body weight (%)*	−9.5	8.0
	34	Ingested amount of food per meal*	7.00	1.97
	41	Necessity for additional meals	1.98	0.81
	38–40	Quality of ingestion subscale*	3.78	0.92
	42	Ability for working	1.84	0.88
QOL	43	Dissatisfaction with symptoms	1.87	0.95
	44	Dissatisfaction at the meal	2.32	1.13
	45	Dissatisfaction at working	1.79	0.97
	43–45	Dissatisfaction for daily life subscale	2.00	0.87
	1–8	Physical component summary*	50.4	5.6
	1–8	Mental component summary*	49.7	5.8
Domain	Item number (#)	Other outcome measures (symptom)	Mean	SD
Symptoms	9	Abdominal pains	1.74	0.96
	10	Heartburn	1.76	1.02
	11	Acid regurgitation	1.81	1.12
	12	Sucking sensations in the epigastrium	1.50	0.82
	13	Nausea and vomiting	1.50	0.94
	14	Borborygmus	1.87	1.06
	15	Abdominal distension	2.00	1.12
	16	Eructation	1.70	0.97
	17	Increased flatus	2.72	1.43
	18	Decreased passage of stools	2.13	1.25
	19	Increased passage of stools	2.13	1.29
	20	Loose stools	2.10	1.18
	21	Hard stools	1.96	1.12
	22	Urgent need for defecation	2.19	1.30
	23	Feeling of incomplete evacuation	2.43	1.16
	24	Bile regurgitation	1.77	1.07
	25	Sense of foods sticking	1.79	1.08
	26	Postprandial fullness	2.39	1.21
	27	Early satiation	2.41	1.21
	28	Lower abdominal pains	1.87	1.11
	30	Early dumping general symptoms	1.96	1.20
	31	Early dumping abdominal symptoms	2.34	1.31
	33	Late dumping symptoms	1.81	1.17

Table 2 continued

Domain	Item number (#)	Other outcome measures (dumping)	Mean	SD
Symptoms	29	Existence of early dumping general symptoms [Y/N]	915	802
	29	Existence of early dumping abdominal symptoms [Y/N]	1,175	542
	29	Existence of either early dumping symptoms [Y/N]	1,293	424
	32	Existence of late dumping symptoms [Y/N]	715	891
	29	Number of early dumping general symptoms	1.95	1.30
	29	Number of early dumping abdominal symptoms	1.94	1.11
	29	Number of any early dumping symptoms	2.87	2.04
	32	Number of late dumping symptoms	1.85	1.24
Domain	Item number (#)	Other outcome measures (meals)	Mean	SD
Living status	35	Ingested amount of food per day*	7.30	2.02
	36, 37	Frequency of daily meals	4.99	1.45
	38	Appetite*	4.27	1.11
	39	Hunger feeling*	3.21	1.30
	40	Satiety feeling*	3.85	1.19

In items or subscales with *, higher score indicates better condition

In items or subscales without *, higher score indicates worse condition

have characteristics in common were aggregated. The item pool was further reduced by excluding items that were considered to represent symptoms with a low incidence or are not definitely related to the PGS. To speed up the process of compiling a valid scale, a decision was made to include items from relevant and internationally acclaimed questionnaires. All items from Short Form-8 Health (SF-8) and Gastrointestinal Symptom Rating Scale (GSRS) surveys were subsequently selected for inclusion with permissions from relevant organizations for this study. Thus, PGSAS-45 was established in April 2009.

Structure of the PGSAS-45 (Tables 1, 2; Fig. 1)

PGSAS-45, the end product of the current project with 45 items, became a HRQOL instrument with multidimensional structure consisting of three domains: symptom domain, living status domain, and QOL domain, each consisting of several subdomains (Tables 1, 2; Fig. 1). Twenty-two of the items that had originally been proposed by the JPGSWP members were selected to be retained and added to all 8 items from SF-8 (items 1–8) and all 15 items from GSRS (items 9–23) to constitute the PGSAS-45.

As a symptom domain, 10 original items proposed by the JPGSWP members (items 24–33) were added to the 15 items from GSRS. Of these 10 items, 8 items inquire intensity of symptoms that are actually observed as PGS but had not been evaluated by the conventional questionnaires. The other 2 items (items 29 and 32) inquire whether the patients suffer from early or late dumping syndrome, and the number and types of symptoms if they do. The living status domain consists entirely of the original items proposed by the JPGSWP members and can be stratified into three subdomains (Table 1; Fig. 1). Items 34–37 and 41 constitute the subdomain for the amount of food ingested, and items 38–40 constitute the subdomain for quality of food intake. A subdomain for social activity consists of a single item (item 42). The QOL domain consists of all 8 items from the SF-8 and 3 original items proposed by the JPGSWP members. These 3 items focused on the issue of dissatisfaction in everyday life caused by symptoms (item 43), feeding problems (item 44), and impaired social activity (item 45), and constitute the dissatisfaction subdomain (Table 1; Fig. 1). Twenty-three of the 25 items in the symptom domain (items 29 and 32 excepted) inquire about intensity of symptoms and are rated on a 7-point Likert scale. One of the 5 items of the amount of food ingested subdomain, all 3 items of the quality of food intake subdomain, the single item for social activity subdomain, and all 3 items of the dissatisfaction subdomain were rated on a 5-point Likert scale (Table 1). High scores denote favorable outcome in items 1–8 and items 34, 35, and 38-40, whereas low scores indicate superior outcome in items 9–28, 30, 31, 33, and 41–45.

PGSAS (PGS assessment) study, a multi-institutional cross-sectional study

A multi-institutional cross-sectional study involving 52 institutions (25 university hospitals, 8 cancer centers, and 19 community hospitals) was conducted by the JPGSWP to assess the patient-reported outcome using the PGSAS-45

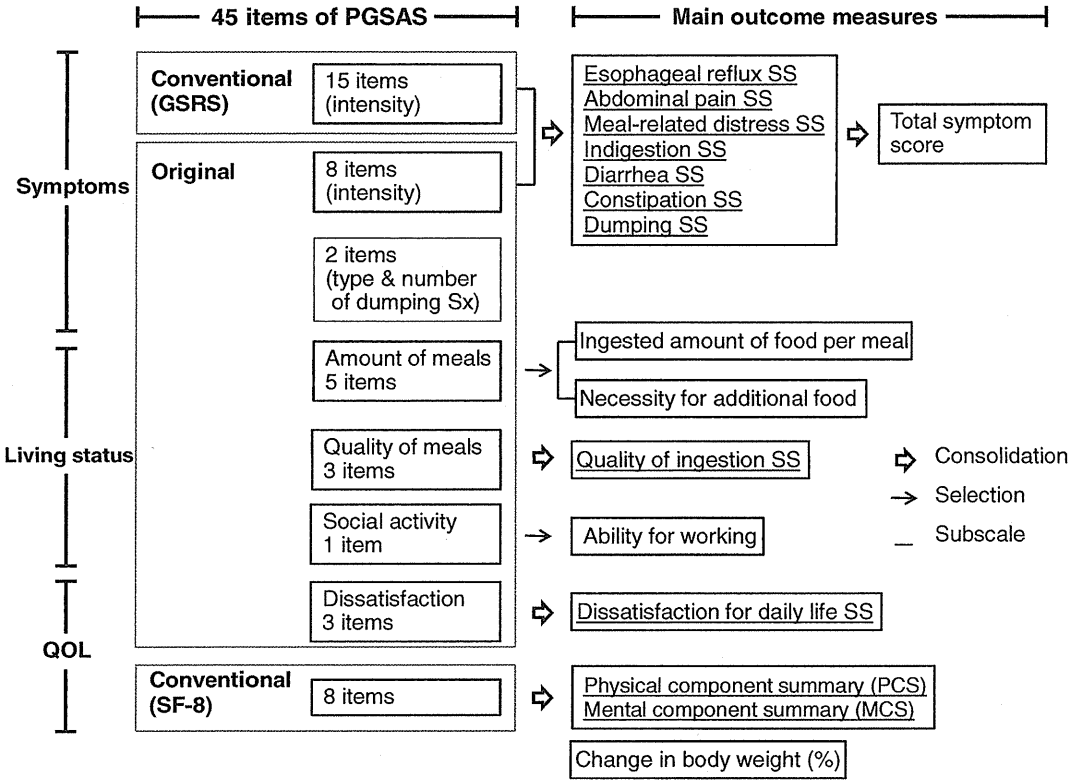

Fig. 1 The process of consolidation and selection to constitute main outcome measures

and to validate this instrument. This study was approved by the institutional review committee (IRB) of Jikei University and subsequently by the IRBs of all participating institutions.

Patients who underwent surgery for gastric cancer and were confirmed pathologically to have stage I disease were eligible. In addition, the patient had to be between 20 and 75 years of age, have undergone no chemotherapy, have lived for more than 1 year after surgery, have no signs of recurrence at the point of assessment, and be without active cancer in other sites. Consecutive sampling of the eligible patients in the outpatient clinic was conducted after obtaining written informed consent. The patients were given the questionnaire sheets together with a stamped and addressed envelope and were asked to fill in the answers and post the sheets to the data cancer. In addition, data regarding background of the patients such as age, gender, height, body weight before surgery and at the time of assessment, time interval since the surgery, the extent of lymphadenectomy (D-number), surgical approach, and details of the surgery performed were retrieved from the medical records and sent to the data center by the medical staff.

Of the 2,922 patients who were handed the questionnaire sheets between July 2009 and December 2010, 2,520 (86 %) responded and 2,368 were confirmed to be eligible for the

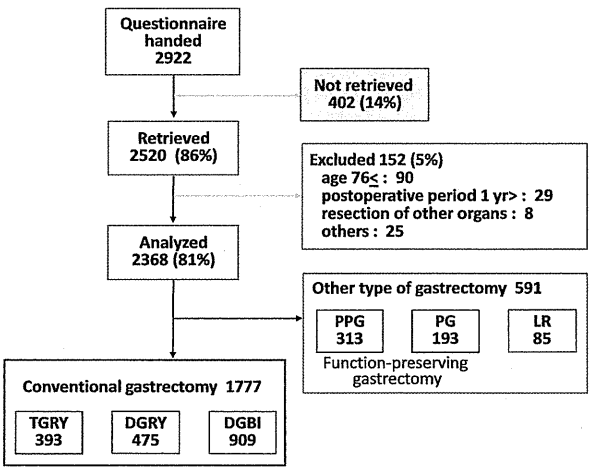

Fig. 2 Outline of the study

study. Of these, data from 1,777 patients who underwent either total or distal gastrectomy were used in the current study to assess construct validity for the PGSAS-45 (Fig. 2). Using these data, we explored relevance of the eight original items proposed by the JPGSWP members that were selected and added to the items derived from the GSRS to constitute the symptom domain of the PGSAS-45.

In addition to validation of the PGSAS-45, we intended to evaluate the PGS of patients who underwent radical gastrectomy for gastric cancer, and to what extent the symptoms influence the patients' living status or QOL.

Statistical analyses

Statistical analyses were performed by the biostatisticians mainly using StatView for Windows Ver. 5.0 (SAS Institute, Cary, NC, USA).

Bivariate and multivariate regression analyses were performed to evaluate correlations between the sum of scores for the 15 symptom-related items derived from GSRS or the 8 symptom-related items proposed by the JPGSWP members and scores related to living status and QOL. Factor analysis was used to decide which of the 23 symptom-related items should be clustered to form each symptom subscale. Cronbach's α was calculated from the pairwise correlations between items to verify the internal consistency of the items in each subscale. Correlations between the scores for each of the 7 symptom subscales were calculated in terms of Pearson's r, where effect size is considered to be large when $r > 0.5$.

Results

Characteristics and living status of the patients after conventional gastrectomy

Of the 1,777 patients, 1,188 (66.9 %) were male; the patients had a mean age of 62.1 ± 9.2 years. Of the patients, 393 underwent total gastrectomy, 909 underwent distal gastrectomy with Billroth type I reconstruction, and 475 underwent distal gastrectomy with Roux-en-Y reconstruction. The mean time interval between surgery and retrieval of the questionnaires was 37 ± 27 months. Table 2 summarizes the mean values and standard deviation of the main outcome measures and other items evaluated in the PGSAS study. The mean values of the symptom subscales indicate that the symptoms that adversely affect patient well-being are, in the order of importance, meal-related distress, constipation, diarrhea, indigestion, dumping, esophageal reflux, and abdominal pain. The mean loss of body weight at the time the patients were evaluated was 9.5 ± 8.0 %. The amount of food consumed per meal was approximately 70 % of the amount ingested before surgery, and the mean number of meals per day was five. Patient dissatisfaction with life was more closely related to meals rather than their symptoms or their jobs. In contrast, physical and mental components as evaluated by SF-8 were not seriously affected because both scores were around 50 by norm-based scoring.

Factor structure after weighting 23 symptom-related items of the PGSAS-45

Related items were clustered into a subscale to allow more simplified evaluation with a smaller number of scores when necessary. Items 1–8 derived from the SF-8 constitute the physical component summary (PCS) and the mental component summary (MCS). Items 38–40 constitute the quality of ingestion subscale and items 43–45 constitute the dissatisfaction for daily life subscale.

Similarly, the 23 symptom-related items of the PGSAS-45, which are rated on a 7-point Likert scale, were clustered into subscales, each consisting of 3–4 related items (GSRS actually has five symptom subscales). For this purpose, factor analysis using the principal factor method with Promax rotation was performed for the observed responses to the 23 symptom-related items of the PGSAS-45 (Table 3). Consequently, the 23 items were stratified into seven subgroups in which factor loading took maximal values for all the items and sufficiently large values of 0.7 or higher for most of the items. Thus, factor analysis identified seven clinically relevant subscales, which were named from their content as follows: esophageal reflux subscale (items 10, 11, 13, 24), abdominal pain subscale (items 9, 12, 28), meal-related distress subscale (items 25–27), indigestion subscale (items 14–17), diarrhea subscale (items 19, 20, 22), constipation subscale (items 18, 21, 23), and dumping subscale (items 30, 31, 33). Five of these seven subscales were named the same way as the subgroups of the GSRS, which are termed syndromes, of which three subscales (indigestion, diarrhea, and constipation) had similar content with the corresponding syndromes whereas two other subscales (esophageal reflux and abdominal pain) were dissimilar.

All these seven subscales could further be aggregated as a total symptom score, which is calculated as a mean value of the seven symptom subscales.

Clinical relevance of the eight additional items proposed by the JPGSWP members

The 8 symptom-related JPGSWP items, rated on a 7-point Likert scale, were compared with the 15 items derived from GSRS in terms of the correlation between the sum of these scores and the scores of the items reflecting either the living status, QOL, or change in body weight. The standardized partial regression coefficients (β) took larger values for the JPGSWP items in almost the items reflecting either the living status or QOL, with the exception of the MCS. The R^2 values of the JPGSWP items as evaluated by bivariate regression analysis were larger than that of the GSRS items across all outcome measures assessing living status and QOL and were