

ORIGINAL**Assessment of Perioperative Symptoms of Patients with Gastric Cancer Using The Edmonton Symptom Assessment System Revised Japanese version (ESAS-r-J)**

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Abstract: *Purpose* To evaluate the perioperative symptoms of gastric cancer patients undergoing gastrectomy using the Edmonton Symptom Assessment System Revised Japanese version (ESAS-r-J), which is a nine-item visual analogue scale to rate patient symptoms. *Methods* Between February 2015 and March 2017, 246 patients completed the ESAS-r-J before and after gastrectomy. We evaluated the changes in the prevalence and score of each ESAS-r-J item before and after gastrectomy. In addition, we compared them after gastrectomy between patients who underwent the different approaches. *Results* Before gastrectomy, anxiety and well-being were the most prevalent items (80%), followed by depression (45%). After gastrectomy, well-being was the most prevalent item (87%), followed by pain (68%). The prevalence of anxiety decreased from 80% to 59% ($P = 0.002$). The depression and anxiety scores decreased from 1.6 to 1.1 ($P < 0.001$) and from 2.6 to 1.7 ($P = 0.002$), respectively. The total score was higher in patients who underwent open surgery than in patients who underwent laparoscopic surgery (16.9 vs 12.9; $P = 0.031$). *Conclusions* After gastrectomy, psychological symptoms such as depression and anxiety improved despite more physical complaints than before gastrectomy. The laparoscopy was less invasive. It is very important to take care of psychological aspects before gastrectomy. *J. Med. Invest.* 68: 90-95, February, 2021

Keywords: ESAS, Gastrectomy, Gastric cancer, Quality of life, Questionnaire

INTRODUCTION

Although the long-term survival of patients with gastric cancer has improved because of early diagnosis and advances in multimodality management, patients sometimes suffer from various symptoms, including early satiety, loss of appetite, heartburn, dysphagia, nausea, and vomiting. When evaluating treatment for cancer, health-related quality of life (QOL) has been acknowledged to be an important endpoint in addition to oncologic outcomes and safety issues (1, 2).

Korenaga *et al.* (3) developed their own sets of questions to evaluate the QOL of postgastrectomy patients. Recently, generic QOL instruments designed in the form of questionnaires have been developed. These include the Functional Assessment of Cancer Therapy-General (FACT-G) by the Functional Assessment of Chronic Illness Therapy QoL group, the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) by the EORTC QoL group (4), and the site-specific module for gastric cancer (EORTC QLQ-STO22) (5); the validity of these questionnaires have been reported (6).

The Edmonton Symptom Assessment System Revised Japanese version (ESAS-r-J) is a self-report symptom measurement tool that includes six items related to physical symptoms and three related to psychologic symptoms such as depression, anxiety, and well-being (7). A series of validation studies complemented the rapid clinical implementation of the ESAS, providing further evidence for its psychometric properties and clinical utility (8).

There are few studies examining the QOL of patients with gastric cancer in the perioperative period using the ESAS-r-J.

To our knowledge, this is the first study evaluating the perioperative symptoms of patients with gastric cancer underwent gastrectomy using ESAS-r-J.

PATIENTS & METHODS

Between February 2015 and March 2017, a total of 246 patients with gastric cancer underwent total gastrectomy (TG), proximal gastrectomy (PG) or distal gastrectomy (DG) and completed the ESAS-r-J before and after (before discharge) gastrectomy.

Usually, we explained the clinical stages and the type of operation to the patients in the outpatient department and the preoperative assessment using the ESAS-r-J was performed the day before gastrectomy. The postoperative assessment using the ESAS-r-J was performed the day before discharge, at which time the pathological stage had been already informed to the patients.

This study was approved by the Ethics Review Board of Ogaki Municipal Hospital. The subject provided informed consent, and patient anonymity was preserved. We retrospectively reviewed the medical records and evaluated the following: (1) patient characteristics; (2) surgical outcomes and histological findings; (3) changes in the prevalence and score of each ESAS-r-J item before and after gastrectomy (The prevalence was considered to be present if the score for the symptom was rated as > 0); and (4) differences in the prevalence and score of each ESAS-r-J item after gastrectomy between patients who underwent TG or PG procedures and those who underwent DG, patients who underwent a laparoscopic approach and those who underwent an open approach, and patients with morbidity and those without morbidity.

Postoperative morbidities were evaluated according to the

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Clavien–Dindo classification (9), and grade II or higher was considered significant.

MEASURES

The ESAS (10) is a self-report symptom assessment measure consisting of nine common symptom-related items for advanced cancer: pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, and shortness of breath, with the option of adding a tenth patient-specific symptom. Patients rated the intensity of each of these symptoms. Each symptom rating is interpreted independently, although it is also possible to calculate a total symptom distress score. The ESAS-r (11) is a modified version of the ESAS. The time frame for the symptom ratings is specified as ‘now’. Patients rated the intensity of each symptom at a point in time (current) using an 11-point numerical rating scale, ranging from 0 (symptom absent or best) to 10 (worst possible) (Fig. 1). The ESAS-r-J was translated into Japanese by Yokomichi *et al.* (7).

INTERVENTIONS

Patients were treated according to our institutional practices for patients with gastric cancer (12, 13). Briefly, patients underwent staging investigations, including computed tomography, endoscopic ultrasonography, and/or laparoscopy. The surgical procedures were classified as follows: distal gastrectomy (DG) if the procedure included the distal stomach and pylorus but not the esophagogastric junction; proximal gastrectomy (PG) if the procedure included the proximal stomach and esophagogastric junction but not the distal stomach; and total gastrectomy (TG) if the entire stomach was resected. Patients who underwent wedge resections were not included in this study. Reconstruction was performed with Billroth I or Billroth II after DG, jejunal interposition after PG (12), and Roux-en-Y after TG. An open

approach was performed for patients over 81 years old, with organ dysfunction (i.e., cardiovascular or respiratory dysfunction or coagulation), who had previous upper abdominal surgery, or who had low-performance status. Preoperatively, if the patients preferred different type of the procedure and the approach, we had a thorough discussion with the patients and ultimately respected the patient’s hopes.

STATISTICAL ANALYSIS

All statistical analyses were performed with EZR, which is a graphical user interface for R (The R Foundation for Statistical Computing, version 2.13.0) (14). The McNemar test was used to compare the prevalence of the nine items, and a paired t-test was used to compare the nine items and total scores before and after gastrectomy. In comparison with the prevalence and scores of each category after gastrectomy, Fisher’s exact test was used to compare categorical variables, and the Mann–Whitney U-test was used to compare continuous variables. A value of $p < 0.05$ was considered statistically significant.

RESULTS

In this study, 246 patients were enrolled. Among these patients, eight patients (3.3%) required blood transfusions due to anemia and two patients (0.8%) required total parenteral nutrition due to gastrointestinal obstruction as preoperative management. There were no patients required analgesics for cancer pain.

The clinical characteristics and surgical outcomes and histological findings of the patients are summarized in Tables 1 and 2, respectively. Laparoscopic surgery was performed for 133 patients (54%). The most frequent procedure was DG (57%), followed by TG (39%), and PG (3.7%). The mean operation time was 165 min (range, 60–326), and the mean estimated blood loss was

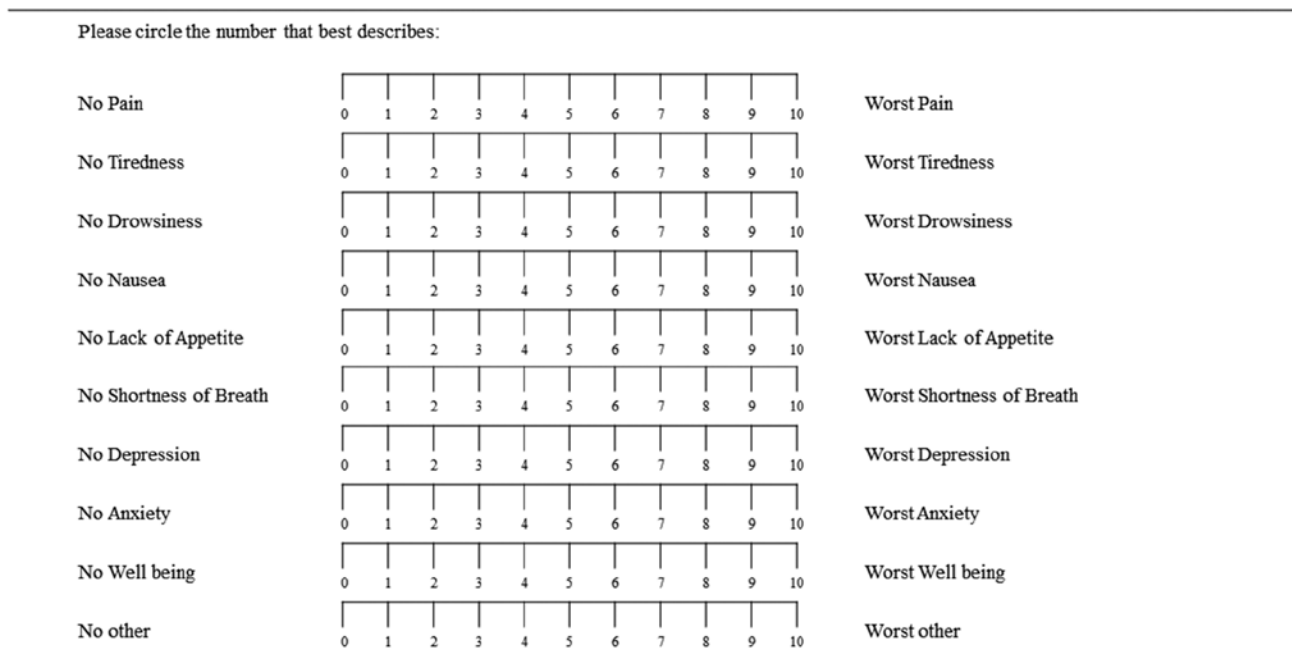


Fig 1. ESAS-r (Edmonton Symptom Assessment System-revised).

133 mL (range, 1–1250). The overall incidence of postoperative complications (CD \geq grade II) was 14%. There was no postoperative mortality. The detail of postoperative complications are demonstrated in Table 3. Among Leakage (n = 7), anastomotic leakage at the esophagojejunostomy site occurred in 3 patients, duodenal stump leakage in 2 patients, jejunum stump leakage in 1 patient, and 1 patient developed pancreatic fistula followed by secondary anastomotic leakage at the gastroduodenostomy site. Reoperation was required in 1 patient. The causes of reoperation was anastomotic stenosis at the gastrojejunostomy site. 25 patients (10%) were required a temporary fast to cure the complication.

The prevalence of each ESAS-r-J item before and after gastrectomy is shown in Table 4. Before gastrectomy, anxiety and well-being were the most prevalent items (80%), followed by

depression (45%). After gastrectomy, well-being was the most prevalent item (87%), followed by pain (68%). The prevalence of anxiety decreased from 80% before gastrectomy to 59% after gastrectomy (P = 0.002). Depression showed a tendency to decrease after gastrectomy without statistically significant differences. Other than these items, the other items increased significantly after gastrectomy. Fig. 2 shows the changes in the ESAS-r-J item scores before and after gastrectomy. The anxiety and depression scores decreased from 2.6 to 1.7 (P = 0.002) and from 1.6 to 1.1 (P < 0.001), respectively. Except for well-being, the scores of the other items and total scores increased significantly after gastrectomy. Particularly, large fluctuations were observed in pain and lack of appetite. Table 5 shows a comparison of the prevalence and score of each ESAS-r-J item after gastrectomy. The depression score was higher in patients who underwent TG or PG than in patients who underwent DG (1.5 vs 0.9; P = 0.046). The total score was higher in patients who underwent the open surgery than those who underwent laparoscopic surgery (16.9 vs 12.9; P = 0.031). The patients with morbidity had more shortness of breath than those without morbidity (47% vs 30%; P = 0.049). There were no significant differences in the prevalence and score of each ESAS-r-J item between groups of patients of different sexes and tumor stages (data not shown).

Table 1. Clinical Characteristics

Number of patients	246
Age (years), mean (range)	68.9 (34-81)
Male	175 (71%)
BMI (kg/m ²), mean (range)	23.4 (14.1-38.3)
Comorbidities	133 (54%)
Hypertension	76 (31%)
Diabetes mellitus	36 (15%)
Ischemic heart disease	15 (6.1%)
COPD	10 (4.0%)
Cerebral vascular disease	20 (8.1%)
Anti-coagulant therapy	14 (5.7%)

BMI, body mass index; COPD, chronic obstructive pulmonary disease.

Table 2. Surgical Outcomes and Histological Findings (UICC)

Laparoscopic approach	133 (54%)
Procedure	
Total	97 (39%)
Proximal	9 (3.7%)
Distal	140 (57%)
Operation time (min), mean (range)	165 (60-326)
Blood loss (mL), mean (range)	133 (1-1250)
Morbidity (\geq Grade II)	34 (14%)
Mortality	0
Postoperative hospital stay (days)	
mean (range)	16.4 (9-99)
Stage*	
I (IA/IB)	146 (126/20)
II (IIA/IIB)	38 (26/12)
III (IIIA/IIIB/IIIC)	52 (16/19/17)
IV	10

*Data are shown as number of patients.
Grade is according to the Clavien–Dindo classification.
UICC, UICC TNM classification, 7th edition.

Table 3. Postoperative Complications

Any complication (\geq Grade II)	34 (14%)
Pancreatic fistula	11 (4.5%)
Leakage	7 (2.8%)
Pneumoniae	6 (2.4%)
Anastomotic stenosis	4 (1.6%)
Bowel obstruction	3 (1.2%)
Anastomotic bleeding	2 (0.8%)
Abdominal abscess	2 (0.8%)
Abdominal bleeding	1 (0.4%)
Requiring reoperation	1 (0.4%)

Grade is according to the Clavien–Dindo classification

Table 4. Prevalence of the Symptoms

ESAS-r items	Prevalence (%)		P
	Before Gastrectomy	After Gastrectomy	
Pain	24	68	< 0.001
Tiredness	26	49	< 0.001
Drowsiness	35	53	< 0.001
Nausea	8.5	24	< 0.001
Lack of Appetite	21	57	< 0.001
Shortness of Breath	16	32	< 0.001
Depression	45	42	0.50
Anxiety	80	59	0.002
Well-being	80	87	0.041

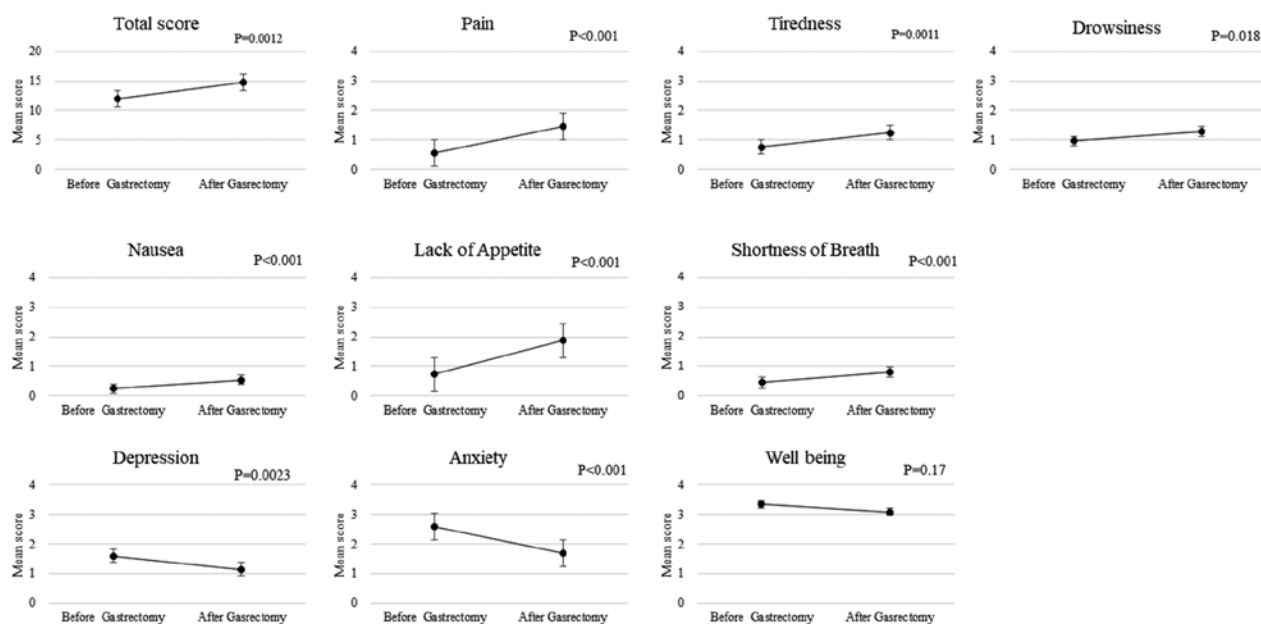


Fig 2. The mean scores of all patients who underwent gastrectomy for gastric cancer were calculated before and after gastrectomy. The mean scores are presented with s.e. (bars).

DISCUSSION

Cancer patients may have poor QOL due to the disease itself before surgery. After surgery, the patients may still suffer from poor QOL due to oncologic problems and the consequences of surgery. In the current study, the perioperative symptoms of gastrectomy were evaluated using the ESAS-r-J. After gastrectomy, psychological symptoms, such as depression and anxiety, improved despite more physical complaints than before gastrectomy. The recognition of this result is an important metric for the delivery of optimal quality of care.

In fact, health-related QOL should include physical, social and psychological aspects. Several studies have investigated the post-surgical QOL of patients with gastric cancer. Among these studies, the EORTC QLQ-C30 and QLQ-STO22 questionnaires have been well validated. The EORTC QLQ-C30 is a cancer-specific 30-question instrument. The EORTC QLQ-STO22 takes into consideration 22 additional items relating to gastric cancer. The average time required to complete the EORTC QLQ-C30 was approximately 11 minutes (4). The ESAS-r was first described in a group of palliative care patients in a hospice setting (10). Because of its brevity and ease of administration, the ESAS-r has received much interest as a bedside clinical instrument. In a review of QOL tools for patients with cancer, the proposed criteria for an ideal instrument included the following characteristics: simple to read and follow, quick and easy to complete and analyze, and based on a categorical or visual analogue scale. The average time required to complete the ESAS-r was considered to be shorter than that to complete the EORTC QLQ-C30 and the EORTC QLQ-STO22 because there are only nine items. Chang VT *et al.* (15) validated the ESAS-r in 240 patients with cancer and reported that the ESAS-r may be a valid instrument to use in a medical oncology population and that the ESAS-r distress score may predominantly reflect physical well-being.

In this study, the prevalence and scores of the psychological symptoms, such as depression and anxiety, in contrast those of the other items, were highest before surgery and steadily improved after surgery. Since the preoperative ESAS-r-J was taken after being diagnosed with gastric cancer, the psycholog-

ical symptoms from being diagnosed with cancer could have affected the preoperative prevalence and score, and the relief from the disease burden after surgery perhaps improved the symptoms after surgery. These results are consistent with those from the study (n = 36) by Schmidt-Matthiesen A *et al.* who used the Eypasch (self-assessment) (16) and those from the study (n = 272) by Kong H *et al.* who used the EORTC QLQ-C30 (17).

The prevalence and scores of the other items such as pain, tiredness, drowsiness, nausea, lack of appetite, and shortness of breath increased significantly after surgery. Particularly large fluctuations were observed for pain and lack of appetite. Kobayashi *et al.* (18) and Kong H *et al.* (17) reported that pain did not show any statistically significant patterns in their study. This may be because the questionnaire was taken at 1 month and 3 months after surgery, respectively. We expected the prevalence and score of pain to rapidly recover afterwards. The lack of appetite can be explained as one of the detrimental adverse effects of gastrectomy. The other items, other than pain and lack of appetite, are physical symptoms, and the cause of these patterns can be explained as one of the detrimental adverse effects of surgery. Kong H *et al.* (17) reported that many of these symptoms were worse at 3 months after surgery and improved or did not fully recover 1 year postoperative. Therefore, further follow-ups are necessary to confirm if these symptoms will recover.

Moreover, to compare the outcomes of different surgical procedures (DG vs TG or PG), approaches (laparoscopic vs open), and morbidity status (with vs without), we analyzed subgroup of patients in terms of QOL. Although the extent to which the different types of resection or approach affected QOL remains poorly defined, it has been well documented that DG is superior to TG (3, 19, 20) and that laparoscopic surgery shows an advantage over open surgery for a few weeks after surgery (21). In this study, there were no differences between the different surgical procedure (DG vs TG, PG) groups, except for the depression score. A limitation of this study is that the time interval from the date of surgery to the first time the questionnaire was completed was too short. Therefore, further follow-ups are necessary to confirm if there were differences. The total symptom score was lower in the laparoscopy group than in the open group. This result

Table 5. Prevalence and mean scores of the symptoms after gastrectomy
 DG, Distal gastrectomy ; TG, Total gastrectomy ; PG, Proximal gastrectomy

(A) DG vs TG or PG

(B) Laparoscopic approach vs open approach

(C) with morbidity vs without morbidity

A

ESAS-r Item	Prevalence (%)			ESAS-r Score (Mean [SD])		
	Procedure		P	Procedure		P
	DG (n = 140)	TG, PG (n = 106)		DG (n = 140)	TG, PG (n = 106)	
Pain	73	61	0.072	1.5 (1.5)	1.4 (1.7)	0.18
Tiredness	50	48	0.80	1.2 (1.6)	1.3 (1.9)	0.98
Drowsiness	50	57	0.37	1.2 (1.6)	1.4 (1.7)	0.27
Nausea	23	26	0.55	0.5 (1.0)	0.6 (1.3)	0.46
Lack of Appetite	56	59	0.80	1.7 (2.0)	2.1 (2.5)	0.42
Shortness of Breath	31	33	0.89	0.8 (1.5)	0.8 (1.4)	0.84
Depression	39	47	0.19	0.9 (1.5)	1.5 (2.1)	0.046
Anxiety	58	60	0.70	1.5 (1.8)	2.0 (2.3)	0.18
Well-being	85	89	0.45	2.9 (1.9)	3.3 (2.1)	0.19
Total	-	-	-	13.7 (10.2)	16.0 (14.0)	0.39

B

ESAS-r Item	Prevalence (%)			ESAS-r Score (Mean [SD])		
	Approach		P	Approach		P
	Laparo (n = 133)	Open (n = 113)		Laparo (n = 133)	Open (n = 113)	
Pain	68	67	0.89	1.3 (1.3)	1.6 (1.8)	0.37
Tiredness	50	49	0.90	1.1 (1.5)	1.4 (1.9)	0.65
Drowsiness	52	54	0.80	1.1 (1.4)	1.5 (2.0)	0.24
Nausea	20	29	0.14	0.4 (0.8)	0.8 (1.4)	0.051
Lack of Appetite	57	58	1.00	1.8 (2.0)	2.0 (2.5)	0.74
Shortness of Breath	29	35	0.34	0.6 (1.2)	1.0 (1.7)	0.18
Depression	38	47	0.20	0.9 (1.4)	1.4 (2.1)	0.07
Anxiety	57	61	0.60	1.5 (1.8)	1.9 (2.3)	0.17
Well-being	86	88	0.71	2.9 (1.9)	3.3 (2.2)	0.15
Total	-	-	-	12.9 (9.6)	16.9 (14.1)	0.031

C

ESAS-r Item	Prevalence (%)			ESAS-r Score (Mean [SD])		
	Morbidity		P	Morbidity		P
	Yes (n = 34)	No (n = 212)		Yes (n = 34)	No (n = 212)	
Pain	56	70	0.11	1.3 (1.9)	1.5 (1.5)	0.16
Tiredness	47	50	0.85	1.6 (2.2)	1.2 (1.6)	0.73
Drowsiness	50	53	0.85	1.3 (1.7)	1.3 (1.7)	0.99
Nausea	32	23	0.28	0.6 (1.1)	0.5 (1.2)	0.32
Lack of Appetite	62	57	0.71	2.6 (2.9)	1.8 (2.1)	0.23
Shortness of Breath	47	30	0.049	1.1 (1.7)	0.76 (1.4)	0.10
Depression	41	43	1.00	1.4 (2.4)	1.1 (1.7)	0.87
Anxiety	53	60	0.46	2.0 (2.7)	1.6 (1.9)	0.92
Well-being	94	85	0.18	3.7 (2.4)	3.0 (2.0)	0.12
Total	-	-	-	17.4 (15.6)	14.3 (11.3)	0.45

suggested that the laparoscopy was less invasive, which is in line with the findings of a previous study (21, 22). The prevalence of shortness of breath was higher in patients with morbidity than in those without morbidity. This may have resulted because some patients with complications may not have been completely cured before being discharged. The details are unknown.

The most important result in this study is that many patients with gastric cancer have the psychological symptoms, such as depression and anxiety before gastrectomy. Nowadays, the Palliative Care Certified Nurse is present in the informed consent before gastrectomy and takes care of psychological aspects.

The current study has several limitations. First, there were not enough cases for each type of surgery. We did not separate each case by the type of surgery to review the overall picture. Another limitation is that marked differences in background (e.g., sex, age, incidence of combined resection) were observed between patients who underwent different procedures and approaches. Therefore, further studies comparing the type of surgery will be necessary.

In conclusions, after gastrectomy, psychological symptoms, such as depression and anxiety, improved despite more physical complaints than before gastrectomy. However, it is very important to take care of psychological aspects before gastrectomy. Also, further follow-ups would be helpful in determining which scales are permanently affected and which are need time to recover.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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