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ORIGINAL ARTICLE

Long-term quality of life after open and laparoscopic total gastrectomy for stage I gastric cancer: A prospective multi-institutional study (CCOG1504)

Chie Tanaka[1] | Mitsuro Kanda[1] | Kazunari Misawa[2] | Yoshinari Mochizuki[3] | Masashi Hattori[4] | Satoshi Sueoka[5] | Takuya Watanabe[6] | Takanobu Yamada[7] | Kenta Murotani[8] | Yasuhiro Kodera[1]

[1]Department of Gastroenterological Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan

[2]Department of Gastroenterological Surgery, Aichi Cancer Center Hospital, Nagoya, Japan

[3]Department of Surgery, Komaki Municipal Hospital, Komaki, Japan

[4]Department of Surgery, NHO Nagoya Medical Center, Nagoya, Japan

[5]Department of Surgery, Ichinomiya Municipal Hospital, Ichinomiya, Japan

[6]Department of Surgery, Gifu Prefectural Tajimi Hospital, Tajimi, Japan

[7]Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan

[8]Biostatistics Center, Graduate School of Medicine, Kurume University, Kurume, Japan

Correspondence
Yasuhiro Kodera, Department of Gastroenterological Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8560, Japan.
Email: ykodera@med.nagoya-u.ac.jp

Abstract

Background: Little information is available from prospective clinical trials on the influences of surgical approaches on postoperative quality of life (QOL). We aimed to prospectively compare chronological changes in postoperative body weight and QOL between laparoscopic and open total gastrectomy for stage I gastric cancer (GC).

Methods: We conducted a multi-institutional prospective study (CCOG1504) of patients who undergo laparoscopic or open total gastrectomy. Body weight was measured at the baseline and at the 1st, 2nd, and 3rd postoperative years (POY). QOL using the European Organization for Research and Treatment of Cancer quality of life questionnaire-C30 (EORTC QLQ-C30) and the Post-Gastrectomy Syndrome Assessment Scale-37 (PGSAS-37) questionnaires were measured at the baseline and at the 1st, 3rd, 6th, 12th, and 36th postoperative months (POM).

Results: We enrolled 84 patients from 15 institutions, and finally 43 patients for the laparoscopic group and 16 for the open group were eligible for data analysis. There were no significant differences in body weight change between the two groups. The role functioning score among the EORTC QLQ-C30 tended to be higher (i.e., better QOL) in the laparoscopic group at POM 1 and 12 after surgery compared to the open group. The dissatisfaction at working score among the PGSAS-37 at 1 month after surgery was lower (i.e. better QOL) in the laparoscopic group compared to the open group.

Conclusions: The results of CCOG1504 indicated that laparoscopic approach for total gastrectomy was associated with a more favorable dissatisfaction at working score (PGSAS-37).

KEYWORDS
gastric cancer, laparoscopic surgery, quality of life, total gastrectomy

1 | INTRODUCTION

Although the incidence of gastric cancer (GC) continues to decline in Japan, GC remains the main cause of cancer-related death worldwide.[1,2] Since a high curability is expected for patients with early GC, maintenance of quality of life (QOL) after gastrectomy has been considered an important goal for these patients. Laparoscopic gastrectomy for GC, first reported in 1994,[3] has now become one of standard surgical procedures to treat early GC.[4]

The short-term outcome benefits of laparoscopic gastrectomy compared with open surgery are reduced blood loss, shorter time to pass the first flatus, and less use of analgesics after 5 postoperative days.[5] When we retrospectively evaluated chronological changes in QOL after laparoscopic and open distal gastrectomy for early GC,[6] we found that the lowest scores for most of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) scales were observed 1 month postoperatively and improved thereafter in both groups. Benefits of laparoscopic surgery were observed for certain functioning scores which lasted for a year. Moreover, some symptom scale scores including fatigue, pain, eating restriction, taste problem, and anxiety were superior after laparoscopic surgery during early postoperative periods.[6]

Since reconstruction after the resection was technically more demanding, introduction of the laparoscopic approach was delayed for total gastrectomy. The proportion of patients with major complications, especially the incidence of esophagojejunal anastomotic leakage, was found to be relatively low and the postoperative recovery was favorable in the hands of the experts,[7] but the safety issue remained rather uncertain in the setting of real world data.[8] Moreover, only limited evidence is available on the advantages of laparoscopic surgery associated with postoperative QOL and body composition.

We therefore designed a multi-institutional prospective study to test the validity of the hypothesis that a laparoscopic approach for total gastrectomy is beneficial for patients with GC through maintenance of postoperative QOL. Since the Japanese Treatment Guidelines at the time the patients were recruited recommended laparoscopic gastrectomy only for clinical stage I GC, prospective comparisons of body weight and QOL were conducted only among such a cohort of patients.

2 | METHODS

2.1 | Study design and ethics

Here we conducted a multi-institutional prospective study to compare the QOL of patients selected to undergo open or laparoscopic total gastrectomy for stage I GC. The internal review boards of 15 participating institutions reviewed the scientific and ethical validity of the protocol, which was registered in the University Hospital Medical Information Network (UMIN) Clinical Trial Registry as UMIN000018808 (http://www.umin.ac.jp/ctr/index.htm).

2.2 | Patient selection

The inclusion criteria were as follows: (1) histologically confirmed adenocarcinoma of the stomach; (2) clinical stage IA (T1N0) or IB (T1N1, T2N0) tumor according to the classification of gastric carcinoma stated in the Japanese Classification of Gastric Carcinoma[9]; (3) total gastrectomy (TG) according to the Japanese Gastric Cancer Treatment Guidelines was planned; (4) no invasion of the esophagus; (5) ages 20–80 years; (6) Eastern Cooperative Oncology Group Performance Status 0 or 1; (7) no history of gastrointestinal surgery; and (8) patient's written informed consent provided. The exclusion criteria included other active malignancies, simultaneous surgery other than cholecystectomy, body mass index (BMI) >30, and any other condition judged unsuitable for inclusion, according to the investigator's opinion. Patients diagnosed with pathological stages II–IV were excluded from the analyses. Patients who underwent conversion from laparoscopic to open surgery were included in the laparoscopic surgery group.

2.3 | Surgical procedure and perioperative treatment

Laparoscopic total gastrectomy was regarded as an investigational approach according to the Japanese Gastric Cancer Treatment Guidelines until the enrollment terminated. Thus, during the time when patients were registered for the current study, the surgical approach was selected according to institutional policy as well as patients' wishes. Most cases of open surgery were therefore conducted in institutions where laparoscopic total gastrectomy had not been introduced. Although the current study was a multi-institutional prospective study with a preplanned design, it was not a randomized trial. Furthermore, bursectomy was not performed, and omentectomy was not prescribed. D1+ lymphadenectomy was performed for T1N0 GC and D2 lymphadenectomy was performed for T2N0 or T1N1 GC according to the Japanese Gastric Cancer Treatment Guidelines 2021 (ver.6).[10] Preoperative transfusion and enteral nutrition were not administered. Oral intake and postoperative nutritional support were not prescribed in the study protocol.

2.4 | Assessment of body weight and QOL

Body weight was measured before surgery, and 1 year, 2 years, and 3 years after surgery. Patients who required conversion from laparoscopic to open surgery were included in the laparoscopic surgery group. Postoperative QOL was assessed using the EORTC QLQ-C30 and PGSAS-37 questionnaires. Patients were asked to complete the questionnaires by themselves before surgery and then 1 month, 3 months, 6 months, 1 year, and 3 years after surgery.

The EORTC QLQ-C30 comprises global health status, five functional scales (physical, role, cognitive, emotional, and social), and nine symptom scales (fatigue, pain, nausea and vomiting, dyspnea,

sleep disturbance, appetite loss, constipation, diarrhea, and financial difficulties).[11] All scales were converted to scores of 0–100.[11] A high score for a functional scale represents a high/healthy functional level, and a high score for global health status and QOL represents high QOL. In contrast, a high score for a symptom scale or item indicates a high level of symptoms and associated problems.[11]

PGSAS-37 is an integrated questionnaire specifically designed to assess postoperative symptoms and QOL after gastrectomy. Main outcome measures of the PGSAS-37 comprise seven symptom subscales (esophageal reflux, abdominal pain, meal-related distress, indigestion, diarrhea, constipation, and dumping), four living status scales (ingested amount of food per meal, necessity for additional food, quality of ingestion subscale, and ability for working), and four QOL scales (dissatisfaction with symptoms, dissatisfaction at the meal, dissatisfaction at working, and dissatisfaction for daily life subscale).[12,13] The total symptom score was calculated according to the average of seven symptom scales. In the PGSAS-37 questionnaire, high scores represented favorable outcomes regarding ingested amount of food per meal and quality of ingestion subscale, whereas low scores on the symptom subscales, necessity for additional food, ability for working, and QOL scales indicated favorable outcomes. The questionnaires were directly sent from the data center to all patients after surgery and returned to the registration center after completion by patients.

2.5 | Study endpoints

The primary objective was an exploratory comparison of QOL after total gastrectomy between the open surgery and laparoscopic surgery groups. The other exploratory endpoints included chronological changes in body weight, operating time, blood loss, postoperative complication rate according to the Clavien–Dindo classification,[14] and number of retrieved lymph nodes.

2.6 | Sample size

The present study was an exploratory trial. Therefore, previous reports and historical data to estimate the sample size were unavailable. First, the patient enrollment period was set at 5 years. In average, 20 open total gastrectomies and 30 laparoscopic total gastrectomies for cStage I gastric cancer had been performed at the participating institution in a year. We estimated a consent acquisition rate at 70%, and then set the target sample size as 70 patients for open total gastrectomy group. To match the sample size for each group, we decided to set it for laparoscopic total gastrectomy as 70 patients.

2.7 | Statistical analysis

Comparisons of continuous variables were conducted using the Student's *t* test, and Fisher's exact test was used to compare categorical variables. Results are presented in delta values with 95% confidence interval (CI) between two time points. No statistical adjustments for multiplicity were conducted because this was a hypothetical exploratory analysis. $p < 0.05$ indicates statistical significance. Cohen's *d* was calculated according to the guidance issued by the PGSAS program. Interpretation of effect sizes were 0.2 < small, 0.5 < medium, and 0.8 < large in Cohen's *d*. Statistical analysis was performed using JMP software (version 16, SAS Institute, Inc, Cary, NC) and R version 4.2.2.

3 | RESULTS

3.1 | Patients

Patient registration began in December 2015. However, due to low patient accrual and enrollment especially in the open approach, only 27 patients were registered in the open group as of July 2020. Since the safety of LATG/LAPG was confirmed by the JCOG1401 trial and expected to be established as one of the standard treatments for clinical stage I gastric cancer, we terminated this study on July 31, 2020.[7] Figure 1 shows that 14 patients in the laparoscopic group were excluded because of pathological stage II, and 11 patients were excluded in the open group (10 were diagnosed with pStage II and one questionnaire was not received) after surgery. We finally analyzed 43 and 16 patients in the laparoscopic and open groups, respectively. Table 1 summarizes patients' baseline characteristics and shows that there were no significant differences in age, sex, preoperative body mass index, and preoperative hemoglobin levels, serum albumin levels, serum tumor marker levels, and clinical stages between the two groups.

3.2 | Perioperative factors

Table 2 presents the surgical procedures, intraoperative findings, pathological stages, and postoperative outcomes. D1+

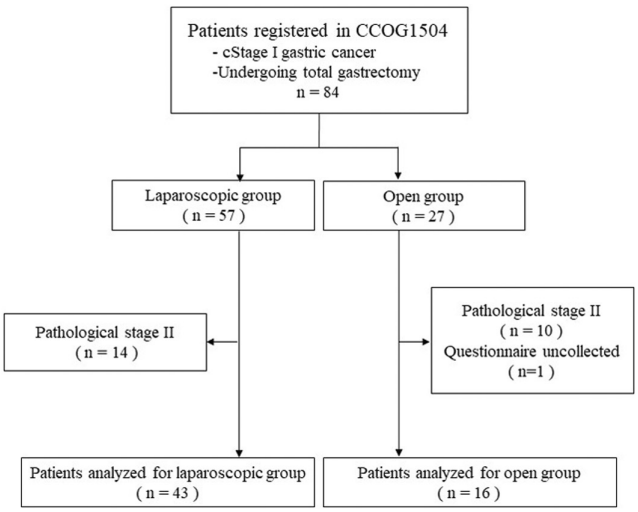

FIGURE 1 Flowchart of patient selection.

TABLE 1 Patient baseline characteristics.

Characteristic	Laparoscopic group ($n=43$)	Open group ($n=16$)	p[a]
Demographic characteristics			
Age (years), mean ± SD	65.3 ± 10.2	66.4 ± 8.4	0.698
Sex male/female	31/12	14/2	0.216
Body mass index, mean ± SD	23.1 ± 2.3	22.9 ± 3.4	0.799
Performance status			
0	43 (100%)	16 (100%)	–
1	0 (0%)	0 (0%)	
Blood test			
WBC (/μL), mean ± SD	6071.9 ± 1349.9	6412.5 ± 1756.5	0.431
Hb (g/dL), mean ± SD	13.6 ± 2.1	13.9 ± 1.5	0.643
Albumin (g/dL), mean ± SD	4.2 ± 0.3	4.1 ± 0.3	0.912
CEA (ng/mL), mean ± SD	2.4 ± 1.4	2.6 ± 2.0	0.782
CA19-9 (IU/mL), mean ± SD	12.2 ± 14.1	12.3 ± 17.5	0.986
Tumor size (cm), mean ± SD	4.4 ± 4.6	5.5 ± 7.6	0.507
Tumor type			
0–I	1 (2%)	1 (6%)	0.839
0–IIa	3 (7%)	2 (12%)	
0–IIb	1 (2%)	0 (0%)	
0–IIc	33 (77%)	11 (70%)	
1	1 (2%)	1 (6%)	
2	2 (5%)	1 (6%)	
3	2 (5%)	0 (0%)	
Clinical T stage			
cT1a	6 (14%)	2 (12%)	0.918
cT1b	30 (70%)	12 (76%)	
cT2	7 (16%)	2 (12%)	
Clinical N stage			
cN0	41 (95%)	15 (94%)	0.804
cN1	2 (5%)	1 (6%)	
Clinical stage			
cStage IA	34 (79%)	13 (82%)	0.853
cStage IB	9 (21%)	3 (18%)	

Abbreviation: SD, standard deviation.

[a]Comparison between laparoscopic and open group.

lymphadenectomy was performed for 30 (69%) and 12 (75%) patients in the laparoscopic and open groups, respectively. All patients in both groups were treated using the Roux-en-Y method. Operative time was significantly longer in the laparoscopic group than that of the open group, whereas the laparoscopic group experienced significantly smaller volumes of intraoperative blood loss. There were no significant differences in the number of resected lymph nodes between the two groups. Postoperative morbidity rates (any grade) of the laparoscopic and open groups were 7% and 25%, respectively ($p=0.078$), of which the incidence of ≥ Grade 3 complications were 7% and 13%, respectively ($p=0.498$). There was no significant difference in the duration of postoperative hospitalization between the two groups (Table 2).

3.3 | Postoperative changes in body weight

Body weight declined to the lowest level at postoperative year (POY) 1 in the laparoscopic and open groups (−16.8% and −15.1%, respectively) and then slightly recovered in both groups. Furthermore, there were no significant differences at all time points between the two groups (Table S1).

TABLE 2 Perioperative data.

Characteristic	Laparoscopic group ($n=43$)	Open group ($n=16$)	p[a]
Conversion to open surgery	1 (2%)	–	–
Reconstruction method			
Roux-en-Y	43 (100%)	16 (100%)	–
Antecolic	35 (81%)	4 (25%)	<0.001
Retrocolic	8 (19%)	12 (75%)	
Lymphadenectomy			
D1	2 (5%)	0 (0%)	0.674
D1+	30 (69%)	12 (75%)	
D2	11 (26%)	4 (25%)	
Operation time (min), mean ± SD	338.9 ± 84.6	252.7 ± 53.9	<0.001
Blood loss (mL), median (range)	60 (0–690)	368 (14–920)	<0.001
Intraoperative transfusion	1 (2%)	0 (0%)	0.538
Resected lymph nodes, mean ± SD	51.5 ± 24.2	44.1 ± 23.8	0.303
Pathological T stage			
pT1a	16 (37%)	1 (6%)	0.065
pT1b	23 (54%)	13 (81%)	
pT2	4 (9%)	2 (13%)	
Pathological N stage			
pN0	39 (91%)	16 (100%)	0.206
pN1	4 (9%)	0 (0%)	
Pathological stage			
pStage IA	34 (79%)	14 (88%)	0.460
pStage IB	9 (21%)	2 (12%)	
Postoperative complication			
Any	3 (7%)	4 (25%)	0.078
Bleeding	2 (5%)	0 (0%)	0.380
Intraabdominal abscess	1 (2%)	0 (0%)	0.538
Anastomotic leakage	0 (0%)	1 (6%)	0.098
Pancreas fluid leakage	1 (2%)	1 (6%)	0.459
Pneumonia	0 (0%)	1 (6%)	0.098
Other	1 (2%)	2 (13%)	0.114
Clavien–Dindo classification			
3≤	3 (7%)	2 (13%)	0.498
Postoperative hospital stay (days), median (range)	11 (8–56)	14 (6–53)	0.113

Abbreviation: SD, standard deviation.

[a]Comparison between laparoscopic and open group.

3.4 | Postoperative QOL assessed using EORTC QLQ-C30 and PGSAS-37 assessments

Table S2 summarizes the data collection rates. The questionnaires were retrieved from 100%, 89.8%, 94.9%, 89.8%, 89.8%, and 100% of patients at baseline, and postoperative months (POMs) 1, 3, 6, 12, and 36, respectively.

Table 3 summarizes the results of the EORTC QLQ-C30 questionnaires after surgery at POM 1 and POY 1. Among the parameters of EORTC QLQ-C30, role functioning score tended to be higher (i.e. better QOL) in the laparoscopic group at both times after surgery compared with the open group. Similarly, the fatigue score tended to be lower (i.e. better QOL) in the laparoscopic group at 1 month after surgery compared with the open group. Table 4 summarizes the results of the PGSAS-37 symptom survey at POM 1 and POY 1. The dissatisfaction at working score at 1 month after surgery was lower (i.e. better QOL) in the laparoscopic group compared with the open group. There were no differences between the other parameters between the two groups during POY 1.

TABLE 3 Comparison of scores of EORTC QLQ-C30 parameters.

Parameters	1 month after surgery			1 year after surgery		
	Laparoscopic group ($n=43$)	Open group ($n=16$)	p	Laparoscopic group ($n=43$)	Open group ($n=16$)	p
Global health status	−26.2 ± 39.1	−12.5 ± 24.5	0.198	−16.7 ± 36.4	−3.6 ± 35.5	0.224
Physical functioning	−6.3 ± 23.0	−15.4 ± 12.3	0.142	−1.3 ± 20.1	−6.3 ± 14.5	0.374
Role functioning	−14.0 ± 31.9	−31.3 ± 25.7	0.057	0.0 ± 23.8	−13.5 ± 22.1	0.053
Emotional functioning	8.7 ± 27.6	5.7 ± 10.9	0.677	15.7 ± 24.3	8.9 ± 27.0	0.354
Cognitive functioning	1.6 ± 31.5	0.0 ± 13.6	0.850	2.3 ± 28.3	1.0 ± 24.7	0.874
Social functioning	−3.1 ± 29.6	−9.4 ± 25.1	0.455	7.8 ± 26.1	7.3 ± 29.2	0.954
Fatigue	11.9 ± 29.5	27.8 ± 25.0	0.061	7.0 ± 30.0	6.3 ± 28.4	0.933
Nausea and vomiting	5.4 ± 24.3	14.6 ± 16.0	0.169	4.3 ± 21.2	8.3 ± 19.2	0.505
Pain	3.1 ± 27.0	13.5 ± 22.1	0.173	−5.0 ± 23.7	3.1 ± 20.4	0.228
Dyspnea	6.2 ± 33.5	16.7 ± 24.3	0.260	−1.6 ± 27.2	6.3 ± 25.0	0.321
Insomnia	−2.4 ± 36.4	12.5 ± 16.7	0.122	−10.1 ± 33.8	−4.2 ± 26.9	0.532
Appetite loss	22.5 ± 39.7	35.4 ± 39.4	0.269	4.7 ± 33.0	8.3 ± 25.8	0.689
Constipation	−6.2 ± 38.0	8.3 ± 46.3	0.224	−7.0 ± 34.5	−8.3 ± 28.5	0.889
Diarrhea	17.8 ± 40.1	14.6 ± 32.1	0.772	8.5 ± 38.6	14.5 ± 38.4	0.593
Financial difficulties	3.1 ± 33.2	8.3 ± 25.8	0.572	−9.3 ± 28.5	−2.1 ± 28.5	0.390

Note: Values are indicated by mean ± standard deviation.

TABLE 4 Comparison of scores of PGSAS-37 symptom parameters.

Parameters	1 month after surgery				1 year after surgery		
	Laparoscopic group ($n=43$)	Open group ($n=16$)	p	Cohen's d value	Laparoscopic group ($n=43$)	Open group ($n=16$)	p
Esophageal reflux subscale	0.6 ± 1.2	0.8 ± 1.2	0.596		0.5 ± 1.0	0.6 ± 1.1	0.714
Abdominal pain subscale	0.6 ± 1.0	0.6 ± 0.9	0.938		0.1 ± 1.0	0.5 ± 1.2	0.210
Meal-related distress subscale	1.3 ± 1.6	1.9 ± 1.7	0.267		0.9 ± 1.4	0.8 ± 1.2	0.885
Indigestion subscale	0.7 ± 1.3	0.9 ± 0.8	0.531		0.6 ± 1.3	1.0 ± 0.7	0.269
Diarrhea subscale	1.2 ± 1.7	0.6 ± 1.2	0.260		0.8 ± 1.6	0.5 ± 1.1	0.607
Constipation subscale	0.1 ± 1.6	−0.0 ± 1.5	0.821		−0.2 ± 1.5	−0.3 ± 1.3	0.835
Dumping subscale	1.1 ± 1.6	1.1 ± 1.6	0.980		0.6 ± 1.3	0.4 ± 1.3	0.537
Total symptom score	0.8 ± 1.1	0.9 ± 0.8	0.956		0.5 ± 1.0	0.5 ± 0.6	0.803
Ingested amount of food per meal	−5.7 ± 2.7	−4.6 ± 3.0	0.211		−3.6 ± 3.7	−2.4 ± 3.3	0.288
Necessity for additional food	1.2 ± 1.4	1.4 ± 0.9	0.699		0.7 ± 1.3	0.9 ± 1.3	0.544
Quality of ingestion subscale	−1.6 ± 1.8	−1.4 ± 1.7	0.607		−1.1 ± 1.9	−0.6 ± 1.8	0.293
Ability for working	1.2 ± 1.6	1.6 ± 0.9	0.317		0.1 ± 1.3	0.3 ± 1.1	0.711
Dissatisfaction with symptoms	1.5 ± 1.4	2.0 ± 1.3	0.207		0.9 ± 1.3	1.4 ± 1.3	0.188
Dissatisfaction at the meal	2.1 ± 1.5	2.6 ± 0.9	0.274		1.3 ± 1.3	1.9 ± 1.6	0.104
Dissatisfaction at working	1.4 ± 0.2	2.3 ± 0.3	0.027	−0.666	0.7 ± 1.1	1.1 ± 1.4	0.181
Dissatisfaction for daily life subscale	1.7 ± 1.3	2.3 ± 1.0	0.100		0.9 ± 1.1	1.5 ± 1.4	0.123

Note: Values are indicated by mean ± standard deviation.

Table S3 lists the changes of EORTC QLQ-C30 scores from baseline at POM 1, 3, 6, 12, and 36. Figure 2 shows that role functioning and fatigue level of EORTC QLQ-C30 scores declined to their lowest level at POM 1 and stabilized until POM 36 in both groups. Table S4 documents the change of PGSAS-37 symptom scores from baseline to POM 1, 3, 6, 12, and 36. The scores of PGSAS-37 in total symptom score and dissatisfaction at working also declined to their lowest levels at POM 1, subsequently recovered, but did not reach the baseline level at POY 3 in both groups (Figure S1).

4 | DISCUSSION

Recent evidence indicates the importance of safety, oncological outcomes, and QOL after gastrectomy. Here we employed the EORTC QLQ-C30 and PGSAS-37 assessment questionnaires to evaluate postoperative long-term QOL associated with laparoscopic total gastrectomy compared with open total gastrectomy of patients with stage I gastric cancer. The results suggest that laparoscopic total gastrectomy is superior to the open approach for improving postoperative QOL, particularly the scores observed in role functioning and dissatisfaction at working scores.

We previously evaluated QOL using EORTC QLQ-C30 and STO22 assessment data after open total gastrectomy, open distal gastrectomy, and laparoscopic distal gastrectomy.[15] In this study, a trend of more favorable scores was observed among the patients who received laparoscopic distal gastrectomy. However, because the laparoscopic approach was exclusively used to treat early gastric cancer, which is resectable through distal gastrectomy, the study inevitably suffered from selection bias.

We therefore proceeded to conduct a prospective multi-institutional QOL comparison up to POM 12 after surgery between the two approaches administered to patients undergoing distal gastrectomy for early GC.[6] Furthermore, this study shows that role, emotional, cognitive, and social functioning scores of EORTC QLQ-C30 were superior in the laparoscopic group when assessed at POM 6 and POM 12.[6] Symptom scales including fatigue, pain, eating restriction, taste problems, and anxiety were more favorable in the laparoscopic group before POM 6 but not at POM 12. These findings motivated us to examine whether the laparoscopic approach may confer a benefit upon QOL for patients undergoing total gastrectomy.

We used PGSAS-37, which is a self-reported questionnaire that provides comprehensive assessments of outcomes of patients undergoing surgery for gastric cancer.[16] This study is among the few that used PGSAS-37 questionnaires in a prospective and longitudinal study, unlike previous reports that were limited by their retrospective and cross-sectional nature.[17,18] Consequently, this questionnaire revealed the benefits of laparoscopic total gastrectomy associated with scores for dissatisfaction at working. We found here that postoperative symptoms were lowest at POM 1 to POM 3 and gradually recovered thereafter, except for constipation scores. Furthermore, recovery to the baseline level was not observed within POY 3 after surgery for most symptom scales. Moreover, we found that bodyweight loss and post-gastrectomy maldigestion and malabsorption persisted through POY 3.

We registered patients who underwent total gastrectomy for clinical stage I GC to minimize bias inherent in evaluating the differences between laparoscopic and open approaches. If preoperative scores of patient function scales differ, there is a risk that postoperative function scales will be overestimated or underestimated when compared according to an absolute value. This is likely to occur in patients with clinical stage I, because they are usually asymptomatic. Thus, we evaluated the QOL scores at each time point according to changes compared with preoperative values.

Although the smaller wound and avoidance of destruction of the abdominal wall employing the laparoscopic approach was expected to decrease the postoperative pain,[19] the advantage of this approach was not apparent in the present study, whereas fatigue score tended to more favorable during POM 1. Our assumption here was that the expected differences in these symptoms would manifest as differences in the physical functioning score, although they were not observed. One of possible explanations for this finding is that successful pain control by appropriate administration of analgesics have nullified the difference in postoperative physical activity between the two groups despite large difference in the wound lengths.

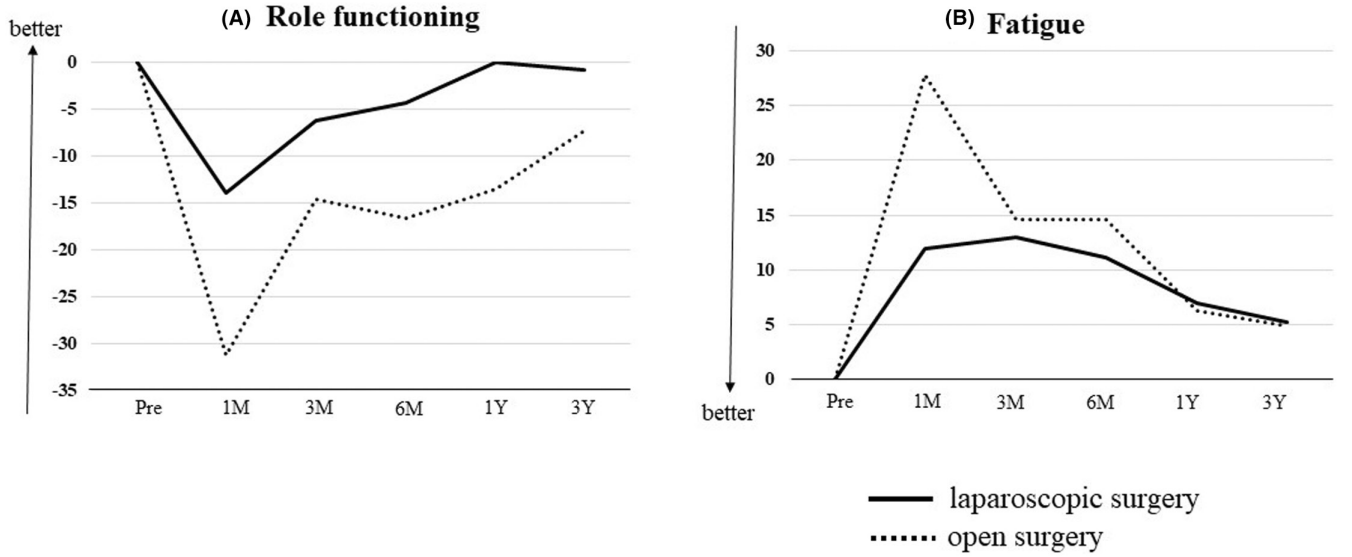

FIGURE 2 Chronological changes in role functioning and fatigue level assessed using EORTC QLQ-C30.

Nevertheless, benefits of the minimally invasive approach were achieved for the role functioning scores of the EORTC QLQ-C30 and dissatisfaction at working scores in the PGSAS-37, which are encouraging signs for surgeons who employ laparoscopic surgery. In contrast, differences between the two approaches were not detected, which were associated with symptom scales related to the functional aspect of the digestive tract such as reflux, diarrhea, abdominal pain, meal-related distress, dumping, and indigestion. These results may represent obvious consequences of the loss of stomach tissue regardless of the surgical approach. However, these findings further suggest that the complex procedures required for reconstruction under the laparoscopic approach did not translate into an observable disadvantage compared with more familiar open surgery procedures.

The limitations of the present study are as follows: First, due to early termination, the sample size was small. Second, laparoscopic total gastrectomy was approved by social insurance despite its status as an investigational treatment in the treatment guidelines at that time and was performed almost routinely for early-stage cancers in some of the institutions. Therefore, it was not possible to plan a randomized trial design in a study group that included several nonspecialized centers. This resulted in potential selection bias in that laparoscopic surgery was apt to be selected by surgeons with greater expertise in gastric cancer surgery. Third, adjustments for multiplicity were not conducted because of the study's exploratory analysis. A larger sample size is therefore required to perform statistical adjustments for multiplicity, which was not conducted here. Finally, it was difficult to set a reasonable sample size based on previous evidence because the CCOG1504 was an exploratory study.

5 | CONCLUSION

The present multi-institutional prospective study, designed to compare long-term QOL between laparoscopic and open total gastrectomy using PGSAS-37, demonstrated more favorable scores for the laparoscopic approach, especially in the dissatisfaction at working score.

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CONFLICT OF INTEREST STATEMENT

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ETHICS STATEMENT

Approval of the research protocol: All procedures were in accordance with the ethical standards of the responsible committee on human experimentation and in compliance with the Helsinki Declaration of 1964 and later versions. The internal review boards of participating institutions reviewed the scientific and ethical validity of the protocol.

Informed consent: Patients who were registered and analyzed in the CCOG1504 study and from whom written informed consent was obtained for this observational study were eligible.

Registry and the Registration No. of the study/Trial: N/A.

Animal Studies: N/A.

ORCID

Chie Tanaka https://orcid.org/0000-0002-7931-8753

Yasuhiro Kodera https://orcid.org/0000-0002-6173-7474

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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