

# Severity of postgastrectomy syndrome and quality of life after advanced gastric cancer radical gastrectomy

SHINICHI KINAMI<sup>1</sup>, NAOHIKO NAKAMURA<sup>1</sup>, JIANG ZHIYONG<sup>1</sup>, TAKASHI MIYATA<sup>1</sup>, HIDETO FUJITA<sup>1</sup>, HIROYUKI TAKAMURA<sup>1</sup>, NOBUHIKO UEDA<sup>1</sup>, YASUO IIDA<sup>2</sup> and TAKEO KOSAKA<sup>1</sup>

<sup>1</sup>Department of Surgical Oncology, Kanazawa Medical University; <sup>2</sup>Department of Mathematics, Division of General Education, Kanazawa Medical University, Kahoku, Ishikawa 920-0293, Japan

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**Abstract.** It has previously been suggested that postgastrectomy syndrome (PGS) is more severe in patients after surgery for advanced gastric cancer than in patients with early gastric cancer. Using the postgastrectomy syndrome assessment scale-45 (PGSAS-45), the present study aimed to determine whether PGS for postgastrectomy patients, in Kanazawa Medical University Hospital, with advanced gastric cancer was more severe than for patients with early gastric cancer. A questionnaire survey was conducted using PGSAS-45 for curative gastric cancer gastrectomy cases at Kanazawa Medical University Hospital. The questionnaire data were combined with patient background data, anonymized and moved to an unlinked file for patient privacy. Using this dataset, non-recurrent cases of distal partial gastrectomy were extracted and divided into two groups, stage IA or IB patients (group E), and stage IIA or higher (group A). The main outcome measures (MOMs) of PGSAS-45 were compared between the two groups. The participants in the present study included 35 cases in group E and 22 cases in group A. The results of a univariate analysis to compare the MOMs between the two groups showed that only the dumping subscale was significantly different in group A and was judged to be caused by the underlying bias of the background factor. There were no MOMs with significant differences in the pathological stage based on multiple regression analyses. In cases of distal partial gastrectomy, the PGS and quality of life (QoL) of patients following advanced gastric cancer surgery were similar to those of patients with early gastric cancer. The standardized treatment for advanced gastric cancer did not induce notable postoperative failures, and QoL was not impaired. In contrast, for early-stage gastric cancer cases, the present study suggests

that it is necessary to distinguish metastasis-negative cases to indicate an appropriate, function-preserving curative gastrectomy.

## Introduction

A certain percentage of patients with gastric cancer who have undergone a gastrectomy suffer from distinct, subjective symptoms (e.g., heartburn, nausea, hypochondralgia, dumping syndrome, diarrhea), which is called postgastrectomy syndrome (PGS) (1-3). PGS impairs the quality of life (QoL) of patients (4). Various factors are involved in the occurrence and severity of PGS, including age, sex, gastrectomy procedure, reconstruction method, degree of lymph node dissection, and chemotherapy (5). In advanced gastric cancer cases, gastrectomies with a higher degree of lymph node dissection are performed more often than in early-stage cancer cases. In contrast to early gastric cancer cases, adjuvant chemotherapy is often performed for advanced cases. Therefore, it has been suggested that PGS is more severe and QoL more impaired for advanced gastric cancer patients than for early gastric cancer.

Although many postgastrectomy symptoms are subjective and scientific approaches to quantify them have been difficult, a specific questionnaire, the postgastrectomy syndrome assessment scale-45 (PGSAS-45), was developed as a psychometric measurement of PGS. PGSAS-45 measures outcomes from the patient's point of view, and nearly 2,400 questionnaires were collected during the PGS assessment study (PGSAS study), thus providing essential data to verify PGS scientifically (4-7). The subjects of the PGSAS study were stage IA or IB cases at least one year after surgery. Advanced cases, including stage II or higher were not included (6). Thus, the extent of PGS in cases of advanced gastric cancer has not been adequately studied. Using PGSAS-45, we determined whether PGS in patients, in our hospital, with stage II or more advanced gastric cancers, was more severe than for patients with stage I gastric cancer.

## Patients and methods

The details of the PGSAS-45 have been precisely stated in previous research articles (6). The PGSAS-45 questionnaire consists of 45 items, including from the 8-item short-form

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*Correspondence to:* Professor Shinichi Kinami, Department of Surgical Oncology, Kanazawa Medical University, 1-1 Daigaku, Kahoku, Ishikawa 920-0293, Japan  
E-mail: kinami@kanazawa-med.ac.jp

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generic health-related QoL questionnaire (SF-8) (8,9) and the Gastrointestinal Symptom Rating Scale (GSRS) (10). The items of the PGSAS-45 are classified into three domains—the symptom domain, the living status domain, and the QoL domain. Each domain consists of several main outcome measures (MOMs). The Japanese version of SF-8 was used in this study under the licensing of the copyright holder iHope.

A PGSAS-45 questionnaire survey was conducted in 2016 for curative gastric cancer gastrectomy cases at Kanazawa Medical University Hospital (Ishikawa, Japan) in 2009–2014. The questionnaire was handed or mailed to the patients, along with a written informed consent form. In the outpatient department, a nurse or nutritionist handed the questionnaire to the patient. The questionnaire was mailed from the clinical trial center of Kanazawa Medical University Hospital, a hospital department independent of the principal researchers' department of Surgical Oncology. Only the questionnaires for which written informed consent was obtained were validated for use in this study. In the outpatient department, a medical clerk collected the questionnaires. The mailed questionnaires were sent back to the clinical trial center using a provided return envelope. All questionnaires were collected in the clinical trial center. Questionnaires with missing data were excluded. First, the questionnaire data was combined with patients' background data to create the study data set. The background factors were: Sex, age, pathological stage, gastrectomy procedure, degree of lymph node dissection, surgical approach (conventional open surgery or laparoscopic surgery), reconstruction method, size of remnant stomach, preservation of the hepatic branch of the vagus, preservation of the celiac branch of the vagus, and history of adjuvant chemotherapy; these factors were the same as in the original PGSAS study (6). The dataset was then anonymized, and an unlinkable file was created to protect patient privacy. The clerks of the clinical trial center did not know the details of patients or surgeries and carried out this process.

From this dataset, we extracted non-recurrent cases of distal partial gastrectomy, without preoperative chemotherapy, and not currently undergoing chemotherapy, for this study. These cases were divided into two groups, patients of stage IA or IB (group E) and those of stage IIA or higher (group A). The MOMs of PGSAS-45 were compared between the two groups.

All surgeries in this study were performed by skilled surgeons (SK and TK). The treatment policy for these cases is as per the Gastric Cancer Treatment Guidelines of the Japanese Gastric Cancer Association (11), and the descriptions of the findings comply with the Japanese Classification of Gastric Carcinoma (12). A 2/3 resection refers to a distal gastrectomy at the line connecting the first descending branch of the left gastric artery and one-proximal branch of the last branch of the left gastroepiploic artery.

A Chi-square test was used to compare background factors. The Student's t-test or Welch's test was used for comparing the MOMs. Multiple regression analyses were then performed for each of the MOMs to investigate the effect of each background factor on the MOMs. A stepwise variable selection reduction method with P-values was used to narrow down the statistically significant independent factors.  $P < 0.05$  was considered significant. Cohen's *d* was used to evaluate effect sizes. The interpretation of effect sizes was  $\geq 0.2$  small,  $\geq 0.5$  medium,

and  $\geq 0.8$  large. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University), which is a graphical user interface of R (The R Foundation for Statistical Computing). EZR is a modified version of R Commander designed to add statistical functions frequently used in biostatistics (13).

Finally, Billroth I reconstruction cases were extracted from group E and A, and the PGSAS statistic kit was used to compare the data with the values of the Japanese standards of the Billroth I method cases obtained by the PGSAS study.

This study was approved by the Ethics Committees of Kanazawa Medical University (Trial Number E264) and registered with the University Hospital Medical Information Network's Clinical Trials Registry as trial number 000018531.

## Results

The participants in this study included 35 cases in group E and 22 cases in group A (70% of the patients for which a questionnaire was requested). The characteristics of these cases are shown in Table I. Because Group A is a more advanced stage than Group E, there were substantial differences in many background factors. Group A had a higher degree of lymph node dissection, less vagal preservation, smaller remnant stomach size, fewer cases of Billroth I reconstruction, and more cases of adjuvant chemotherapy. Two early gastric cancer patients in group A had nodal metastasis up to pN2, and two advanced gastric cancer patients in group E with node-negative MP cancers.

Table II shows the comparisons between the two groups for MOMs of the PGSAS. Only the dumping subscale was significantly different, group A had a value of 1.22 lower than group E of 1.58, but there were no differences between the two in other items, and there were no items in which group A was inferior to group E.

Tables III and IV show a multiple regression analysis of the dumping subscale value to investigate the effect of each background factor on that subscale. Among the background factors, the factors that were important and should not be deleted were chosen to ensure the reliability of the results with few cases. Only the size of the remnant stomach was selected as a factor influencing the dumping subscale. That is, the difference between the two groups for the dumping subscale in the univariate analysis was caused by the bias of the background factor, not by the pathological stage.

Table V shows the results of multiple regression analyses performed on all MOMs in the same manner as the dumping subscale. Some background factors influenced the MOMs, but there were no items in which differences in the pathological stage affected the MOMs.

Using the PGSAS statistic kit, the data of the Billroth I reconstruction cases were compared with the values of the Japanese standard data from the PGSAS study. Table VI compares standard data with group E, and Table VII with group A. The MOMs of group E were not inferior to that of the PGSAS study, and the dumping subscale and the change in body weight were significantly better than those of the PGSAS study with small effect sizes. On the other hand, compared to the PGSAS study, dumping subscale (medium effect size), dissatisfaction during meal (medium effect size),

Table I. Characteristics of the cases.

Characteristics	Group A (n=22)	Group E (n=35)	P-value
p Stage			
I	0	35	
II	10	0	
III	11	0	
IV	1	0	
Age (mean ± SD)	68.3 ± 7.5	68.9 ± 6.8	>0.1
Sex			>0.1
Male	14	21	
Female	8	14	
Period from surgery (years), median (range)	4.1 (2.0-7.7)	4.5 (2.1-7.8)	>0.1
Surgical approach			0.085
Laparoscopy <sup>a</sup>	4	14	
Open <sup>b</sup>	18	21	
Size of remnant stomach			<0.001
≤1/3	22	22	
>1/3	0	13	
Hepatic branch of vagus			0.025
Cut	7	3	
Saved	15	22	
Celiac branch of vagus			0.015
Cut	21	24	
Saved	1	11	
Degree of nodal dissection			0.007
D0-1	4	19	
D2-3	18	16	
Reconstruction			0.031
Billroth I	13	30	
Others <sup>c</sup>	9	5	
Adjuvant chemotherapy			<0.0001
None <sup>d</sup>	3	31	
History	19	4	

<sup>a</sup>Laparoscopic assisted distal partial gastrectomy; <sup>b</sup>conventional distal partial gastrectomy under laparotomy; <sup>c</sup>Billroth II or Roux-en Y reconstruction; <sup>d</sup>no history of adjuvant chemotherapy. SD, standard deviation.

dissatisfaction with daily life subscale (small effect size), and mental component summary (small effect size) were significantly better, and there were no inferior items, in group A.

### Discussion

This study showed that PGS, living status, and QoL in patients with stage II-IV gastric cancer who had undergone distal gastrectomy and no recurrence were not judged by the patients to be poor, and were equivalent to those with stage I cancer.

Besides, the MOMs of stage II-IV cases who underwent distal partial gastrectomy and Billroth I reconstruction in our hospital were not inferior to those of the Japanese standard stage I cases.

In the PGSAS study, stage IA and IB recurrent-free cases were recruited (6), because it was designed to evaluate the PGS, living status and QoL induced purely by gastrectomy, and to exclude the adverse effects of recurrence and chemotherapy. However, among the PGSAS study cases, there were some advanced cancer cases with proper muscle cancers without nodal metastasis, although most of them were early cancer cases. Unfortunately, the rate of advanced gastric cancer cases having distal partial gastrectomy with Billroth I reconstruction in the PGSAS study is not shown. In our dataset, 94.2% of patients in group E were early gastric cancer cases. On the other hand, 91% had advanced gastric cancer in group A except for two early gastric cancer patients with pN2. Therefore, the present study may be interpreted as a study in which the PGS, living status, and QoL of patients after surgery for advanced gastric cancer were comparable to those of patients with early gastric cancer.

The surgical strategies for advanced gastric cancer differ from those for early gastric cancer. These differences include the extent of nodal dissection, the degree of autonomic nerve injury, approach (conventional open surgery or laparoscopic surgery), the extent of gastrectomy, and the presence or absence of omentectomy (14). Moreover, advanced gastric cancer patients often received postoperative adjuvant chemotherapy (15). In addition, since all patients were informed of their stage and life prognosis before treatment, patients with advanced cancer were expected to have considerable anxiety about recurrence and impact on their lives. Considering these three viewpoints, it is generally considered that the PGS seemed to be worse, and the living status and QoL lower in advanced gastric cancer cases than in early gastric cancer cases (16,17).

However, in our study, the PGS, living status, and QoL were less dependent on the pathological stage of gastric cancer. The factor that influenced the PGS was only the size of the remnant stomach. The factors influencing living status and QoL were mainly age, degree of lymph node dissection, and laparoscopic surgery. There are two reasons why the results were different than expected. First, differences in gastric surgical procedures, such as D1 and D2, vagal preservation and dissection, or omental preservation and resection, may not lead to significant differences in the PGS between early cancer and advanced cancer. Indeed, between D1+ and D2, the difference in the extent of dissection is only the difference of #11p and #12a (11). The preservation of the celiac branch of the vagus has been reported to reduce the frequency of diarrhea (18,19), but this may not lead to the detection of differences unless a large number of cases are studied. The preservation of the omentum is thought to prevent adhesions of the small intestine to the abdominal wall and reduce the incidence of ileus (20), but the occurrence rate of ileus is not high. The other reason is due to the timing of the investigation. All patients were more than one year after surgery, which was the time when chemotherapy had ended, and a certain amount of time has also passed for those who received adjuvant chemotherapy. Chemotherapy undoubtedly impairs

Table II. Comparisons of the main outcome measures of the PGSAS-45 between the two groups.

Main outcome measures <sup>d</sup>	Group A <sup>a</sup>	Group E <sup>a</sup>	P-value <sup>e</sup>
<b>Symptom</b>			
Esophageal reflux subscale	1.50±0.54	1.87±0.98	0.072
Abdominal pain subscale	1.45±0.45	1.79±0.85	0.058
Meal-related distress subscale	1.73±0.80	1.90±0.96	>0.1
Indigestion subscale	1.80±0.83	1.96±0.89	>0.1
Diarrhea subscale	1.91±1.07	2.06±0.92	>0.1
Constipation subscale	2.11±0.98	2.37±1.14	>0.1
Dumping subscale	1.22±0.43	1.58±0.88	0.047
Total symptom score	1.68±0.54	1.93±0.78	>0.1
<b>Living status</b>			
Change in body weight (%) <sup>b</sup>	96±11	95±7	>0.1
Ingested amount of food per meal	7.26±2.52	6.87±1.63	>0.1
Necessity for additional meals	1.64±0.58	1.74±0.66	>0.1
Quality of ingestion subscale	3.61±1.09	3.60±0.90	>0.1
Ability for working	1.81±0.68	2.00±0.97	>0.1
<b>Quality of life</b>			
Dissatisfaction: Symptom	1.45±0.67	1.51±0.78	>0.1
Dissatisfaction: Meal	1.68±0.89	2.03±1.10	>0.1
Dissatisfaction: Working	1.50±0.67	1.68±0.93	>0.1
Dissatisfaction Subscale	1.54±0.66	1.74±0.87	>0.1
PCS <sup>c</sup>	48.5±6.1	50.4±5.5	>0.1
MCS <sup>c</sup>	51.7±4.8	48.5±7.6	0.056

<sup>a</sup>All data are mean ± standard deviation; <sup>b</sup>Data for 'change in body weight' shows the rate of weight compared to the preoperative condition; <sup>c</sup>PCS and MCS of SF-8 were calculated according to the Japanese standard calculation method (9); <sup>d</sup>Higher scores indicate worse conditions, except for 'change in body weight', 'ingested amount of food', 'quality of ingestion subscale', 'PCS', and 'MCS'; <sup>e</sup>P-values for the univariate analysis. PCS, physical component summary; MCS, mental component summary.

Table III. The multiple regression analysis of the dumping subscale value to investigate the effect of each background factor, before stepwise selection.

Background factor	Variables	Estimated value of regression coefficient	Standard error	t-value	P-value
(Intercept)		1.41346	1.04640	1.35078	0.18310
Age		0.01090	0.01414	0.77059	0.44473
Sex	Male:Female	0.37671	0.19885	1.89446	0.06420
Approach	Laparoscope <sup>a</sup> :Open <sup>b</sup>	0.39851	0.25086	1.58860	0.11872
Size of remnant stomach	≤1/3:>1/3	0.58377	0.25824	2.26061	0.02836
Degree of nodal dissection	D0-1:D2-3	-0.24272	0.27186	-0.89281	0.37641
Reconstruction	Billroth I:Others <sup>c</sup>	-0.04000	0.23713	-0.16869	0.86675
Adjuvant chemotherapy	None <sup>d</sup> :History	-0.25197	0.29517	-0.85364	0.39755
Group	A:E	-0.08367	0.30108	-0.27791	0.78227

Multiple regression analysis was performed to investigate the effect of each background factor on the dumping subscale. The background factor of the preservation of vagus was excluded from the calculation because it had to be deleted according to the sample size. A stepwise variable selection reduction method with P-values was used to narrow down the statistically significant independent factors. <sup>a</sup>Laparoscopic assisted distal partial; gastrectomy; <sup>b</sup>Conventional distal partial gastrectomy under laparotomy; <sup>c</sup>Billroth II or Roux-en Y reconstruction; <sup>d</sup>No history of adjuvant chemotherapy.

the QoL of patients, and multiple-regression analyses of this study also showed low PCS in patients undergoing adjuvant chemotherapy. However, this study was a comparison at a

time when the effects of adjuvant chemotherapy had almost disappeared, and the adverse effects of chemotherapy were probably not significant.

Table IV. The multiple regression analysis of the dumping subscale value to investigate the effect of each background factor, after stepwise selection.

Background factor	Variables	Estimated value of regression coefficient	Standard error	t-value	P-value
Age					
Sex	Male:Female				
Approach	Laparoscope <sup>a</sup> :Open <sup>b</sup>				
Size of remnant stomach	≤1/3 >1/3	0.68648	0.22077	3.10949	0.00297
Degree of nodal dissection	D0-1:D2-3				
Reconstruction	Billroth I:Others <sup>c</sup>				
Adjuvant chemotherapy	None <sup>d</sup> :History				
Group	A:E				

Only size of remnant stomach was selected as a factor influencing the dumping subscale; <sup>a</sup>laparoscopic assisted distal partial gastrectomy; <sup>b</sup>conventional distal partial gastrectomy under laparotomy; <sup>c</sup>Billroth II or Roux-en Y reconstruction; <sup>d</sup>no history of adjuvant chemotherapy.

Table V. Multiple regression analyses was performed on all values of main outcome measures to investigate the effect of each background factor.

Main outcome measures	Age	Sex [Female]	Approach [Open]	RS Size [Large]	DLND [D2-3]	RCP [Others]	Adj Ch [History]	Stage [Gr E]
Symptom								
Esophageal reflux subscale								
Abdominal pain subscale				0.639				
Meal-related distress subscale								
Indigestion subscale								
Diarrhea subscale								
Constipation subscale								
Dumping subscale				0.686				
Total symptom score				0.471				
Living status								
Change in body weight (%)								
Ingested food amount per meal								
Necessity for additional meals								
Quality of ingestion subscale	-0.047							
Ability for working	0.042		0.851		-0.796			
Quality of life								
Dissatisfaction: Symptom								
Dissatisfaction: Meal								
Dissatisfaction: Working		0.485	0.585		-0.538			
Dissatisfaction subscale								
Physical component summary	-0.210				3.646		-5.249	
Mental component summary			-4.622	-5.286	5.882			

The values of this table represent the estimated value of the regression coefficient of the multiple regression analysis after a stepwise variable selection reduction method with P-values. Only columns with values are items selected as significant. The main outcome measures of change in body weight, ingested amount of food, quality of ingestion subscale, physical component summary, and mental component summary indicate higher numerical scores and therefore good condition, on the other hands, the other main outcome measures indicate higher scores and therefore worse condition. If the value is positive, then the score of the main outcome measures of the patient in the category in [brackets] is higher when the factor has a nominal scale, and the score of the main outcome measures of the patient with a larger value is higher when the factor has a numeric scale; RS size, size of remnant stomach; DLND, degree of lymph nodal dissection; RCP, reconstruction procedure; Adj Ch, history of adjuvant chemotherapy; Gr E, group E.

Table VI. Comparison between the study's group A data of distal partial gastrectomy with Billroth I reconstruction with the values of the Japanese standard data of the PGSAS study using the PGSAS statistic kit.

Main outcome measures	PGSAS study	Group A	Cohen's d	t-value	P-value
<b>Symptom</b>					
Esophageal reflux subscale	1.70	1.58	0.15	0.75	>0.1
Abdominal pain subscale	1.69	1.54	0.21	1.12	>0.1
Meal-related distress subscale	2.05	1.90	0.18	0.66	>0.1
Indigestion subscale	1.99	1.71	0.33	1.45	>0.1
Diarrhea subscale	2.12	2.00	0.11	0.41	>0.1
Constipation subscale	2.23	1.97	0.25	1.03	>0.1
Dumping subscale	1.96	1.26	0.71	5.66	0.000
Total symptom score	1.96	1.71	0.37	1.58	>0.1
<b>Living status</b>					
Change in body weight (%)	92.07%	94.75%	0.33	1.61	>0.1
Ingested amount of food per meal	7.12	7.52	0.21	0.76	>0.1
Necessity for additional meals	1.86	1.62	0.32	1.35	>0.1
Quality of ingestion subscale	3.80	3.69	0.11	0.33	>0.1
Ability for working	1.75	1.77	0.02	0.09	>0.1
<b>Quality of life</b>					
Dissatisfaction:Symptom	1.81	1.54	0.30	1.48	>0.1
Dissatisfaction:Meal	2.19	1.62	0.53	2.65	0.008
Dissatisfaction:Working	1.67	1.38	0.33	2.01	0.044
Dissatisfaction subscale	1.89	1.51	0.46	2.25	0.025
Physical component summary	50.52	51.37	0.15	0.95	>0.1
Mental component summary	49.86	52.39	0.44	2.94	0.003

The main outcome measures of change in body weight, ingested amount of food, quality of ingestion subscale, physical component summary, and mental component summary indicate higher numerical scores and therefore good condition; the other main outcome measures indicate higher scores and therefore a worse condition. The effect size of the data depends on the value of Cohen's d. Interpretation of effect sizes were  $\geq 0.2$  small,  $\geq 0.5$  medium, and  $\geq 0.8$  large; PGSAS, postgastrectomy syndrome assessment scale-45.

Interestingly, in the multiple regression analyses of this study, we found that the MOMs of living status and QoL was affected by age, degree of lymph node dissection, and surgical approach. These MOMs worsened in the geriatric patients, and they were mitigated in cases with a higher degree of lymph node dissection or laparoscopic surgery. The geriatric patients had lower dietary quality, lower work status, and lower PCS, which may be associated with aging (5). In laparoscopic surgery, the ability of work was better than conventional open surgery, and the MCS was also superior, which suggests that the difference of the incision types may impact personal lifestyle (5). More interestingly, D2 patients had better ability to work and better QoL than D1+ patients. Direct comparisons between groups A and E were similar, but D2 was primarily used in patients diagnosed with advanced gastric cancer, suggesting that survival without recurrence in advanced gastric cancer patients may have relieved anxiety about recurrence, improved mental status, and improved ability to work. The MCS of Group A in this study were better than the Japanese standards in the PGSAS study.

In our study, PGS in early gastric cancer cases was not relieved when fewer lymph nodes were dissected. Given this, what strategies are effective to improve PGS in early gastric

cancer patients after gastrectomy? A function-preserving curative gastrectomy has been proposed as a potential approach. The function-preserving gastrectomy is a surgical procedure aimed at preserving gastric functions lost by gastrectomy by and involves preservation of the part of the stomach, such as pylorus, cardia, antrum, or body. The specific surgical procedures are pylorus-preserving gastrectomy, proximal gastrectomy, minimal-distal gastrectomy, segmental gastrectomy, and local resection. These procedures require bold omission of lymph node dissection and should be applied to node-negative cases in principle. Therefore, many researchers have applied function-preserving gastrectomy by first using sentinel lymph node biopsy to distinguish node-negative cases (14,21-25). Although the PGS and QoL associated with function-preserving curative gastrectomy have not yet been estimated, Isozaki (24) performed a scientifically high-quality study using PGSAS and reported extremely good results. Therefore, for patients with early gastric cancer, further application of function-preserving curative gastrectomy should be pursued in order to obtain a lower PGS and achieve better QoL.

This present research has several limitations. The greatest is that group E of this study contained only part of the early

Table VII. Comparison between group E data of distal partial gastrectomy with Billroth I reconstruction with the values of the Japanese standard data of the PGSAS study using the PGSAS statistic kit.

Main outcome measures	PGSAS study	Group E	Cohen's d	t-value	P-value
<b>Symptom</b>					
Esophageal reflux subscale	1.70	1.85	0.18	-0.83	>0.1
Abdominal pain subscale	1.69	1.80	0.14	-0.66	>0.1
Meal-related distress subscale	2.05	1.86	0.23	1.08	>0.1
Indigestion subscale	1.99	1.94	0.05	0.27	>0.1
Diarrhea subscale	2.12	2.10	0.02	0.12	>0.1
Constipation subscale	2.23	2.44	0.21	-1.01	>0.1
Dumping subscale	1.96	1.58	0.39	2.33	0.020
Total symptom score	1.96	1.94	0.03	0.14	>0.1
<b>Living status</b>					
Change in body weight (%)	92.07%	95.00%	0.36	-2.30	0.022
Ingested amount of food per meal	7.12	6.95	0.09	0.57	>0.1
Necessity for additional meals	1.86	1.70	0.21	1.33	>0.1
Quality of ingestion subscale	3.80	3.60	0.22	1.20	>0.1
Ability for working	1.75	2.07	0.36	-1.67	0.096
<b>Quality of life</b>					
Dissatisfaction:Symptom	1.81	1.53	0.30	1.83	0.067
Dissatisfaction:Meal	2.19	1.97	0.20	1.03	>0.1
Dissatisfaction:Working	1.67	1.70	0.03	-0.15	>0.1
Dissatisfaction subscale	1.89	1.73	0.19	0.94	>0.1
Physical component summary	50.52	49.85	0.12	0.65	>0.1
Mental component summary	49.86	48.20	0.28	1.13	>0.1

The main outcome measures of change in body weight, ingested amount of food, quality of ingestion subscale, physical component summary, and mental component summary indicate higher numerical scores and therefore good condition; the other main outcome measures indicate higher scores and therefore a worse condition. The effect size of the data depends on the value of Cohen's d. Interpretation of effect sizes were  $\geq 0.2$  small,  $\geq 0.5$  medium, and  $\geq 0.8$  large. PGSAS, postgastrectomy syndrome assessment scale -45.

gastric cancer patients. In our department, we are conducting a clinical trial for sentinel node biopsy and function-preserving curative gastrectomy (segmental gastrectomy, local resection, and mini proximal gastrectomy) for node-negative early gastric cancer (21,22). Therefore, we carried out the function-preserving curative gastrectomy for about a half of the early gastric cancer patients, and the cases of the E group in this study were the patients out of the indication of the sentinel node biopsy because it occupied the L region, or the node-positive cases diagnosed intraoperatively by sentinel node biopsy. Therefore, the proportion of patients who underwent D2 gastrectomy is high in group E. However, the results of group E are not inferior to those of the PGSAS study Japanese standards (6,7), and it seems to be unproblematic to consider group E to be common early gastric cancer surgery cases.

Another limitation is that this study was a retrospective study in which there were substantial biases between groups E and A, and direct comparisons might not be reasonable. However, it is not possible to carry out this type of research in a prospective study because it is natural that major differences exist in the treatment for early gastric cancer and advanced gastric cancer patients.

In conclusion, as long as distal partial gastrectomy was applied, the PGS and QoL of patients after advanced gastric cancer surgery were similar to those of early gastric cancer patients. The standardized treatment for the advanced gastric cancer cases did not induce the notable postoperative failure, and QoL was not impaired; the present treatment plan seemed to be appropriate. On the other hand, our results suggest the necessity of distinguishing metastasis-negative cases and seeking function-preserving curative gastrectomy for patients with early-stage gastric cancer (14,21-25).

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### Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

### Authors' contributions

SK was responsible for the scientific context. SK and TK performed surgery as operators. SK, NN, JZ, TM and HF treated the patients. NN, HT and NU helped SK as assistant surgeons. SK wrote the manuscript. YI was responsible for the biostatistical analysis. NN, HT and NU edited the manuscript. TK finalized the manuscript. All authors read and approved the final manuscript.

### Ethics approval and consent to participate

The present study was conducted in accordance with the Good Clinical Practice guidelines and Declaration of Helsinki, approved by the ethics committees of Kanazawa Medical University (Trial no. E264), and registered with the University Hospital Medical Information Network's Clinical Trials Registry as trial no. 000018531. The present study obtained informed consent from all patients.

### Patient consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

### References

- Davis JL and Ripley RT: Postgastrectomy syndromes and nutritional considerations following gastric surgery. *Surg Clin North Am* 97: 277-293, 2017.
- Bolton JS and Conway WC II: Postgastrectomy syndromes. *Surg Clin North Am* 91: 1105-1122, 2011.
- Carvajal SH and Mulvihill SJ: Postgastrectomy syndromes: Dumping and diarrhea. *Gastroenterol Clin North Am* 23: 261-279, 1994.
- Nakada K, Takahashi M, Ikeda M, Kinami S, Yoshida M, Uenosono Y, Kawashima Y, Nakao S, Oshio A, Suzukamo Y, *et al.*: Factors affecting the quality of life of patients after gastrectomy as assessed using the newly developed PGSAS-45 scale: A nationwide multi-institutional study. *World J Gastroenterol* 22: 8978-8990, 2016.
- Kinami S, Takahashi M, Urushihara T, Ikeda M, Yoshida M, Uenosono Y, Oshio A, Suzukamo Y, Terashima M, Kodera Y and Nakada K: Background factors influencing postgastrectomy syndromes after various types of gastrectomy. *World J Clin Cases* 6: 1111-1120, 2018.
- Nakada K, Ikeda M, Takahashi M, Kinami S, Yoshida M, Uenosono Y, Kawashima Y, Oshio A, Suzukamo Y, Terashima M and Kodera Y: Characteristics and clinical relevance of post-gastrectomy syndrome assessment scale (PGSAS)-45: Newly developed integrated questionnaires for assessment of living status and quality of life in postgastrectomy patients. *Gastric Cancer* 18: 147-158, 2015.
- Terashima M, Tanabe K, Yoshida M, Kawahira H, Inada T, Okabe H, Urushihara T, Kawashima Y, Fukushima N and Nakada K: Postgastrectomy syndrome assessment scale (PGSAS)-45 and changes in body weight are useful tools for evaluation of reconstruction methods following distal gastrectomy. *Ann Surg Oncol* 21 (Suppl 3): S370-S378, 2014.
- Ware JE, Kosinski M, Dewey JE and Gandek B: How to score and interpret single-item health status measures: A manual for users of the SF-8 health survey. Quality Metric Inc., Lincoln, RI, 2001.
- Fukuhara S and Suzukamo Y: Manual of the SF-8 Japanese version (in Japanese). Institute for health outcomes and process evaluation research, Kyoto, 2004.
- Svedlund J, Sjödin I and Dotevall G: GSRS-a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. *Dig Dis Sci* 33: 129-134, 1988.
- Japanese Gastric Cancer Association: Japanese gastric cancer treatment guidelines 2018 (ver. 5). Kanehara Shuppan, Tokyo, 2018.
- Japanese Gastric Cancer Association: Japanese classification of gastric carcinoma 2017 (The 15th edition). Kanehara Shuppan, Tokyo, 2018.
- Kanda Y: Investigation of the freely available easy-to-use software 'EZ' for medical statistics. *Bone Marrow Transplant* 48: 452-458, 2013.
- Kinami S, Nakamura N, Tomita Y, Miyata T, Fujita H, Ueda N and Kosaka T: Precision surgical approach with lymph-node dissection in early gastric cancer. *World J Gastroenterol* 25: 1640-1652, 2019.
- Sasako M, Sakuramoto S, Katai H, Kinoshita T, Furukawa H, Yamaguchi T, Nashimoto A, Fujii M, Nakajima T and Ohashi Y: Five-year outcomes of a randomized phase III trial comparing adjuvant chemotherapy with S-1 versus surgery alone in stage II or III gastric cancer. *J Clin Oncol* 29: 4387-4393, 2011.
- Rausei S, Mangano A, Galli F, Rovera F, Boni L, Dionigi G and Dionigi R: Quality of life after gastrectomy for cancer evaluated via the EORTC QLQ-C30 and QLQ-STO22 questionnaires: Surgical considerations from the analysis of 103 patients. *Int J Surg* 11 (Suppl 1): S104-S109, 2013.
- Kundes MF, Kement M, Yegen F, Alkan M, Kaya S and Kaptanoglu L: Effects of clinical factors on quality of life following curative gastrectomy for gastric cancer. *Niger J Clin Pract* 22: 661-668, 2019.
- Miwa K, Kinami S, Sato T, Fujimura T and Miyazaki I: Vagus-saving D2 procedure for early gastric carcinoma. *Nihon Geka Gakkai Zasshi* 97: 286-290, 1996 (In Japanese).
- Kojima K, Yamada H, Inokuchi M, Kawano T and Sugihara K: Functional evaluation after vagus-nerve-sparing laparoscopically assisted distal gastrectomy. *Surg Endosc* 22: 2003-2008, 2008.
- Sugimachi K, Korenaga D, Tomikawa M, Ikeda Y, Tsukamoto S, Kawasaki K, Yamamura S and Takenaka K: Factors influencing the development of small intestinal obstruction following gastrectomy for early gastric cancer. *Hepatogastroenterology* 55: 496-499, 2008.
- Kinami S, Oonishi T, Fujita J, Tomita Y, Funaki H, Fujita H, Nakano Y, Ueda N and Kosaka T: Optimal settings and accuracy of indocyanine green fluorescence imaging for sentinel node biopsy in early gastric cancer. *Oncol Lett* 11: 4055-4062, 2016.
- Kinami S, Funaki H, Fujita H, Nakano Y, Ueda N and Kosaka T: Local resection of the stomach for gastric cancer. *Surg Today* 47: 651-659, 2017.
- Takeuchi H, Goto O, Yahagi N and Kitagawa Y: Function-preserving gastrectomy based on the sentinel node concept in early gastric cancer. *Gastric Cancer* 20 (Suppl 1): S53-S59, 2017.
- Isozaki H, Matsumoto S, Murakami S, Takama T, Sho T, Ishihara K, Sakai K, Takeda M, Nakada K and Fujiwara T: Diminished gastric resection preserves better quality of life in patients with early gastric cancer. *Acta Med Okayama* 70: 119-130, 2016.
- Kinami S and Kosaka T: Laparoscopic sentinel node navigation surgery for early gastric cancer. *Transl Gastroenterol Hepatol* 2: 42, 2017.



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