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Original Article

Diminished Gastric Resection Preserves Better Quality of Life in Patients with Early Gastric Cancer

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Using the Postgastrectomy Syndrome Assessment Scale (PGSAS)-45, we compared the surgical outcomes and the quality of life (QOL) between patients undergoing limited gastrectomies and those undergoing conventional gastrectomies. In Oomoto Hospital between January 2004 and December 2013, a total of 124 patients who met the eligibility criteria were enrolled. Using the main outcome measures of PGSAS-45, we compared 4 types of limited gastrectomy procedures (1/2 distal gastrectomy [1/2DG] in 21 patients; pylorus-preserving gastrectomy [PPG] in 15 patients; segmental gastrectomy [SG] in 26 patients; and local resection [LR] in 13 patients) with conventional gastrectomy (total gastrectomy [TG] in 24 patients and 2/3 or more distal gastrectomy [WDG] in 25 patients). The TG group showed the worst QOL in almost all items of the main outcome measures. The 1/2DG, PPG, and SG groups showed better QOL than the WDG group in many of the main outcome measures, including the body weight ratio, total symptom score, ingested amount of food per meal, and the dissatisfaction for daily life subscale. The LR group showed a better intake of food than the 1/2DG, PPG, and SG groups. The body weight ratio of the LR group was better than that of the SG group. Diminished gastric resection preserved better QOL in patients with early gastric cancer.

Key words: limited gastrectomy, early gastric cancer, function preserving gastrectomy, quality of life, post-gastrectomy syndrome

The incidence of early gastric cancer has markedly increased in Japan. Although procedures such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) have provided remarkable progress [1], many patients with early gastric cancer require a gastrectomy with lymphadenectomy in order to be cured.

The conventional surgical treatment for gastric cancer in Japan encompasses the removal of at least two-thirds of the stomach and dissection of the first and second levels of lymph nodes [2]. However, after a conventional gastrectomy, many patients suffer from postgastrectomy syndrome (PGS), which includes numerous symptoms related to the loss of the stomach, leading to impaired quality of life (QOL) [3–5].

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To maintain QOL after a gastrectomy, especially in patients with early gastric cancer, limited surgery has been applied in which the extent of gastric resection is smaller and the lymph node dissection is less invasive compared to conventional gastrectomy. Function-preserving gastrectomy (FPG), a procedure that is known to improve long-term QOL by avoiding PGS, is an example. However, the procedures of FPG have not been clearly defined [6, 7].

The lack of suitable instruments to assess PGS comprehensively has made comparisons of QOL after various types of gastrectomy difficult. However, the Postgastrectomy Syndrome Assessment Scale (PGSAS)-45 was developed in recent years [8], providing a valid and reliable integrated index for the evaluation of symptoms, living status, and QOL in patients who have undergone a gastrectomy.

In the last 10 years, we have performed various types of limited gastrectomy using mainly sentinel node navigation surgery (SNNS) [9]. In the present study, we used the PGSAS-45 to compare PGS after limited gastrectomies with conventional gastrectomies, and we obtained data that can be used to help maintain the QOL of patients following gastrectomy.

Patients and Methods

In Oomoto Hospital between January 2004 and December 2013, 407 gastric cancer patients underwent a gastrectomy. Between November 2014 and January 2015, the PGSAS-45 questionnaire [8] was distributed to patients who gave written informed consent to participate in this study and met the following eligibility criteria: (1) pathologically confirmed stage IA or IB gastric cancer; (2) first-time gastrectomy; (3) between 20 and 85 years of age; (4) no history of chemotherapy; (5) no recurrence or distant metastasis; (6) gastrectomy conducted ≥ 1 year prior to the enrollment date; (7) Eastern Cooperative Oncology Group Performance Status (ECOG-PS) ≤ 1 ; (8) full capacity to understand and respond to the questionnaire; (9) no history of other diseases or surgeries that might influence responses to the questionnaire; and (10) no presence of organ failure or mental illness. Patients with dual malignancies or a concomitant resection of other organs (co-resection equivalent to cholecystectomy being the exception) were excluded.

Patients undergoing the following 6 types of gastrectomy were selected. There are 2 types of conventional gastrectomy: total gastrectomy (TG), in which the whole stomach is resected, and wide extent or subtotal distal gastrectomy (WDG), in which approximately two-thirds or more of the whole stomach is resected. There were 4 types of limited gastrectomy procedures: (1) 1/2 distal gastrectomy (1/2DG), in which approximately the distal half of the whole stomach is resected; (2) pylorus-preserving gastrectomy (PPG) with SNNS, in which the distal part of the stomach is resected, while retaining 3–5 cm (average 4 cm) of the pyloric cuff and preserving the hepatic, pyloric, and celiac branches of the vagus nerve; (3) segmental gastrectomy (SG) with SNNS, in which the annular part of the middle or upper part of the stomach is transected, while preserving the hepatic, pyloric, and celiac branches of the vagus nerve; and (4) local resection (LR) with SNNS, in which the gastric wall is locally resected, including the cancerous lesion with a 2-cm safety margin endoscopically marked by clips before the operation, while preserving the hepatic, pyloric, and celiac branches of the vagus nerve.

Out of the 132 patients who met the above requirements, we distributed the questionnaire to 129 patients. For 83 patients, questionnaires were handed out and retrieved when the patients presented to our hospital, and of the 46 questionnaires distributed by mail, 44 were retrieved. Among these, 3 patients undergoing jejunal pouch reconstruction (two TG, one WDG) were excluded, leaving a total of 124 patients who were enrolled in the study.

Fig. 1 shows the location of the early gastric cancer lesions and the limited gastrectomy procedures performed. 1/2DG is indicated for early gastric cancer (A) located in the lower third of the stomach close to the pylorus. PPG is indicated for early gastric cancer (B) located in the lower or middle third of the stomach, ≥ 5 cm away from the pylorus. SG is indicated for early gastric cancer (C) located in the middle third (including the lower portion of the upper third) of the stomach. Commonly, in Japan, WDG is used for (A), (B), and (C) early gastric cancer lesions as a conventional gastrectomy.

SNNS is indicated in patients with early gastric cancer from whom informed consent has been obtained. SNNS is performed according to methods that we

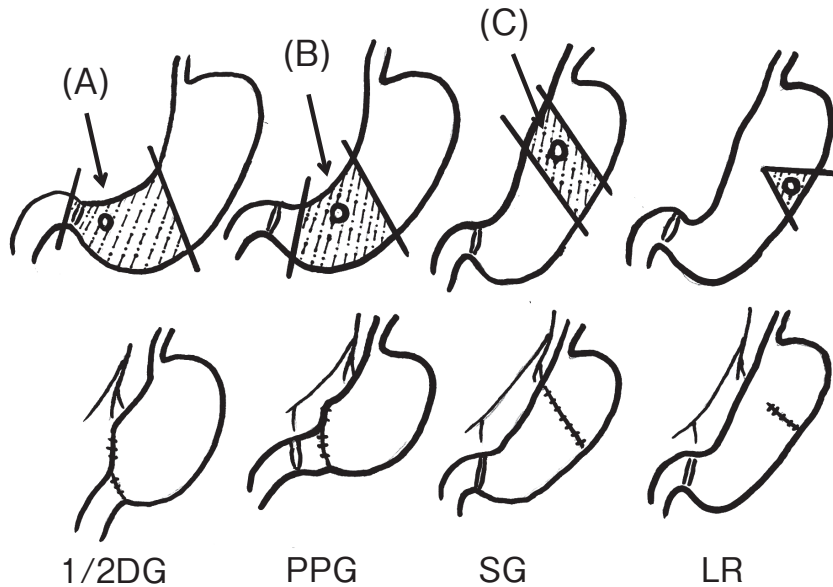


Fig. 1 Limited gastrectomy procedures. DG, 1/2 distal gastrectomy; PPG, pylorus-preserving gastrectomy; SG, segmental gastrectomy; LR, local resection; Gastric cancer lesion, ○; vagus nerve, ∟.

described in a multicenter trial [10]. After opening the abdomen, a total of 1ml of Patent Blue (2.5%) (Wako Pure Chemical Industries, Osaka, Japan) is injected endoscopically into the gastric wall at 4 sites around the gastric cancer lesion (cT1, N0, <4 cm). Approximately 5-10min later, the stained nodes (sentinel lymph nodes, SLNs) around the stomach are resected. When rapidly frozen sections of SLNs reveal no metastasis, a limited resection of the stomach with lymphatic basin resection, including SLN stations, is performed.

Consequently, the LR procedure is performed in patients in whom the SLNs are observed in only one lymphatic basin; for example, when sentinel nodes are observed only in the greater gastric curvature (lymph nodes along the greater curvature and infrapyloric lymph nodes) or only in the lesser gastric curvature (lymph nodes along the lesser curvature, lymph nodes along the left gastric artery, and lymph nodes along the celiac artery). When sentinel nodes are observed in both the greater and lesser curvatures, 1/2DG, PPG or SG procedures are performed.

The PGSAS-45 comprises 45 items: 8 items from SF-8, 15 items from the Gastrointestinal Symptom Rating Scale (GSRS), and an additional 22 items selected by 47 gastric surgeons. In this study, we used the main outcome measures of PGSAS-45 [8]. The change in the body weight (body weight ratio) was calculated by the following formula:

$$\text{present body weight/preoperative body weight} \times 100 (\%)$$

For patients who presented to our hospital, we directly measured their body weight. For patients who answered by mail, we used the recorded weight in the questionnaire as the present weight and obtained the preoperative body weight from the patients' medical records.

The statistical analysis was conducted using JMP version 10.0.2 for Windows (SAS, Cary, NC, USA). To compare the patient characteristics among the patient groups of the 6 types of gastrectomy, we used an analysis of variance (ANOVA) and the Chi-squared test. *P*-values < 0.05 were considered significant. To compare the intensity of main outcome measures of the PGSAS-45 among the 6 types of gastrectomy, the analysis of means method (ANOM) was used. The significance of differences between control groups and each opposed group was assessed using Dunnett multiple comparisons. In general, *p*-values < 0.05 in the ANOM or Dunnett test are considered significant. We calculated Cohen's *d* as the effect size. The value of Cohen's *d* reflects the impact of each causal variable; a value of 0.20 to < 0.50 denotes a small but clinically meaningful difference between groups, and values of 0.50 to < 0.80 and ≥ 0.80 indicate medium and large effects, respectively.

The procedures of the study were approved by the Ethical Committee of Oomoto Hospital.

Results

Patient characteristics. The background data of the patients following the 6 types of gastrectomy are shown in Table 1. The age of the LR group was higher than that in all the other groups. The celiac branch of the vagus nerve was preserved in 14 (67%) 1/2DG procedures and all of the PPG, SG, and LR procedures. The reconstruction methods after TG were double tract in 19 patients (79.2%) and Roux-Y (RY) in 5 patients (20.8%), and those after WGD were Billroth I (BI) in 21 patients (84%) and RY in 4 patients (16%). The depth of cancerous invasion was significantly different among the groups, and that of the limited gastrectomy groups (1/2DG, PPG, SG and LR) was shallower than that of the conventional gastrectomy groups (TG and WDG).

Concerning the frequency of lymph node metastasis, there was no significant difference among the 6 types of gastrectomy. The tumor size of the TG group was significantly larger and those of the SG and LR groups were significantly smaller than the average of the 6 types of gastrectomy by ANOM. In all patients except one WDG patient, the approach of operation was open laparotomy.

The main outcome measures of PGSAS-45 following the 6 types of gastrectomy and the ANOM. The mean \pm SD values of the main outcome measures following the 6 types of gastrectomy and the ANOM analysis are shown in Table 2. Of the 19 main outcome measures, 15 items in the TG group and 2 items in the WGD group were significantly worse than the average of all the operations together. Three items of the 1/2DG group, 2 items of the PPG group, 3 items of the SG group, and 5 items of the LR group were significantly better than the average of all the operations.

Fig. 2 shows the particularly important main outcome measures: (a) the total symptom score, (b) the ingested amount of food per meal, (c) the dissatisfaction for daily life subscale, (d) the change in body weight [body weight ratio, post/preoperative weight \times 100 (%)], and (e) the patients' ability for working.

Comparison of the main outcome measures of PGSAS-45 between the WDG group and the 1/2DG, PPG, or SG groups. We compared the main outcome measures following WDG with those of the 1/2DG, PPG, and SG groups (Table 3). Many of

the main outcome measures of the 1/2DG, PPG, and SG groups were significantly better than those of the WDG group. The total symptom score of the 1/2DG (1.3 ± 0.3), PPG (1.4 ± 0.3), and SG (1.4 ± 0.4) groups were significantly better than that of the WDG group (2.0 ± 0.7) with a large effect size. The ingested amount of food per meal of the 1/2DG (8.6 ± 1.4) and PPG (8.7 ± 1.3) groups were significantly greater than that of the WDG group (7.2 ± 1.8) with a large effect size. The ingested amount of food per meal of the SG group (7.6 ± 1.4) was greater than that of the WDG group with a small effect size, but there was no significant difference between the groups.

The dissatisfaction for the daily life subscale of the 1/2DG (1.2 ± 0.4), PPG (1.3 ± 0.5), and SG (1.2 ± 0.4) groups were significantly better than that of the WDG group (1.8 ± 0.7) with a middle or large effect size. The body weight ratio of the 1/2DG (96.8 ± 7.8) and PPG (98.3 ± 5.3) groups were significantly higher than that of the WDG group (90.6 ± 10.3) with a middle to large effect size. Although the body weight ratio of the SG group (93.8 ± 4.7) was higher than that of the WDG group with a small effect size, there was no significant difference between the groups. The ability for working of the 1/2DG (1.5 ± 0.5), PPG (1.4 ± 0.5), and SG (1.5 ± 0.6) groups were better than that of the WDG group (1.9 ± 1.0) with a middle effect size, but there was no significant difference.

Comparison of the main outcome measures of PGSAS-45 between the LR group and the 1/2DG, PPG, or SG groups. The main outcome measures following LR were compared with those of 1/2DG, PPG, and SG (Table 4). Many of the main outcome measures of the LR group were better than those of the 1/2DG, PPG, or SG groups with small to large effect sizes. The ingested amount per meal had an especially large effect size. However, only a few of the main outcome measures of the LR groups were significantly better than those of the SG or PPG groups, namely, LR was superior to SG in body weight ratio and ingested amount of food per meal, and was superior to PPG in the necessity for additional meals.

Discussion

This study addressed the question of what type of gastrectomy should be performed to maintain QOL

Table 1 Patient characteristics

	TG	WDG	1/2DG	PPG	SG	LR	<i>p</i> -value
Number of patients	24	25	21	15	26	13	
Postoperative period (years)	6.8 ± 1.9	6.2 ± 3.0	5.5 ± 2.5	4.6 ± 3.2	6.0 ± 3.2	4.8 ± 2.1	0.1074 ^a
Age	58.6 ± 10.1	61.0 ± 10.0	63.2 ± 10.7	61.2 ± 12.4	65.1 ± 8.5	(+) 70.7 ± 8.9	0.0222 ^a
Gender							
Male	16	17	13	6	12	7	0.3657 ^b
Female	8	8	8	9	14	6	
Extent of lymph node dissection							<.0001 ^b
D0	0	0	2	0	24	13	
D1	5	2	3	6	2	0	
D1+	0	3	4	5	0	0	
D2	19	20	12	4	0	0	
Sentinel LN navigation							<.0001 ^b
Yes	0	2	10	15	26	13	
No	24	23	11	0	0	0	
Preservation of the celiac branch							<.0001 ^b
Preserved	2	3	14	15	26	13	
Divided	22	22	7	0	0	0	
Reconstruction method							<.0001 ^b
BI	0	21	21	0	0	0	
RY	5	4	0	0	0	0	
Double tract	19	0	0	0	0	0	
Gastro-gastric anastomosis	0	0	0	15	26	0	
Suture of gastric wall	0	0	0	0	0	13	
Depth of cancerous invasion							<.0001 ^b
T1a (m)	9	9	14	9	11	10	
T1b (sm)	11	10	7	5	13	2	
T2 (mp)	4	6	0	1	2	1	
Lymph node metastasis							0.8498 ^b
N0	21	24	19	14	25	12	
N1	3	1	2	1	1	1	
Tumor size (cm)	(+) 4.9 ± 2.4	3.2 ± 1.6	2.8 ± 1.7	2.5 ± 9.9	(-) 2.2 ± 1.1	(-) 1.8 ± 1.7	<.0001 ^a

a, ANOVA; b, Chi-square test.

Analysis of means method (ANOM); a *p* value less than 0.05 was considered as statistically significant.

(+) Significantly larger compared with the overall mean of 6 types of gastrectomy by ANOM (*p* < 0.05).

(-) Significantly smaller compared with the overall mean of 6 types of gastrectomy by ANOM (*p* < 0.05).

TG, Total gastrectomy; WDG, Wide-extent distal gastrectomy (2/3 or more resection of the stomach); 1/2 DG, 1/2 distal gastrectomy (approximately half resection of the stomach); PPG, Pylorus-preserving gastrectomy; SG, Segmental gastrectomy; LR, Local resection of the stomach.

after surgery. Many gastric surgeons have not considered this issue. In terms of PGS, many studies have compared the outcomes between different surgical procedures. However, because of the lack of instruments focusing on the evaluation of PGS, the results

of these studies are not necessarily comprehensive or convincing. The PGSAS-45 questionnaire has provided a breakthrough in this problem. The PGSAS-45 was developed by the Japanese Postgastrectomy Syndrome Working Party (JPGSWP) in 2009, and it

Table 2 Comparison of main outcome measures of PGSAS-45 following 6 types of gastrectomy

	TG		WDG		1/2DG		PPG		SG		LR	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Body weight ratio* post/pre × 100 (%)	(-) 88.4	±7.3	90.6	±10.3	96.8	±7.8	98.3	±5.3	93.8	±4.7	(+) 99.5	±5.0
Esophageal reflux subscale (a)	1.8	±1.0	1.7	±0.8	1.2	±0.5	1.3	±0.4	1.3	±0.4	1.4	±0.8
Abdominal pain subscale (a)	(-) 1.9	±0.7	1.6	±0.8	1.2	±0.4	1.2	±0.3	1.3	±0.5	1.0	±0.1
Meal-related distress subscale (a)	(-) 2.7	±1.2	2.0	±0.7	1.5	±0.7	1.4	±0.5	(+) 1.4	±0.5	(+) 1.2	±0.4
Indigestion subscale (a)	(-) 2.0	±0.9	(-) 2.0	±0.7	1.4	±0.4	1.5	±0.5	1.5	±0.6	1.4	±0.3
Diarrhea subscale (a)	(-) 2.8	±1.4	2.4	±1.5	1.5	±0.7	1.3	±0.6	1.5	±0.9	1.2	±0.5
Constipation subscale (a)	2.3	±1.3	2.4	±1.4	1.6	±0.6	1.8	±1.2	1.8	±1.1	2.2	±1.1
Dumping subscale (a)	(-) 2.3	±0.9	1.8	±1.2	1.3	±0.6	1.0	±0.2	1.2	±0.5	1.0	±0.0
Total symptom score (a)	(-) 2.3	±0.8	(-) 2.0	±0.7	(+) 1.3	±0.3	1.4	±0.3	1.4	±0.4	1.4	±0.3
Ingested amount of food per meal*	(-) 6.3	±1.5	7.2	±1.8	(+) 8.6	±1.4	(+) 8.7	±1.3	7.6	±1.4	(+) 9.6	±0.8
Necessity of additional meals	(-) 2.3	±0.8	1.9	±1.1	1.5	±0.7	1.8	±0.7	1.5	±0.6	1.2	±0.4
Quality of ingestion subscale* (a)	3.7	±0.8	4.1	±1.0	4.2	±0.9	(+) 4.7	±0.4	3.8	±1.0	4.0	±1.2
Ability for working	(-) 2.2	±0.8	1.9	±1.0	1.5	±0.5	1.4	±0.5	1.5	±0.6	1.2	±0.4
Dissatisfaction with symptoms	(-) 2.2	±1.2	1.8	±0.8	1.2	±0.5	1.3	±0.6	1.2	±0.4	1.1	±0.3
Dissatisfaction at the meals	(-) 2.8	±1.2	1.9	±0.9	1.3	±0.8	1.5	±0.7	(+) 1.3	±0.5	1.2	±0.6
Dissatisfaction at working	(-) 2.0	±1.1	1.6	±0.9	1.1	±0.3	1.2	±0.4	1.2	±0.4	1.0	±0.0
Dissatisfaction for daily life subscale (a)	(-) 2.3	±1.0	1.8	±0.7	(+) 1.2	±0.4	1.3	±0.5	(+) 1.2	±0.4	(+) 1.1	±0.2
Physical component summary (PCS)* (a)	(-) 46.4	±7.5	51.6	±6.7	52.0	±5.3	52.5	±4.2	50.1	±4.7	52.5	±5.2
Mental component summary (MCS)* (a)	49.5	±5.3	50.0	±5.1	51.9	±5.6	51.6	±5.7	53.2	±4.2	(+) 55.3	±2.9

Analysis of means method (ANOM); a *p* value less than 0.05 was considered as statistically significant.

(+) Significantly better compared with the overall mean of 6 types of gastrectomy by ANOM (*p* < 0.05).

(-) Significantly worse compared with the overall mean of 6 types of gastrectomy by ANOM (*p* < 0.05).

TG, Total gastrectomy; WDG, Wide extent distal gastrectomy (2/3 or more resection of stomach); 1/2 DG, 1/2 distal gastrectomy (approximately half resection of stomach); PPG, Pylorus-preserving gastrectomy; SG, Segmental gastrectomy; LR, Local resection of the stomach.

Outcome measures with* higher score indicates better condition. Outcome measures without* higher score indicates worse condition. (a) Integrated subscales

has been shown to be a useful multidimensional integrated QOL measure. The PGSAS study, a multi-institutional cross-sectional study involving 52 institutions, addressed several factors of PGS following

various operations or reconstructions [11-14]. Until now, in many studies, the benefits to QOL following limited surgery for gastric cancer have been reported using inadequate evaluation tools. In this study, we

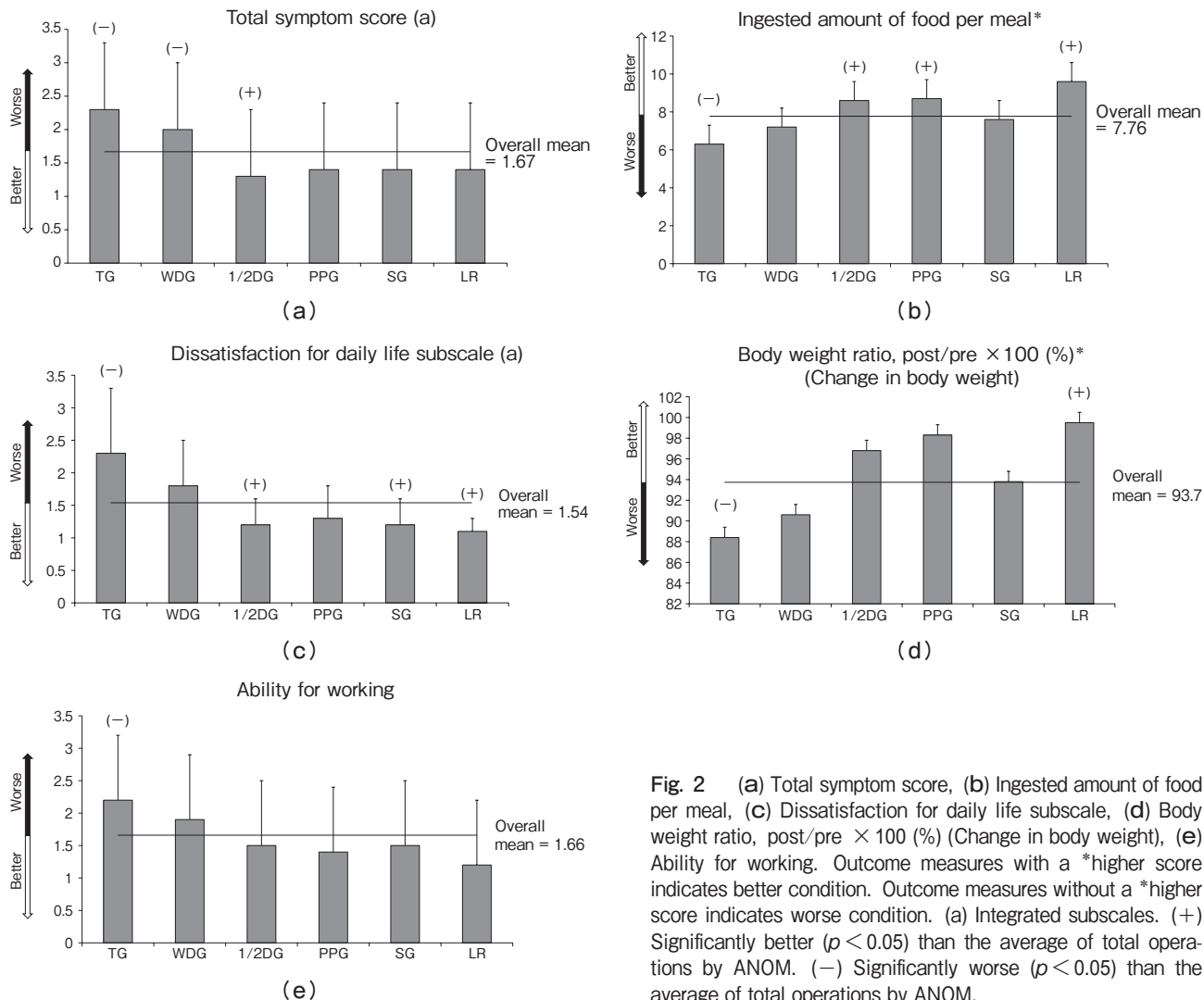


Fig. 2 (a) Total symptom score, (b) Ingested amount of food per meal, (c) Dissatisfaction for daily life subscale, (d) Body weight ratio, post/pre × 100 (%) (Change in body weight), (e) Ability for working. Outcome measures with a *higher score indicates better condition. Outcome measures without a *higher score indicates worse condition. (a) Integrated subscales. (+) Significantly better ($p < 0.05$) than the average of total operations by ANOM. (-) Significantly worse ($p < 0.05$) than the average of total operations by ANOM.

evaluated QOL following various limited operations for gastric cancer by using the PGSAS-45, and although this study was performed at a single institution, the PGSAS-45 revealed a powerful ability to detect PGS.

Using the ANOM and Dunnett's test, our present findings revealed that PGS after limited gastrectomy procedures (1/2DG, PPG, SG, and LR) was much better than that after conventional gastrectomy procedures (TG and WDG).

Our TG patients showed the worst PGS with the lowest body weight ratio among the 6 types of gastrectomy. Using the ANOM, we observed that almost all items of the main outcome measures of TG were sig-

nificantly worse than the average of all the operations. Representatively, the total symptom score, ingested amount of food per meal, ability for working, dissatisfaction for daily life subscale, and the physical component summary (PCS) of the TG patients were worse than those of the other groups. These results indicate that TG should be avoided for early gastric cancer whenever possible.

WDG is widely accepted in Japan as a radical operation for early gastric cancer located in the lower or middle part (including the lower portion of the upper third) of the stomach. However, using the ANOM, we observed that the total symptom score and indigestion subscale in patients following WDG were

Table 3 Comparison of main outcome measures of PGSAS-45 between WDG vs. 1/2DG, PPG or SG

	1/2DG vs. WDG		PPG vs. WDG		SG vs. WDG	
	<i>p</i> -value	Cohen's <i>d</i>	<i>p</i> -value	Cohen's <i>d</i>	<i>p</i> -value	Cohen's <i>d</i>
Body weight ratio* post/pre ×100 (%)	0.0193	<u>0.68</u>	0.0065	0.9	≥0.1	0.42
Esophageal reflux subscale (a)	0.0129	<u>0.73</u>	0.0402	<u>0.7</u>	0.0118	<u>0.75</u>
Abdominal pain subscale (a)	0.0226	<u>0.7</u>	0.0418	<u>0.68</u>	≥0.1	0.46
Meal-related distress subscale (a)	0.0298	<u>0.69</u>	0.0138	<u>0.92</u>	0.0025	<u>0.98</u>
Indigestion subscale (a)	0.0005	<u>1.19</u>	0.0172	<u>0.86</u>	0.0038	<u>0.84</u>
Diarrhea subscale (a)	0.0164	<u>0.73</u>	0.0065	<u>0.88</u>	0.014	<u>0.7</u>
Constipation subscale (a)	0.0617	<u>0.7</u>	≥0.1	0.46	≥0.1	0.49
Dumping subscale (a)	0.0578	<u>0.56</u>	0.0122	<u>0.78</u>	0.0234	<u>0.64</u>
Total symptom score (a)	0.0001	<u>1.12</u>	0.0005	<u>1.07</u>	0.0004	<u>0.96</u>
Ingested amount of food per meal*	0.0074	<u>0.86</u>	0.0068	<u>0.97</u>	≥0.1	0.26
Necessity of additional meals	≥0.1	0.4	≥0.1	<0.2	≥0.1	0.46
Quality of ingestion subscale* (a)	≥0.1	<0.2	≥0.1	<u>0.74</u>	≥0.1	0.28
Ability for working	≥0.1	<u>0.54</u>	0.0885	<u>0.61</u>	0.0772	<u>0.54</u>
Dissatisfaction with symptoms	0.0024	<u>0.94</u>	0.0491	<u>0.67</u>	0.0028	<u>0.94</u>
Dissatisfaction at the meals	0.0231	<u>0.72</u>	≥0.1	<u>0.51</u>	0.0121	<u>0.86</u>
Dissatisfaction at working	0.0055	<u>0.8</u>	0.0572	<u>0.59</u>	0.0094	<u>0.72</u>
Dissatisfaction for daily life subscale (a)	0.0003	<u>1.07</u>	0.0163	<u>0.75</u>	0.0003	<u>1.05</u>
Physical component summary (PCS)* (a)	≥0.1	<0.2	≥0.1	<0.2	≥0.1	0.26
Mental component summary (MCS)* (a)	≥0.1	0.36	≥0.1	0.32	0.0732	<u>0.7</u>

Dunnett multiple comparison test; a *p* value less than 0.05 was considered as statistically significant.

Interpretation of effect size in Cohen's *d*: ≥0.20 as small, ≥0.50 as medium, ≥0.80 as large.

Outcome measures with* higher score indicates better condition. Outcome measures without* higher score indicates worse condition.

(a) Integrated subscales

significantly worse than those of the average of the total operations in this series. The main outcome measures of the WDG group were better than those of the TG group with small to large Cohen's effect size (data not shown). However, many of the main outcome measures of the WDG group were significantly worse than those of the limited operations, with small to large effect sizes.

As mentioned above, WDG is commonly used as a conventional gastrectomy procedure for early gastric cancer located in the lower or middle part of the stomach. On the other hand, as limited procedures, 1/2DG, PPG, and SG are used depending on the location of the early gastric cancer. However, the

present report is of the only study comparing PGS following 1/2DG, PPG or SG, and WDG.

Our 1/2DG patients demonstrated significantly better QOL after surgery in many of the main outcome measures, with a higher body weight ratio (96.8%) than the WDG patients. The better QOL following 1/2DG compared to WDG was also proven by small to large effect sizes. Nomura *et al.* [15] reported the actual benefits (in terms of postoperative body weight, food intake, and postprandial symptoms) of 1/2 distal gastrectomy compared to the typical 2/3 after laparoscopic distal gastrectomy for early stage gastric cancer. Thus, diminished resection in distal gastrectomy maintained better QOL than conventional

Table 4 Comparison of main outcome measures of PGSAS-45 between LR vs. 1/2DG, PPG, or SG

	1/2DG vs. LR		PPG vs. LR		SG vs. LR	
	<i>p</i> -value	Cohen's <i>d</i>	<i>p</i> -value	Cohen's <i>d</i>	<i>p</i> -value	Cohen's <i>d</i>
Body weight ratio* post/pre ×100 (%)	≥0.1	0.41	≥0.1	0.23	0.0165	<u>1.21</u>
Esophageal reflux subscale (a)	≥0.1	0.34	≥0.1	0.31	≥0.1	0.34
Abdominal pain subscale (a)	≥0.1	0.46	≥0.1	<u>0.58</u>	0.0717	<u>0.73</u>
Meal-related distress subscale (a)	≥0.1	0.47	≥0.1	0.38	≥0.1	0.33
Indigestion subscale (a)	≥0.1	<0.2	≥0.1	0.39	≥0.1	0.30
Diarrhea subscale (a)	≥0.1	0.43	≥0.1	<0.2	≥0.1	0.40
Constipation subscale (a)	≥0.1	<u>0.69</u>	≥0.1	0.35	≥0.1	0.38
Dumping subscale (a)	≥0.1	<u>0.56</u>	≥0.1	0.30	≥0.1	0.49
Total symptom score (a)	≥0.1	<0.2	≥0.1	<0.2	≥0.1	0.20
Ingested amount of food per meal*	0.0652	<u>0.88</u>	≥0.1	<u>0.85</u>	<.0001	<u>1.68</u>
Necessity of additional meals	≥0.1	<u>0.50</u>	0.0407	<u>1.02</u>	≥0.1	<u>0.51</u>
Quality of ingestion subscale* (a)	≥0.1	<0.2	≥0.1	<u>0.85</u>	≥0.1	<0.2
Ability for working	≥0.1	<u>0.71</u>	≥0.1	<u>0.57</u>	≥0.1	<u>0.55</u>
Dissatisfaction with symptoms	≥0.1	0.27	≥0.1	<u>0.54</u>	≥0.1	0.41
Dissatisfaction at the meals	≥0.1	<0.2	≥0.1	0.49	≥0.1	0.22
Dissatisfaction at working	≥0.1	0.41	≥0.1	<u>0.68</u>	≥0.1	<u>0.52</u>
Dissatisfaction for daily life subscale (a)	≥0.1	0.38	≥0.1	<u>0.74</u>	≥0.1	0.45
Physical component summary (PCS)* (a)	≥0.1	<0.2	≥0.1	<0.2	≥0.1	<u>0.50</u>
Mental component summary (MCS)* (a)	≥0.1	<u>0.75</u>	≥0.1	<u>0.84</u>	≥0.1	<u>0.57</u>

Dunnnett multiple comparison test; a *p* value less than 0.05 was considered as statistically significant.

Interpretation of effect size in Cohen's *d*: ≥0.20 as small, ≥0.50 as medium, >0.80 as large.

Outcome measures with* higher score indicates better condition. Outcome measures without* higher score indicates worse condition. (a) Integrated subscales

WDG.

In addition, the celiac branch of the vagus nerve was preserved in 67% of the 1/2DG cases and all of the PPG, SG, and LR cases in this series. Physiologically, preservation of the celiac branch of the vagus nerve prevents diarrhea and dumping syndrome after gastrectomy [16, 17]; it retains the postprandial motility of the duodenum and jejunum [18], and it controls pancreatic insulin release [19], postprandial plasma ghrelin levels [20], and visceral fat maintenance after distal gastrectomy [21]. The PGSAS study [11], using a multivariate analysis, showed that preservation of the celiac branch of the

vagus was significantly related to reduced weight loss after distal gastrectomy. Further research is needed to clarify the role of the celiac branch of the vagus nerve.

Compared to our WDG patients, the PPG patients showed significantly better QOL after surgery in many main outcome measures with high body weight ratio (98.3%). The better QOL following PPG compared to WDG was also proven by small to large effect sizes. Concerning the surgical technique of PPG in this series, the length of the pyloric cuff was 3–5 cm (average 4 cm), with a layer-to-layer hand-sewn anastomosis, and the size of gastric resection was reduced

by SNNS. There is a general consensus that PPG is associated with less dumping syndrome compared to conventional WDG [22–24].

However, the issue of body weight maintenance and food intake after PPG compared to WDG has been controversial. Some studies [23, 25, 26] from single institutes have reported better postoperative body weight maintenance in patients after PPG than after WDG. However, a multicenter trial comparing PPG and WDG reported no significant differences in postoperative body weight and food intake [22]. Nakane *et al.* [27] reported that patients undergoing PPG (2/3 distal gastrectomy with a 1.5-cm pyloric cuff) complained of gastric fullness after meals and poor food intake. Thereafter, they reported that patients with a 2.5-cm pyloric cuff had better food intake and recovery of body weight than those with a 1.5-cm pyloric cuff after PPG [28].

In contrast, Morita *et al.* [29] reported that there were no significant differences in symptoms, such as dumping syndrome or emptying disturbance, between patients with a pyloric cuff length within 3.0 cm and those with > 3.0 cm. The PGSAS study [13] showed that the size of the remnant stomach following PPG was closely related to patient dissatisfaction for daily life and body weight (*i.e.*, larger is better), and that having a medium pyloric cuff size (3–5 cm) reduced some symptoms after PPG. The PGSAS study also revealed that the nausea score in patients with hand-sewn anastomoses was better than those in whom a linear stapler had been used.

In our study, the QOL after PPG was much better than that after WDG, especially in relation to body weight, total symptom score, the ingested amount of food per meal, and the dissatisfaction for daily life subscale. From the point of view of the PGSAS study, we suspect that the ideal PPG procedure was performed in our series. Therefore, the combination of a plentiful size of proximal gastric remnant, a proper length of the pyloric cuff (approx. 4 cm), and a hand-sewn layer-to-layer anastomosis seem to be important for obtaining greater benefits from PPG.

Our SG group showed significantly better QOL after surgery in many main outcome measures compared to the WDG group. The better QOL following SG compared to WDG was also proven by small to large effect sizes. Following SG, as well as following PPG, better recovery of postoperative body weight

and fewer postprandial symptoms have been reported [30–32]. SG is often lumped together with PPG as a transectional gastrectomy [33]. In the present study however, there were significant differences between the PPG and SG group in body weight ratio (mean 98.3% and 93.8%, respectively), ingested amount of food per meal (mean 8.7 and 7.6, respectively), and the quality of ingestion subscale (mean 4.7 and 3.8, respectively) (unpaired *t*-test, data not shown). There were no significant differences between the PPG and SG groups in the other main outcome measures. Thus, SG was worse than PPG regarding food-related items. The reason for this is important for understanding the mechanism of food intake after gastrectomy. Namely, the size of the proximal gastric remnant may be closely related to the food intake volume in gastrectomized patients.

Using the ANOM, we observed that the LR patients had significantly better body weight ratios (99.5%), abdominal pain subscale scores, ingested amount of food per meal, dissatisfaction for daily life subscale scores, and mental component summary scores compared to the average of all the operations together. The ingested amount of food per meal of the LR patients was better than those of the 1/2DG, PPG, or SG patients, with a large effect size. The body weight ratio of the LR patients was significantly better compared to that of the SG patients. Thus, in our series, the QOL following LR was better than that of 1/2DG, PPG, or SG. However, the differences in QOL between the LR and 1/2DG, PPG, or SG patients were smaller than those between the WDG and 1/2DG, PPG, or SG patients.

Ohgami *et al.* [34] reported that LR should be strictly limited to mucosal gastric cancer using laparoscopy. Seto *et al.* [35] later reported the use of LR in early gastric cancer with lymph node dissection using SNNS. They also reported the nutritional superiority of LR over PPG. Kawamura *et al.* [36], using a ¹³C breath test, reported that reservoir capacity, gastric emptying, and QOL after LR were maintained. The average pre/postoperative body weight ratios in their series (the latter two) were high (99.5% and 97.3%), as observed in our study. In our study, the PGSAS-45 demonstrated that the maintenance of QOL following LR is better. Thus, LR should be performed in patients with early gastric cancer in whom sentinel lymph nodes are observed in only one

lymphatic basin, under the condition that there are no metastases on rapidly frozen sections.

Proximal gastrectomy (PG) is one of the limited surgical procedures for early gastric cancer located in the upper part of the stomach. In this study, however, we could not evaluate PGS following PG because PG was performed in only one patient with early gastric cancer during the study period. In general, we prefer to use LR with SNNS for early gastric cancer in the upper part of the stomach instead of PG. In the PGSAS study, Takiguchi *et al.* [14] reported that PG was significantly better than TG in terms of body weight loss (TG 13.8% vs. PG 10.9%), the necessity of additional meals and the dumping subscale, without any differences in the other main outcome measures. In the present study, LR was much better than TG in many main outcome measures, with large differences. Thus, if possible, LR with SNNS rather than PG should be performed in early gastric cancer.

This retrospective study has limitations. First, the study conducted at single time points, 1–10 years after gastrectomy. Since Kobayashi *et al.* [37] reported that the QOL of the patients after gastrectomy was more or less stabilized at 1 year after surgery, the present study was conducted to evaluate the QOL after limited gastrectomies at a similar steady period. The QOL of the patients in the recovery period (3–6 months after surgery) is also important, and thus a prospective study should be conducted to survey this period.

Second, the sample size of each gastrectomy in this study was relatively small. Nevertheless, the QOLs of the patients who underwent limited gastrectomies were significantly better than those of the conventional gastrectomy patients, with middle to large effect sizes, showing the clinical usefulness of limited gastrectomies. A further accumulation of patients with limited gastrectomies is needed to increase the reliability of our findings. Third, although all of our patients were stage I, the backgrounds of the patients such as the depth of cancerous invasion and the tumor size were different among the conventional gastrectomy and limited gastrectomy groups. This selection bias may have been yielded because we selected conventional gastrectomies whenever a limited gastrectomy was thought to be inadequate for cure.

In conclusion, our study clearly showed that the QOL in patients after limited gastrectomies was significantly better than the QOL after conventional

gastrectomies with middle to large effect sizes, and therefore limited gastric resection (using SNNS) seems preferable for patients with early gastric cancer, unless curability is jeopardized.

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