

# World Journal of *Gastroenterology*

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## Observational Study

**Predictive factors for body weight loss and its impact on quality of life following gastrectomy**

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## Abstract

### AIM

To determine the predictive factors and impact of body weight loss on postgastrectomy quality of life (QOL).

### METHODS

We applied the newly developed integrated questionnaire postgastrectomy syndrome assessment scale-45, which consists of 45 items including those from the Short Form-8 and Gastrointestinal Symptom Rating Scale instruments, in addition to 22 newly selected items. Between July 2009 and December 2010, completed questionnaires were received from 2520 patients with curative resection at 1 year or more after having undergone one of six types of gastrectomy for Stage I gastric cancer at one of 52 participating institutions. Of those, we analyzed 1777 eligible questionnaires from patients who underwent total gastrectomy with Roux-en-Y procedure (TGRY) or distal gastrectomy with Billroth-I (DGBI) or Roux-en-Y (DGRY) procedures.

### RESULTS

A total of 393, 475 and 909 patients underwent TGRY, DGRY, and DGBI, respectively. The mean age of patients was  $62.1 \pm 9.2$  years. The mean time interval between surgery and retrieval of the questionnaires was  $37.0 \pm 26.8$  mo. On multiple regression analysis, higher preoperative body mass index, total gastrectomy, and female sex, in that order, were independent predictors of greater body weight loss after gastrectomy. There was a significant difference in the degree of weight loss ( $P < 0.001$ ) among groups stratified according to preoperative body mass index ( $< 18.5$ ,  $18.5$ - $25$  and  $> 25$   $\text{kg}/\text{m}^2$ ). Multiple linear regression analysis identified lower postoperative body mass index, rather than greater body weight loss postoperatively, as a certain factor for worse QOL ( $P < 0.0001$ ) after gastrectomy, but the influence of both such factors on QOL was relatively small ( $R^2$ ,  $0.028$ - $0.080$ ).

### CONCLUSION

While it is certainly important to maintain adequate body weight after gastrectomy, the impact of body weight loss on QOL is unexpectedly small.

**Key words:** Quality of life; Gastrectomy; Weight loss; Postgastrectomy syndrome assessment scale-45

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**Core tip:** Our study of almost 1800 gastrectomy patients revealed that higher preoperative body mass index, total gastrectomy, and female sex were independent predictors of greater body weight loss after gastrectomy. Moreover, we determined lower postoperative body mass index, rather than greater postoperative weight loss, as a certain factor of worse quality of life (QOL), although the effect was not substantial. We believe that this contribution is theoretically and practically relevant in the current

context of gastric cancer treatment and recovery because early diagnosis and improved treatments have led to increased long-term survival postgastrectomy, highlighting the need for better QOL.

Tanabe K, Takahashi M, Urushihara T, Nakamura Y, Yamada M, Lee SW, Tanaka S, Miki A, Ikeda M, Nakada K. Predictive factors for body weight loss and its impact on quality of life following gastrectomy. *World J Gastroenterol* 2017; 23(26): 4823-4830 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v23/i26/4823.htm> DOI: <http://dx.doi.org/10.3748/wjg.v23.i26.4823>

## INTRODUCTION

Despite its gradually decreasing incidence, gastric cancer remains the second leading cause of cancer death in the world<sup>[1]</sup>. Surgical resection and regional lymphadenectomy are the only curative options for patients with localized gastric tumors<sup>[2-4]</sup>. As early diagnosis and improved treatment have led to longer-term survival, patients are now more aware of the morbidities associated with gastrectomy, which is called postgastrectomy syndrome. Indeed, the gastrectomized patients may experience various nutritional and functional problems that interfere with their quality of life (QOL)<sup>[5-7]</sup>. Loss of body weight is a common complaint after gastrectomy, and is thought as one of few objective indices to measure the well-being of postgastrectomy patients. Some reports suggest that the type of gastrectomy is a certain predictor of postoperative weight loss<sup>[6,8,9]</sup>, however, other predictive factors for postoperative weight loss has yet not been determined. Though the low body mass index (BMI) as well as body weight loss is often identified after gastrectomy and may affects the QOL after gastrectomy<sup>[10]</sup>, their detail implication on the QOL has not been clarified.

The aim of the present study was to determine the predictive factors for postoperative weight loss and to investigate the impact of body weight loss and low BMI on the QOL in patients after gastrectomy using the Postgastrectomy Syndrome Assessment Scale (PGSAS)-45, which was established specifically to assess symptoms, living status and QOL among patients after gastrectomy<sup>[11]</sup>.

## MATERIALS AND METHODS

The PGSAS study, a surveillance study involving 52 institutions, was conducted by the Japanese Postgastrectomy Syndrome Working Party (JPGSWP) and approved by the institutional review boards of all participating institutions. After completion of the informed consent process, patients were enrolled in this study if they met the following eligibility criteria: 20-75 years of age, histologically proven Stage I gastric cancer based on the 13<sup>th</sup> edition of the Japanese

**Table 1 Characteristics of patients after conventional gastrectomy**

Sex [male: <i>n</i> (%)]	1188 (66.9)
Age (yr, mean $\pm$ SD)	62.1 $\pm$ 9.2
Type of gastrectomy ( <i>n</i> : TGRY/DGBI/DGRY)	393/909/475
Period after gastrectomy (mo: mean $\pm$ SD)	37.0 $\pm$ 26.8
Change in body weight (%; mean $\pm$ SD)	-9.5 $\pm$ 8.0
Preoperative BMI (kg/m <sup>2</sup> , mean $\pm$ SD)	22.8 $\pm$ 3.1
Postoperative BMI (kg/m <sup>2</sup> , mean $\pm$ SD)	20.6 $\pm$ 2.8
Approach ( <i>n</i> , open/laparoscopic)	1102 $\pm$ 664
Preservation of celiac branch of vagus (Y/N)	173/1567

BMI: Body mass index.

classification of gastric carcinoma<sup>[12]</sup>, curative resection at least 1 year after surgery, no signs of recurrence at the point of assessment, and no other active malignancy.

The PGSAS-45 questionnaire consists of 45 questions, with 8 items from the Short Form-8 (SF-8)<sup>[13]</sup>, 15 items from the Gastrointestinal Symptom Rating Scale<sup>[14]</sup>, and 22 clinically important items determined by the JPGSWP. Patients were given the questionnaire together with a stamped and addressed envelope in the outpatient clinic and were asked to complete questionnaire and return it by post to the data center. Of the 2922 patients to whom questionnaires were given during July 2009 to December 2010, 2520 (86%) responded and 2368 (81%) were confirmed to be eligible for the original study. Of these, the data from 1777 patients who underwent total gastrectomy with Roux-en-Y (TGRY) and distal gastrectomy with Billroth-I (DGBI) or Roux-en-Y (DGRY) were analyzed in this study.

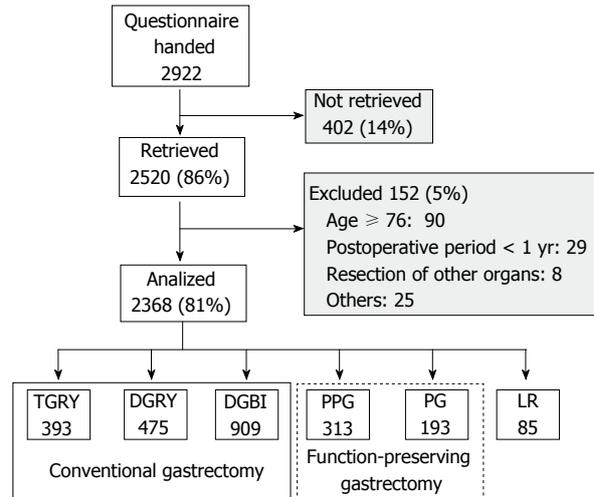
### Statistical analysis

The degree of body weight loss was compared among the three relevant preoperative BMI groups (BMI, < 18.5, 18.5-25 and > 25 kg/m<sup>2</sup>) by multiple comparisons. Multiple regression analysis was performed to determine the factors affecting body weight loss after surgery, and to study the impact of the change in body weight and postoperative BMI on QOL. A *P* value of < 0.05 was considered to indicate statistical significance. To evaluate effect sizes, Cohen's *d*, standardization coefficient of regression ( $\beta$ ) and coefficient of determination (*R*<sup>2</sup>) were used. Interpretation of effect sizes were  $\geq 0.2$  small,  $\geq 0.5$  medium, and  $\geq 0.8$  large in Cohen's *d*;  $\geq 0.1$  small,  $\geq 0.3$  medium, and  $\geq 0.5$  large in  $\beta$ ;  $\geq 0.02$  small,  $\geq 0.13$  medium, and  $\geq 0.26$  large in *R*<sup>2</sup>. All statistical analyses were performed by biostatisticians who primarily used Stat View for Windows Ver. 5.0 (SAS Institute Inc., Cary, NC, United States).

## RESULTS

### Patient characteristics

A CONSORT flowchart of the PGSAS study is shown in Figure 1. A total of 1777 patients (1188 men;



**Figure 1 CONSORT flowchart of the Postgastrectomy Syndrome Assessment Study (PGSAS study).** TGRY: Total gastrectomy with Roux-en-Y reconstruction; DGRY: Distal gastrectomy with Roux-en-Y reconstruction; DGBI: Distal gastrectomy with Billroth-I reconstruction; PPG: Pylorus-preserving gastrectomy; PG: Proximal gastrectomy; LR: Local resection.

66.9%) who underwent conventional gastrectomy were enrolled in this study. The mean age of patients was 62.1  $\pm$  9.2 years. The numbers of patients undergoing each operative procedure were as follows: TGRY, 393; DGRY, 475; and DGBI, 909. The mean time interval between surgery and retrieval of the questionnaires was 37.0  $\pm$  26.8 mo, and the mean body weight loss among postgastrectomy patients was 9.5%  $\pm$  8.0% at that time (Table 1).

### QOL measures in the PGSAS-45

The PGSAS-45 is an integrated questionnaire for assessing the symptoms, the living status and the QOL in patients after gastrectomy, as described previously<sup>[11]</sup>. The structure of the PGSAS-45 is shown in Table 2. QOL scores in the PGSAS-45 were obtained for two subdomains: dissatisfaction and the SF-8 items. The dissatisfaction subdomain consists of four outcome measures based on symptoms (item 43), meals (item 44), working (item 45), and daily life subscale (mean of the item 43-45). The SF-8 consists of eight items and generates two summary measures, the physical component summary and the mental component summary. The mean values of main outcome measures are shown in Table 3.

### Factors affecting postoperative weight loss

To clarify the predictive factors affecting change in body weight after surgery, multiple regression analysis was performed. In order of significance, higher preoperative BMI, type of gastrectomy (TGRY) and female sex were the independent predictors for postoperative weight loss (Table 4).

### Relationship between preoperative BMI and change in body weight

Considering that preoperative BMI was the most

**Table 2 Structure of postgastrectomy syndrome assessment scale-45 (domains/subdomains/items/subscales)**

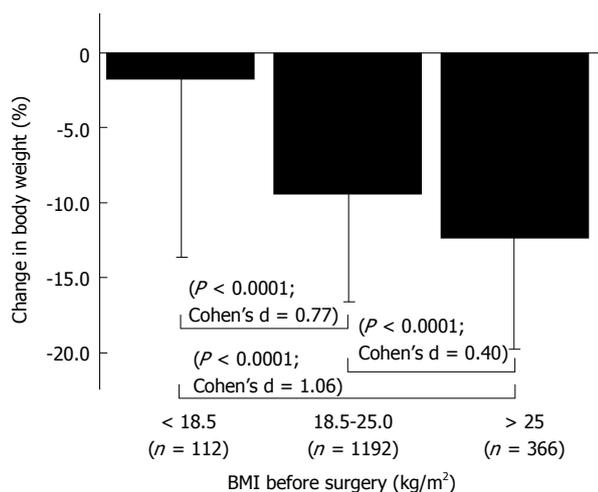
Domains	Subdomains	Items	Subscales			
QOL	SF-8 (QOL)	1	Physical functioning <sup>1</sup>	Physical component summary <sup>1</sup> (item 1-8)		
		2	Role physical <sup>1</sup>		Mental component summary <sup>1</sup> (item 1-8)	
		3	Bodily pain <sup>1</sup>			
		4	General health <sup>1</sup>			
		5	Vitality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

<sup>1</sup>Higher scores indicate better conditions. Each subscales is calculated as the mean of its composite items or subscales, except the physical and mental component summaries of SF-8. Items 29 and 32 do not have scores; these were analyzed separately. PGSAS-45: Postgastrectomy syndrome assessment scale-45; SF-8: Short form-8; QOL: Quality of life; GSRS: Gastrointestinal symptom rating scale.

**Table 3 Main outcome measures of postgastrectomy syndrome assessment scale-45 quality of life domain in patients after conventional gastrectomy (n = 1777)**

Subdomains	Item in PGSAS-45	Main outcomes measures	Scale	mean ± SD
Dissatisfaction	43	Dissatisfaction with symptoms	Five-point Likert scale	1.87 ± 0.95
	44	Dissatisfaction at the meals		1.13
	45	Dissatisfaction at working		1.79 ± 0.97
	43-45	Dissatisfaction for daily life subscale		0.87
SF-8	1-8	Physical component summary <sup>1</sup>	Five or six-point Likert scale	50.4 ± 5.6
	1-8	Mental component summary <sup>1</sup>		49.7 ± 5.8

<sup>1</sup>Higher score indicating better condition. Integrated subscales (SS) are underlined in the Table. PGSAS-45: Postgastrectomy syndrome assessment scale-45; SF-8: Short form-8.



**Figure 2** Preoperative body mass index strongly influences change in body weight postoperatively. Bars represent the mean change in body weight (mean  $\pm$  SD); effect size for group difference are reported as Cohen's *d* ( $P < 0.0001$ ). BMI: Body mass index.

influential factor affecting weight loss postoperatively, we compared the degree of weight loss among three relevant preoperative BMI groups:  $< 18.5$ ;  $18.5-25$ ; and  $25 <$  ( $\text{kg}/\text{m}^2$ ) (Figure 2). There was a significant difference between each group ( $P < 0.0001$ ) with a certain effect size in terms of Cohen's *d*. The patients with higher BMI ( $> 25 \text{ kg}/\text{m}^2$ ) exhibited the greatest weight loss (12.3%) among the groups, while the degree of weight loss in patients with lower BMI  $< (18.5)$  was spare (2%).

### Impact of change in body weight and postoperative BMI on QOL

Finally, we performed multiple regression analysis to compare the influence on postoperative QOL between body weight loss and low postoperative BMI (Tables 5 and 6). The low postoperative BMI significantly affected on all QOL outcome measures with small but clinically meaningful effect size in terms of standardized partial regression coefficient ( $\beta$ ), while the body weight loss only affected on some of QOL outcome measures with smaller effect size in  $\beta$  (approximately of half value compared to that of postoperative BMI). In addition, coefficient of determination  $R^2$ , which indicates the aggregated impact of body weight loss and low postoperative BMI on the QOL, were relatively small for each QOL outcome measures.

## DISCUSSION

This study identified the causal factors affecting body weight loss after gastrectomy and investigated the impact of body weight loss on the postoperative QOL using the PGSAS-45 questionnaire, which was recently developed to assess the QOL following gastrectomy. Our results identified higher preoperative BMI as the most influential factor affecting postoperative weight

**Table 4** Factors influencing body weight loss after gastrectomy (multiple regression analysis)

Variables	Change in body weight	
	$\beta$	<i>P</i> value
Type of gastrectomy (DGBI)	0.204	$< 0.0001$
Type of gastrectomy (DGRY)	0.116	$< 0.0001$
Postoperative period (mo)	(-0.02)	NS
Age (yr)	(-0.04)	0.0746
Gender (male)	0.120	$< 0.0001$
Preoperative BMI ( $\text{kg}/\text{m}^2$ )	-0.356 <sup>1</sup>	$< 0.0001$
Approach (Laparoscopic)	(0.01)	NS
Celiac branch of vagus (Preserved)	(0.074)	0.0010
$R^2$ ( <i>P</i> value)	0.216	$< 0.0001$
The interpretation of effect size	$\beta$	$R^2$
None-very small	$< (0.100)$	$< (0.020)$
Small	$> 0.100$	$> 0.020$
Medium	$> 0.300^1$	$> 0.130^1$
Large	$> 0.500$	$> 0.260$

<sup>1</sup>Integrated subscales. Higher score indicative of a better condition. If  $\beta$  is positive, the score of the outcome measure of the patients belonging to the category in (brackets) is higher in cases when the factor is a nominal scale, and the score of outcome measure of the patients with larger values is higher in cases when the factor is a numeral scale. DGBI: Distal gastrectomy with Billroth-I; DGRY: Distal gastrectomy with Roux-en-Y.

loss, followed by the type of gastrectomy performed (TGRY) and female sex, in order of significance. Moreover, the patients with higher BMI ( $> 25 \text{ kg}/\text{m}^2$ ) preoperatively exhibited the largest postoperative weight loss among three relevant preoperative BMI groups. The patients with low postoperative BMI experienced worse QOL than those with greater body weight loss, though the aggregated impact of low BMI and excess body weight loss on the QOL postoperatively was relatively smaller than generally considered.

Loss of body weight after gastrectomy is thought to be caused by multiple factors, including decreased serum ghrelin<sup>[15]</sup>, reduced food intake due to various abdominal symptoms, and disorder of digestive and absorptive function due to pancreatic exocrine insufficiency or postcibal pancreaticobiliary asynchrony. The degree of weight loss was also affected by the type of gastrectomy employed<sup>[15-19]</sup>. Additionally, body weight loss is also related to tumor progression or chemotherapy after surgery. In this study, we focused on Stage I patients in order to exclude the influence of other factors that may influence the postoperative body weight, and to isolate the effect of the surgical procedures. The findings of present study that patients undergoing TGRY had a greater body weight loss compared to those undergoing DGBI or DGRY were compatible with the previous reports<sup>[19,20]</sup>. However, the influence of the other surgical procedures such as laparoscopic approach or preservation of celiac branch of vagus, which maintains the postprandial motility of the duodenum and jejunum<sup>[21]</sup> and attenuates a dumping syndrome<sup>[22]</sup>, were insignificant as for effect size,  $\beta$ .

Recent analyzes of specific disease processes,

**Table 5 Impact of postoperative lower body mass index and body weight loss on the quality of life (multiple regression analysis)**

Variables	Ability for working		Dissatisfaction with symptoms		Dissatisfaction at the meals		Dissatisfaction at working		Dissatisfaction for daily life subscale		PCS		MCS	
	$\beta$	P value	$\beta$	P value	$\beta$	P value	$\beta$	P value	$\beta$	P value	$\beta$	P value	$\beta$	P value
Postoperative BMI (kg/m <sup>2</sup> )	-0.134	< 0.0001	-0.189	< 0.0001	0.216	< 0.0001	-0.185	< 0.0001	-0.231	< 0.0001	0.148	< 0.0001	0.109	< 0.0001
Change in body weight (%)	(-0.081)	0.0018	(-0.073)	0.0040	-0.112	< 0.001	(-0.097)	< 0.0001	-0.109	< 0.0001	(0.047)	0.066	(0.025)	NS
R <sup>2</sup> (P value)	0.031	< 0.0001	0.048	< 0.0001	0.073	< 0.001	0.054	< 0.0001	0.080	< 0.0001	0.028	< 0.0001	(0.014)	< 0.0001

BMI: Body mass index; QOL: Quality of life; PCS: Physical component summary; MCS: Mental component summary.

**Table 6 Regression analysis of effect size**

The interpretation of effect size	$\beta$	R <sup>2</sup>
None-very small	< (0.100)	< (0.020)
Small	> 0.100	> 0.020
Medium	> 0.300	> 0.130
Large	> 0.500	> 0.260

including sarcopenia and metabolic diseases, have identified the importance of evaluating not only BMI but also body component composition, such as body fat and skeletal muscle<sup>[23-26]</sup>. Siervo *et al*<sup>[27]</sup> also reported that body composition varies with BMI, age and sex. Although a significant reduction in body fat has been reported after gastrectomy, several studies indicated that the reduction in skeletal muscle mass was smaller than reductions in the volume of body fat<sup>[28-31]</sup>. These previous findings may, in part, explain the smaller body weight loss in patients with low BMI (< 18.5), in which, the proportion of the skeletal muscle supposed to be larger than those of the other relevant preoperative BMI groups.

Body weight loss is considered to be one of the objective index which resulting in worse QOL after gastrectomy<sup>[5,8,32,33]</sup>, and also loss of body weight is associated with intolerance to adjuvant chemotherapy<sup>[34]</sup>. However, in clinical setting, excess body weight loss is not always accompanied with worse QOL, therefore, precise features of the impact of body weight loss on the postoperative QOL should be investigated. For this purpose, we studied the impact of body weight loss as well as postoperative BMI on the postgastrectomy QOL using the PGSAS-45 questionnaire, which is the first questionnaire developed to specifically measure QOL in gastrectomized patients<sup>[11,35-38]</sup>, by multiple regression analysis. The results of our study demonstrated that the preoperative BMI rather than the degree of body weight loss was the most influential predictor of worse QOL after gastrectomy. The low postoperative BMI significantly affected on all QOL outcome measures, though the body weight loss only affected few QOL outcome measures with smaller effect size in terms of  $\beta$ . The aggregated impact of low BMI and body weight loss was unexpectedly small for each QOL outcome measures in terms of R<sup>2</sup>. There may be other factors influencing worse QOL postgastrectomy, and future work should focus on investigation of other possible

factors.

Despite above mentioned results, both to maintain postoperative body weight and to avoid low BMI seem yet important for better QOL after gastrectomy, therefore, enhanced perioperative nutritional management should be required particularly in patients with low preoperative BMI.

Several limitations of our study should be acknowledged. This study was not a prospective study and the investigation was performed at a single point in time postoperatively. We focused on long-term QOL, more than 1 year after gastrectomy based on previous findings that most QOL measures are stable at > 1 year postoperatively<sup>[39]</sup>. However, such QOL measurements at a single point in time may be insufficient to reflect the true impact of body weight loss. Further prospective and chronological studies assessing QOL over short- and longer-term periods after gastrectomy are required.

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## COMMENTS

### Background

Body weight loss, a common complaint after gastrectomy, is likely associated with various factors such as tumor progression and chemotherapy. While several reports indicated that the type of gastrectomy may be a determinant of postoperative weight loss, other risk factors have yet to be determined. In the present study, they focused only on patients with Stage I gastric cancer, so as to evaluate the impact of the surgical procedure without the confounding effect of other factors.

### Research frontiers

Previous reports indicated that the type of gastrectomy is a certain postoperative weight loss, suggesting that total gastrectomy resulted in greater weight loss. Additionally, patients with excess weight loss after gastrectomy were shown to have lower performance status and difficulty in continuing chemotherapy. However, few reports have analyzed the relationship between postgastrectomy body weight loss and quality of life (QOL).

### Innovations and breakthroughs

The authors aimed to determine the predictive factors and clarify the quality-of-life impact of postgastrectomy body weight loss and low body mass index. For this purpose, the authors used the postgastrectomy syndrome assessment scale-45, which was established specifically to evaluate QOL following

gastrectomy. Interestingly, the authors found that postoperative body mass index, rather than the degree of weight loss, was a predictor of worse QOL after gastrectomy, but the effect was relatively mild.

### Applications

To minimize the negative effects on QOL after gastrectomy, it is better to maintain the postoperative body weight and avoid low body mass index. Postgastrectomy syndrome is a group of disorders and complications following gastrectomy. It includes early/late dumping syndrome, reflux gastritis, diarrhea, anemia, malabsorption, reflux gastritis, and weight loss.

### Peer-review

The authors have conducted a well-written observational study. The case enrollment and variable choices were appropriate. Despite this study has the limit that QOL measures are conducted only at a single point after surgery, it has some new insights.

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