

# Postoperative relative decrease in skeletal muscle mass as a predictor of quality of life in patients with gastric cancer

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**Abstract.** Low skeletal muscle mass reflects poor nutritional condition, which may impair the functional status and quality of life (QOL) of survivors of gastrectomy. The present cross-sectional study examined the association between a relative change in skeletal muscle mass and perceived postoperative health and QOL in patients with gastric cancer. The study comprised 74 patients (48 men and 26 women; median age, 68.5 years) who underwent surgery for stage I-III gastric cancer. Outcomes were measured using the Postgastrectomy Syndrome Assessment Scale-45, which was specifically developed to measure post-gastrectomy symptoms, living status, dissatisfaction with daily life and generic QOL. The skeletal muscle mass index (SMI) was estimated using computed tomography by tracing the area of the psoas major muscle to calculate the  $\Delta$ SMI, defined as: (SMI before surgery-SMI at completion of the PGSAS-45 survey)/SMI before surgery  $\times$  100. Associations between  $\Delta$ SMI and health outcomes were assessed using univariate and multivariate analyses. The mean  $\Delta$ SMI (SD) was 8.64% (10.6%). The effect size (Cohen's d) of  $\Delta$ SMI <10% compared with  $\Delta$ SMI  $\geq$ 10% was 0.50 (95% CI: 0.02 to 0.97) for total symptom scores, -0.51 (-0.98 to -0.03) for general health, and -0.52 (-0.99 to -0.05) for the physical component summary (PCS). Multiple regression analysis showed that  $\Delta$ SMI was significantly associated with PCS decline, and its standardized regression coefficient was -0.447 (-0.209 to -0.685). Determining  $\Delta$ SMI may help clinicians to facilitate the objective evaluation of low skeletal mass, which reflects poor nutritional condition that can impair functional status and QOL of postoperative patients surviving gastrectomy.

## Introduction

With the advent of diagnostic and therapeutic innovations, recent patients with gastric cancer in Japan have a better chance of being diagnosed in the early stages and living out their lives. The Cancer Statistics in Japan indicated that 64% of gastric cancer patients have Stage I disease, whose 5-year relative survival rate after diagnosis was estimated to be 96.0% (1). Thus, mortality and patients' views-related to their quality of life (QOL) following diagnosis and treatment for gastric cancer-have become immensely important (2,3). Observational studies identified several factors associated with a decline of QOL in patients with gastric cancer, including poor nutritional status and body configurations (3-9). For example, Climent *et al* reported that a loss of body weight of  $\geq$ 10% was associated with a deterioration of the functional aspects of QOL among gastric cancer survivors (6). Likewise, skeletal muscle mass is one of the critical determinants of sarcopenia and is closely related to muscle strength and physical performance. Huang *et al* found that patients with acute muscle wasting of over 10% had a poorer QOL in terms of fatigue and physical functioning (7). However, the effect of its long-term loss remains to be determined. Although computed tomography (CT) equipment is necessary to measure skeletal muscle mass, it is often readily available for postoperative surveillance of disease recurrence in clinical practice. Therefore, we hypothesized that a change in skeletal muscle mass at any time measured using CT images could be associated with impaired QOL in postoperative patients with gastric cancer. We conducted a cross-sectional study to examine the association between a percentage decline from baseline in skeletal muscle mass and postoperative QOL, both generic and disease-specific, among gastric cancer survivors.

## Materials and methods

**Patients.** The study comprised patients who underwent gastrectomy for gastric cancer between April 2008 and September 2015 at the Department of Surgery II of Tokyo Women's Medical University and had agreed to participate in the survey. Patients who met at least one of the following conditions were not eligible for the study: Followed-up less than 18 months after surgery, with distant metastases at initial diagnosis, with

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recurrent disease, and undergoing chemotherapy for other malignancies. In addition, patients whose attending physicians deemed them not suitable as participants were also ineligible.

**Measurements and data collection.** We recognized that the terms of health (or functional) status, health-related QOL, and QOL are often used interchangeably to refer to the same aspect of health (10-12). For the present study, we put two components into the construct of QOL: Disease-related aspects of daily life and overall perception of one's health. The Postgastrectomy Syndrome Assessment Scale-45 (PGSAS-45) questionnaire is a disease-specific and generic QOL questionnaire developed by the Japan Postgastrectomy Syndrome Working Party for the measurement of QOL in patients with gastric cancer (13). It consists of 45 items covering the following 4 domains: Gastrointestinal symptoms (25 items), living status (9 items), dissatisfaction in everyday life (3 items), and generic QOL (8 items). The generic QOL subscale is the standard form-8 (SF-8) questionnaire, and scores of the responses can be aggregated into two summary measures: the physical component summary (PCS) and mental component summary (MCS). Specifically, the items of the SF-8 are used to elicit respondents' general functional status, except for one item which asks, 'Overall, how would you rate your health during the past 4 weeks?', for which responses can range from very poor=1 to excellent=6 on a Likert-type scale (14). The gastrointestinal symptoms component consists of 15 items from the Gastrointestinal Symptom Rating Scale (GSRS) (15) and 10 original items specific to gastroesophageal reflux symptoms and dumping syndrome, which can occur after gastrectomy.

Skeletal muscle mass was measured on axial abdominal CT images that had been obtained both preoperatively and postoperatively to rule out metastasis or the recurrence of cancer. We measured total psoas major muscles area (TPA) between the third and fourth lumbar vertebrae (L3-L4) using an image viewer system (ShadeQuest/View C version 1; Yokogawa Medical Solutions, Tokyo, Japan). We then calculated the skeletal muscle mass index (SMI,  $\text{mm}^2/\text{m}^2$ ) as  $(\text{right TPA} + \text{left TPA})/(\text{height})^2$  because it has been shown to correlate significantly with total skeletal muscle mass (16,17).

Patient characteristics retrieved from medical records included age, body height, body weight, SMI, gender, stage of disease, surgical procedures, and use of adjuvant chemotherapy.

The percentage decline in the SMI ( $\Delta\text{SMI}$ ) from the preoperative value to the postoperative value was calculated as  $(\text{SMI before surgery} - \text{SMI at the survey})/\text{SMI before surgery} \times 100$ . Also, the percentage decline in body mass index ( $\Delta\text{BMI}$ ) was defined as  $(\text{BMI before surgery} - \text{BMI at the survey})/\text{BMI before surgery} \times 100$ . We used  $\Delta\text{SMI}$  to categorize participants into two groups with a cut-off value of 10%: patients whose  $\Delta\text{SMI}$  was  $<10\%$  and those with  $\Delta\text{SMI} \geq 10\%$ . The cut-off value was based on a demarcation noted in the literature (6,7).

**Statistical analyses.** Study data are shown as the number and percentage of patients, mean (standard deviation;  $\pm$  SD), median, or as median (range) values. For numerical data, the assumption of Gaussian distribution was examined using the Shapiro-Wilk test, and the Box-Cox transformation was used where it was appropriate. We used an unpaired *t*-test or the Wilcoxon rank-sum test to examine the statistical significance

of differences in numerical data between patients with a DSMI  $<10\%$  vs.  $\geq 10\%$ , and for categorical data we used chi-squared test. We also calculated the effect size (Cohen's *d*) for each difference to determine clinical significance. An effect size of 0.2 is generally considered small, 0.5 is moderate, and 0.8 is large with clinical importance (18). To explore the relationships between the numerical data, we employed correlation analyses using Pearson's *r* or Spearman's  $\rho$ , depending on the distributions.

We calculated the gender-adjusted Z scores for PCS and MCS of each patient based on national norm data of the SF-8 (14). The QOL of patients with Z scores  $<-1.0$  were deemed moderately or severely impaired. Multiple linear regression analyses were used to explore the association between PCS and DSMI controlling for other potential confounders as follows: Age at survey, gender, disease stage, surgical procedure, and use of chemotherapy. We examined interactions between DSMI and other variables by comparing the models with and without interaction terms using the multiple-partial F test (19,20). The proportion of variance in the dependent variable explained by the explanatory variables was estimated using adjusted  $R^2$ , which accounted for the number of predictors. We used JMP 13 (SAS Institute, Cary, NC, USA) and jamovi version 1.6.23 (21) for the statistical analyses and considered a two-sided  $P < 0.05$  to be statistically significant.

**Ethical considerations.** Written informed consent was obtained from all individual participants included in the study. The study was conducted under approval of the Tokyo Women's Medical University review board (approval no. 4056).

## Results

**Patients' characteristics.** The median follow-up time from gastrectomy to the survey was 48.5 months (range: 18-130). The clinical characteristics of the 74 patients who participated in the study are summarized in Table I. The male/female ratio was 48/26, and the median age at the time of the survey was 68.5 years (range: 41-89). Stage I, II, and III clinical disease was observed in 54 (73%), 13 (17.5%), and 7 (9.5%) patients, respectively. Thirty-eight (51.4%) patients underwent distal gastrectomy, and 17 (23.0%) received total gastrectomy. Adjuvant chemotherapy was administered to 14 (18.9%) patients. Mean values for preoperative body weight, BMI, and SMI were 59.3 kg ( $\pm 11.6$ ),  $22.3 \text{ kg}/\text{m}^2$  ( $\pm 3.31$ ), and  $605 \text{ mm}^2/\text{m}^2$  ( $\pm 161$ ), respectively, and at the postoperative survey they were 52.8 kg ( $\pm 10.6$ ),  $19.8 \text{ kg}/\text{m}^2$  ( $\pm 3.15$ ), and  $552 \text{ mm}^2/\text{m}^2$  ( $\pm 158$ ), respectively.

**$\Delta\text{SMI}$  and its relationship with  $\Delta\text{BMI}$  and other variables.** The mean values for  $\Delta\text{SMI}$  and  $\Delta\text{BMI}$  were 8.64% ( $\pm 10.6$ ) and 10.5% ( $\pm 9.4$ ), respectively. Ten (13.5%) patients showed an increase in  $\Delta\text{SMI}$  and a decrease in  $\Delta\text{BMI}$ , while four (5.4%) patients experienced a decrease in  $\Delta\text{SMI}$  and an increase in  $\Delta\text{BMI}$  (Table II). There was no significant correlation between  $\Delta\text{SMI}$  and years from surgery to the survey [Pearson's  $r=0.026$ ,  $P=0.829$  (data not shown)].

We compared patients whose  $\Delta\text{SMI}$  was  $\geq 10\%$  and those with  $<10\%$  in terms of gender, age at the time of the survey,

Table I. Patient characteristics.

Characteristic	Value
Male/female, n	48/26
Median age, years (min, max)	
Time of surgery	65 (38, 87)
Time of survey	68.5 (41, 89)
Disease stage, n (%)	
I	54 (73)
II	13 (17.5)
III	7 (9.5)
Gastrectomy, n (%)	
Distal gastrectomy	38 (51.4)
Total gastrectomy	17 (23.0)
Proximal gastrectomy	9 (12.2)
Pylorus preserving gastrectomy	6 (8.1)
Segmental gastrectomy	4 (5.4)
Reconstruction method, n (%)	
Billroth I	32 (43.2)
Roux-en-Y	23 (31.1)
Esophageal gastric anastomosis	6 (8.1)
Double tract	3 (4.1)
Other	10 (13.5)
Adjuvant chemotherapy, n (%)	
Not reported	60 (81.1)
Reported	14 (18.9)
Mean body weight, kg (SD)	
Preoperative	59.3 (11.6)
Time of survey	52.8 (10.6)
Mean BMI, kg/m <sup>2</sup> (SD)	
Preoperative	22.3 (3.31)
Time of survey	19.8 (3.15)
Mean SMI, mm <sup>2</sup> /m <sup>2</sup> (SD)	
Preoperative	605 (161)
Time of survey	552 (157)

BMI, body mass index; max, maximum; min, minimum; SMI, skeletal muscle mass index.

pathological stage, use of adjuvant chemotherapy, and the extent of gastrectomy. Patients with  $\Delta$ SMI  $<10\%$  were more likely to have stage I disease (60.6% vs. 82.9%,  $P=0.04$ ) and were less likely to have had a total gastrectomy (9.8% vs. 39.3%,  $P<0.01$ ). There were no statistically significant differences observed in the other variables assessed (Table III).

**Gastrointestinal symptoms and living status.** Patients with a  $\Delta$ SMI  $\geq 10\%$  scored significantly higher than those with a  $\Delta$ SMI  $<10\%$  in the subscale of abdominal pain and total symptom score (Table IV). Corresponding effect sizes were 0.61 [95% confidence interval (CI): 0.13, 1.09] and 0.50 [95% CI: 0.02, 0.97], respectively (data not shown). Observed differences in other subscales and the four domains of living status did not reach statistical significance.

Table II. Number of patients according to  $\Delta$ SMI and  $\Delta$ BMI.

$\Delta$ SMI	$\Delta$ BMI		
	Decrease	No change	Increase
Decrease	56	1	4
No change	0	0	0
Increase	10	1	2

$\Delta$ BMI, percent change in body mass index (preoperative-postoperative);  $\Delta$ SMI, percent change in skeletal muscle mass index (preoperative-postoperative).

**Generic and disease-specific QOL.** For the 74 patients overall, responses to the first question in the SF-8, 'Overall, how would you rate your health during the past 4 weeks?', were distributed as follows: very poor=0; poor=2 (3%), fair=5 (7%); good=44 (59%); very good=23 (31%); and excellent=0. The mean PCS was 50.6 ( $\pm 5.7$ ), which was significantly higher than that of the general population (Cohen's  $d=0.28$ , 95% CI: 0.04, 0.51;  $P=0.0018$ ). The mean MCS was 50.4 ( $\pm 5.5$ ), and it was not higher than the average of the general population (Cohen's  $d=0.15$ , 95% CI: -0.08, 0.38;  $P=0.06$ ). The duration of follow-up was significantly associated with MCS (Spearman's  $\rho=0.243$ ,  $P=0.037$ ) but not with PCS (Spearman's  $\rho=0.040$ ,  $P=0.738$ ). Z scores were  $<-1.0$  for PCS in 5 (6.8%) patients and for MCS in 6 (8.1%) patients. Patients with a  $\Delta$ SMI  $\geq 10\%$  had significantly lower scores than those with a  $\Delta$ SMI  $<10\%$  in the domain of general health and PCS (Table V). Corresponding effect sizes were -0.51 (95% CI: -0.98, -0.03) and -0.52 (95% CI: -0.99 to -0.05), respectively. Observed differences in other domains and MCS did not reach statistical significance (data not shown).

**Associations between  $\Delta$ SMI and summary scores for the SF-8.** There was a positive correlation between  $\Delta$ SMI and  $\Delta$ BMI, and Pearson's correlation coefficient was 0.47 (95% CI: 0.27, 0.63).  $\Delta$ SMI was significantly associated with PCS ( $r=-0.30$ , 95% CI: -0.52, -0.07) but not with MCS ( $r=-0.09$ , 95% CI: -0.32, 0.15).  $\Delta$ BMI had no significant correlations with either PCS ( $r=-0.15$ , 95% CI: -0.38, 0.08) or MCS ( $r=-0.03$ , 95% CI: -0.27, 0.20) (Fig. 1). After controlling for potential confounders, the multiple regression analysis showed that  $\Delta$ SMI was significantly associated with PCS decline, and its standardized regression coefficient was -0.447 (95% CI: -0.209, -0.685) (Table VI).

Multiple regression analyses with and without interaction terms indicated that there were no significant interactions (multiple-partial F test,  $F_{6,60,0.95}=0.45$ ,  $P>0.05$ ; data not shown). The model without interaction terms ( $F_{7,66}=3.18$ ,  $P=0.006$ , adjusted  $R^2=0.173$ ) showed that  $\Delta$ SMI was significantly associated with PCS decline, and its standardized regression coefficient was -0.447 (95% CI: -0.209, -0.685) (Table VI).

## Discussion

Although more than five decades have passed since Elkinton introduced QOL for medical use in 1966 (22), the

Table III. Patient characteristics.

Characteristic	$\Delta$ SMI $\geq 10\%$ (n=33)	$\Delta$ SMI $< 10\%$ (n=41)	P-value
Male/female, n	23/10	25/16	0.47 <sup>b</sup>
Mean age at survey, years (SD)	69.1 (11.5)	69.0 (8.9)	0.99 <sup>a</sup>
Median time from surgery to survey, months (IQR)	48 (33.5, 76)	52 (33, 64.5)	0.94
Pathological stage I disease, n (%)	20 (60.6)	34 (82.9)	0.04 <sup>b</sup>
Adjuvant chemotherapy, n (%)	8 (24.2)	6 (14.6)	0.38 <sup>b</sup>
Total gastrectomy, n (%)	13 (39.3)	4 (9.8)	$< 0.01^b$

<sup>a</sup>Based on the unpaired *t*-test and <sup>b</sup>based on chi-squared test. The Wilcoxon rank-sum test was used for statistical analysis of the other characteristics.  $\Delta$ SMI, percent change in skeletal muscle mass index (preoperative-postoperative).

Table IV. Gastrointestinal symptoms and living status.

Variable	$\Delta$ SMI $\geq 10\%$	$\Delta$ SMI $< 10\%$	P-value
Gastrointestinal symptoms <sup>a</sup>			
Esophageal reflux subscale	1.9 (0.9)	1.6 (0.9)	0.20
Abdominal pain subscale	1.7 (0.9)	1.3 (0.5)	0.01
Meal-related distress subscale	2.4 (1.1)	2.1 (1.0)	0.25
Indigestion subscale	2.2 (1.0)	1.9 (0.8)	0.15
Diarrhea subscale	2.4 (1.2)	1.9 (0.8)	0.06
Constipation subscale	2.4 (1.1)	2.1 (1.1)	0.16
Dumping subscale	1.8 (0.9)	1.5 (0.7)	0.14
Total symptom score	2.1 (0.8)	1.8 (0.6)	0.04
Living status			
Food ingested per meal	6.1 (2.1)	6.9 (1.9)	0.09
Necessity for additional meals <sup>b</sup>	2.1 (1.0)	1.9 (0.7)	0.26
Quality of ingestion subscale <sup>c</sup>	3.8 (1.1)	4.0 (0.9)	0.26
Ability to work <sup>d</sup>	1.9 (0.9)	1.8 (0.7)	0.35

All values are mean (SD). <sup>a</sup>Each subscale of gastrointestinal symptoms is scored by averaging the responses to its items with a 7-point Likert scale ranging from 1 (never bothered) to 7 (always bothered). Total symptom score is a mean of the seven subscales. <sup>b</sup>Necessity for additional meals has 5 responses ranging from 1 (not at all) to 5 (very much). <sup>c</sup>Quality of ingestion subscale is scored by averaging the responses to three items (appetite, hunger feeling, and satiety feeling) with a 5-point Likert scale ranging from 1 (not at all) to 5 (always). <sup>d</sup>Ability to work has 5 responses ranging from 1 (best) to 5 (worst).  $\Delta$ SMI, percent change in skeletal muscle mass index (preoperative-postoperative). The unpaired *t*-test was used for all statistical analyses.

conceptual and methodological clarification of QOL has been challenging (23). Researchers have never unanimously agreed upon what QOL means; the construct has become a kind of umbrella under which many different indexes are included (24). Gill and Feinstein have argued that domains of QOL measured by many researchers have been diverse (11). Since two people with the same clinical conditions may have quite different views on their life quality, researchers need to be cautious about what it is that they measure, health status or QOL (25,26). In this regard, the PGSAS-45 questionnaire used in the present study has distinct domains for post-gastrectomy symptoms, living status, dissatisfaction with daily life, and generic QOL (13).

Clinical and research observations have shown that surgery for gastric cancer led to nutritional sequelae due to anatomical and physiological changes in the digestive tract. Besides, the

reduced production of ghrelin, which is mainly secreted from the stomach and stimulates appetite and food intake, may play a role in metabolic changes following gastrectomy (27-30).

Gastrectomy reduces gastric acid secretion, which reduces calcium absorption in the upper small intestine. Calcium is an extremely important nutrient for the function of skeletal muscles. A study on the relationship between calcium intake and sarcopenia in the elderly showed that those with low calcium intake have a significantly higher rate of sarcopenia, and it is thought that nutritional guidance that considers the balance of minerals, including calcium, plays an important role in suppressing the decline in skeletal muscle mass (31). It is also important to leave a large residual stomach to suppress abdominal symptoms, which is one of the causes of QOL deterioration. Kunisaki *et al* reported that patients with upper gastric cancer who underwent cardiac gastrectomy obtained

Table V. Generic and disease-specific QOL.

QOL factors	$\Delta$ SMI $\geq 10\%$	$\Delta$ SMI $< 10\%$	P-value
SF-8			
General health	50.2 (6.3)	53.0 (5.0)	0.03
Physical functioning	48.4 (7.9)	50.6 (4.5)	0.14
Role physical	49.1 (7.0)	50.7 (5.0)	0.26
Bodily pain	56.5 (7.0)	57.1 (5.2)	0.67
Vitality	50.4 (6.2)	52.2 (4.1)	0.13
Social functioning	49.6 (7.0)	51.3 (6.0)	0.25
Mental health	53.1 (4.6)	51.6 (6.3)	0.25
Role emotional	50.9 (3.7)	51.3 (4.9)	0.70
Physical component summary	49.0 (6.8)	51.9 (4.2)	0.03
Mental component summary	50.9 (4.9)	50.1 (5.9)	0.55
Disease-specific QOL			
Dissatisfaction with symptoms	1.9 (0.8)	1.5 (0.7)	0.06
Dissatisfaction at meals	2.4 (1.2)	2.2 (1.0)	0.57
Dissatisfaction at working	1.8 (0.9)	1.5 (0.8)	0.14
Dissatisfaction with daily life subscale <sup>a</sup>	2.0 (0.9)	1.8 (0.7)	0.14

All values are mean (SD). <sup>a</sup>Dissatisfaction with daily life subscale is scored by averaging the responses to three dissatisfaction items (symptoms, meals, and working) with a 5-point Likert scale ranging from 1 (not at all) to 5 (very much so). QOL, quality of life; SF-8, short form-8;  $\Delta$ SMI, percent change in skeletal muscle mass index (preoperative-postoperative). The unpaired t-test was used for all statistical analyses.

Table VI. Multiple regression analysis with PCS as a dependent variable<sup>a</sup>.

Variable	Standardized regression coefficient (95% CI)	t-value	P-value
$\Delta$ SMI	-0.447 (-0.685, -0.209)	-3.75	$< 0.01$
Age at survey	-0.126 (-0.343, 0.090)	-1.16	0.25
Time from surgery to survey	0.088 (-1.322, 0.308)	0.80	0.43
Female	0.493 (-0.017, 0.896)	1.92	0.06
Stage I disease	0.686 (-0.232, 1.604)	1.49	0.14
Adjuvant chemotherapy	-0.685 (-1.606, 0.235)	-1.49	0.14
Total gastrectomy	-0.605 (-1.339, 0.129)	-1.65	0.10

<sup>a</sup>Adjusted R<sup>2</sup>: 0.173. CI, confidence interval; PCS, physical component summary;  $\Delta$ SMI, percent change in skeletal muscle mass index (preoperative-postoperative).

better scores on many PGSAS items than those who underwent total gastrectomy (32). In addition to the importance of selecting less invasive surgery, they also pointed out the importance of dietary guidance and that close cooperation not only with surgeons but also with allied medical professionals is necessary to suppress the deterioration of postoperative QOL.

These alterations may variously manifest as reflux symptoms, dumping syndrome, and/or chronic pain that may contribute to both a poor nutritional status and QOL (2-5). Rupp and Stengel identified 35 factors potentially associated with QOL, depression, or anxiety in patients with gastric cancer and classified them into nine categories: genetic condition, treatment method, blood markers, nutritional status, daily living, state of health, mental state, supportive care, and alternative treatment (33). Moreover, they are likely

correlated with each other and affect patient QOL in a complex way at the level of the individual (34,35). Nevertheless, it would be helpful to identify clinical characteristics that can predict nutritional status and QOL deterioration. BMI can reflect nutritional status, but its change does not necessarily parallel the change in skeletal muscle mass as observed in the present study. Body weight, the primary variable in the calculation of BMI, can be associated with factors other than muscle volume. Although acute muscle wasting  $\geq 10\%$  within one week after gastric cancer surgery was associated with a poorer QOL (7), the relationship beyond 1 week after surgery has never been reported in the literature. We found that a decrease in SMI ( $\Delta$ SMI)  $\geq 10\%$  at a median follow-up of 4 years was significantly associated with impaired postoperative health status and QOL. However, the mean summary

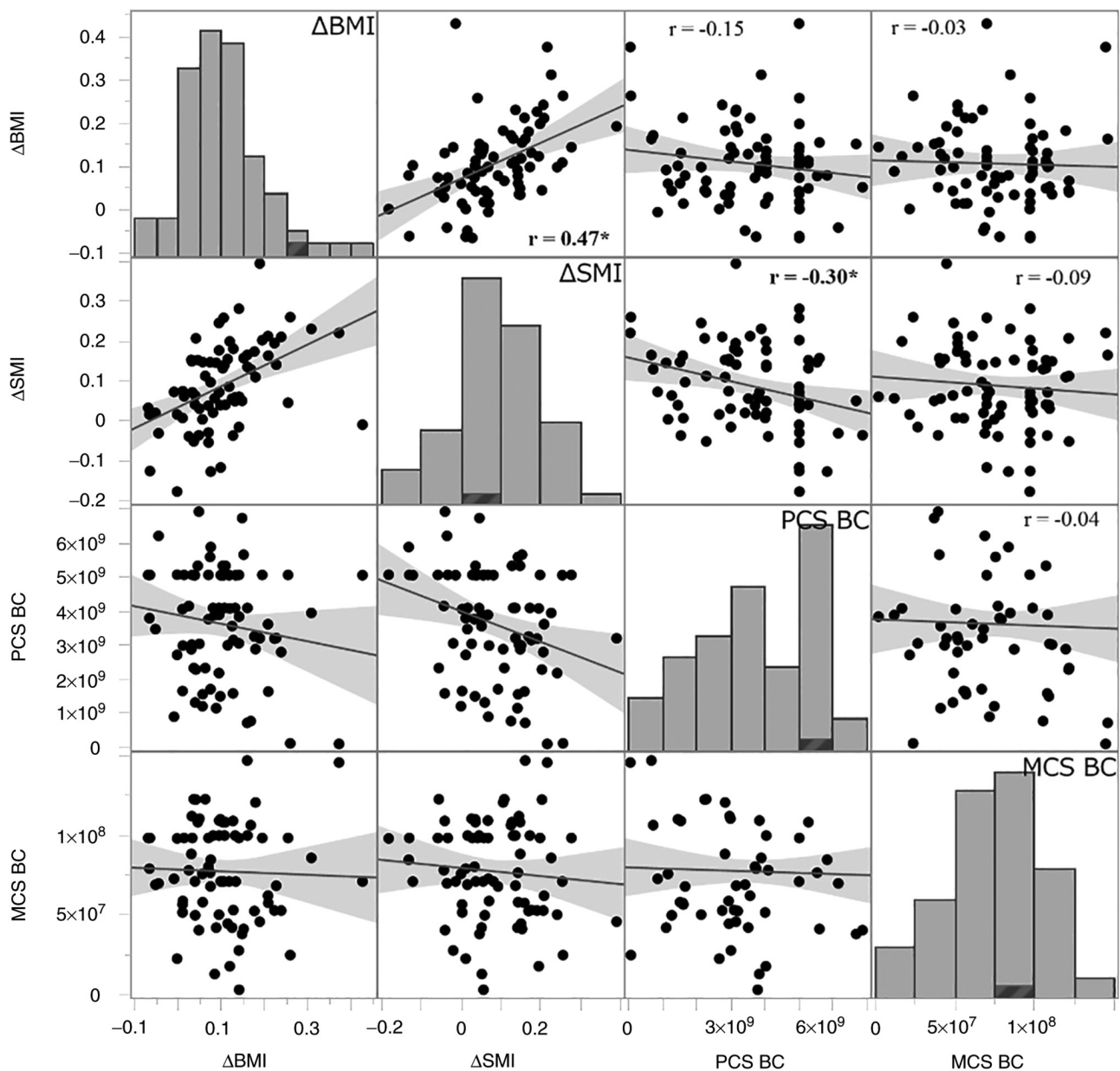


Figure 1. Bar charts show frequency distributions. Scatter plot matrix showing correlations among  $\Delta$ BMI,  $\Delta$ SMI, PCS and MCS. \*Significant difference,  $P < 0.05$ . BC, Box-Cox transformation;  $\Delta$ BMI, percent change in body mass index (before surgery-at the survey); MCS, mental component summary; PCS, physical component summary;  $r$ , Pearson's correlation coefficient;  $\Delta$ SMI, percent change in skeletal muscle mass index (before surgery-at the survey).

scores for generic QOL measured using the SF-8 was equal (mental) to or even superior (physical) to the average of the general population. Furthermore, it is interesting to note that 90% of the respondents indicated their overall QOL (i.e., general health) was good or very good. These observations are caveats to the stereotypical belief that patients with functional or mental difficulties have a lower QOL than those without them (26,36).

Skeletal muscle mass has become a critically important concern of clinicians as sarcopenia and frailty have come into sharper focus in recent years. Its decrease is also associated with surgical complications (36-39). The loss of skeletal muscle mass is multifactorial caused by malnutrition, peri-operative chemotherapy, reduced exercise, aging, or the disease itself (inflammation or cancer cachexia). Of these, nutritional status is a particularly strong predictor of QOL in cancer survivors

and modifiable to the extent that appropriate screening, assessment, and intervention could help patients recovering from such a burden (40,41). Besides, exercise therapy could have beneficial effects on patients' QOL as well as their skeletal muscle mass (42,43).

We acknowledge some concerns that may threaten the validity of the present study. First, periods from surgery to survey varied among the survey participants. A few studies observed that patients' nutritional status and QOL varied depending on surgery time (3,4,44,45). Yet acute effects of surgery on the measurements would be negligible as all patients' time intervals between surgery and the survey were more than 18 months. In particular, the relationship between the changes in skeletal muscle mass and the time elapsed may be non-linear and would not be captured by Pearson's correlation coefficient. Second, the multiple



regression analysis captured only a part of the causal relationships of our observations as it showed an adjusted  $R^2$  of 0.173, which was relatively low. For the complex concept of QOL (23,34,35), mathematical modeling has limitations in exploring the causal pathway when some crucial variables may be unobserved or related in complicated ways. In particular, the surgical procedures may be effect modifiers of the relationship between QoL (PCS) and  $\Delta$ SMI. Subgroup or stratified analyses would be one choice to examine the effect modification. However, such analyses may lead to small stratum-specific sample sizes, resulting in an imprecise estimate (46). Alternatively, we constructed another hierarchically well-formulated multivariable regression model with interaction terms. The multiple-partial F test for regression coefficients of the interaction terms was not statistically significant, indicating no interaction. Third, the SF-8 questionnaire measures health status rather than respondents' life quality (25). In fact, the first item purported to measure overall QOL asks those surveyed to 'rate your health'. This approach does not reflect respondents' views about their circumstances unrelated to health (25). Fourth, we did not measure muscle strength that could be associated with patients' QOL. However, as it is one of the essential components of the definition of sarcopenia (47), measuring muscle strength may become an important consideration when evaluating patients' nutritional status.

In conclusion, determining  $\Delta$ SMI may help clinicians to facilitate the objective evaluation of nutritional status and be aware of the life quality of postoperative patients with gastric cancer.

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## Availability of data and materials

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

## Authors' contributions

YU and AS made substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data. TO made substantial contributions to conception and design, and analysis and interpretation of data. All authors confirm the authenticity of all of the raw data. All authors contributed to the writing of the manuscript, and read and approved the final manuscript.

## Ethics approval and consent to participate

Written informed consent was obtained from all individual participants included in the study. The study was conducted under approval of the Tokyo Women's Medical University review board (approval no. 4056).

## Patient consent for publication

In regard to patient consent for publication, all identifying information was removed, and we obtained written permission for publication from all patients who participated in this study.

## Competing interests

The authors declare that they have no competing interests.

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