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Comparison of the Dietary Intake After Gastrectomy Between Male and Female Patients With Gastric Cancer

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Abstract. *Background/Aim: This study aimed to investigate the differences in the postoperative dietary intake (DI) loss between men and women after radical resection for early gastric cancer (GC), and to identify effective nutritional support for both sexes. Patients and Methods: This prospective, observational study enrolled patients who underwent gastrectomy for GC. DI was assessed using the food frequency questionnaire containing 82 food items (FFQW82) during nutritional counseling before surgery and one and three months postoperatively. Results: The median preoperative DI of all participants was 1,856.3 kcal/day, and DI at 1 and 3 months were 1,532.5 kcal/day and 1,637 kcal/day, respectively. The median preoperative DI was 1805 kcal/day (1,300-2,330 kcal/day) and 1481 kcal/day (1,126-1,957 kcal/day) in men and women, respectively (p<0.0001). The median DI at 1 month was 1627 (1,101-2,195) kcal/day and 1,308 (986-1,915) kcal/day in men and women, respectively (p<0.0001). At 3 months postoperatively, the median DI was 1737 (1,130-2,443) kcal/day in men and 1428 (816-2,005) kcal/day in women (p<0.0001). However, there was no significant difference in the DI loss rate at 1 month (median: –9.7% vs. –9.3%, p=0.765) and 3 months (median: –3.5% vs. –4.8%, p=0.137) between men and women. Conclusion: Although the DI loss rate in men and women after gastrectomy for GC was almost similar, the postoperative DI and DI loss differed significantly. Therefore, differences in DI loss after gastrectomy between men and women should be considered while assessing the efficacy of additional nutritional support such as oral nutritional supplements after gastrectomy.*

Gastric cancer (GC) ranked fifth in incidence, with over 1 million new cases, and fourth in mortality, with 769,000 deaths worldwide in 2020 (1, 2). Although the incidence rate of GC is decreasing, GC is still one of the most prevalent cancers worldwide. The only curative treatment for patients with GC who are not eligible for endoscopic resection is surgical resection (3-5).

Postoperative body composition change is one of the common complications of gastrectomy in clinical practice (6, 7), which has also been associated with adjuvant chemotherapy and long-term prognosis (8-11). Therefore, it is important to identify methods to prevent postoperative body composition change after gastrectomy for GC.

In recent years, clinical trials to evaluate the efficacy of oral nutritional supplements (ONSs) after gastrectomy for GC have been conducted (12-14). However, the efficacy of ONSs in reducing body weight loss after gastrectomy was found to be limited. One possible reason for this is that the clinical benefit may be offset by providing the same caloric supplementation to all patients, regardless of the sex. It is well known that there are differences in the body composition and energy metabolism between men and women. Men tend to have more muscle mass and more

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visceral fat, while women tend to have more subcutaneous fat (15, 16). However, sex differences in the dietary intake (DI) changes after gastrectomy have not been fully investigated. If the differences in the changes in the DI between the two sexes are accurately identified and understood, patients with GC can receive more optimal and aggressive nutritional support and management.

The aim of the present study was to clarify the differences in the postoperative DI changes between men and women after radical resection for early GC, as well as to determine the most effective method of nutritional support for each sex.

Patients and Methods

Patients. This prospective observational study was conducted from May 2011 to November 2014 at the Kanagawa Cancer Center. The eligibility criteria were as follows: 1) underwent radical resection for GC with distal or total gastrectomy; 2) underwent curative (R0) resection; 3) histologically proven gastric adenocarcinoma diagnosed as pathological stage IA or IB according to the Japanese Classification of Gastric Carcinoma; and 4) received nutritional counselling before surgery and one and three months postoperatively. The patients were divided into two groups of male and female patients.

Perioperative care. Perioperative management was standardized by using the enhanced recovery after surgery (ERAS) protocol in both types of gastrectomy. In brief, patients were able to eat a normal diet until dinner on the day before surgery and take a rehydration solution until three hours before surgery. Premedication was not administered. The nasogastric tube was removed at the end of the surgery. Oral intake of water and ONSs was initiated on postoperative day (POD) 1. Soft dietary intake was started on POD2 and progressed to eating regular food every two days (3 steps). Discharge criteria were adequate pain relief, soft food intake, return to preoperative mobility level, and normal laboratory data on POD7 (17, 18).

Study schedule. Perioperative nutritional counselling was conducted before surgery, on the day of discharge, and one and three months postoperatively. During counselling at hospitalization, nutritionists measured the patients' preoperative body weight (BW) and analyzed their preoperative DI. During counselling at discharge, nutritionists provided nutritional education on how to eat meals after gastrectomy, including increasing the intake frequency, decreasing the portion size of each meal, chewing frequently, and eating slowly. During counseling at one and three months postoperatively, nutritionists measured the patients' BW after surgery, analyzed the postoperative DI, and provided education aimed at improving their nutritional status based on the results.

Analysis of the DI. The DI was assessed at each nutritional counselling using the food frequency questionnaire with eighty-two food items (FFQW82) established by Watanabe *et al*. (19). The FFQW82 is a self-administered questionnaire that evaluates the intake frequency and portion size of foods over a period of 1 month from a list of 82 foods according to 16 food groups with pictures. The questionnaire can be answered in approximately 30 min. The frequency of intake was classified into six levels: (0='absolutely do not eat' to 5='eat every day'). The standard intake was defined as 'medium'. Accordingly, 'small' was defined as a half portion of 'medium' and 'large' as a portion 1.5 times the amount of 'medium'. The estimated intake of energy over one whole day was calculated by summing up the estimated amount of intake for each meal. The Microsoft® Excel software program (Microsoft Inc., Redmond, WA, USA) was used to obtain the nutrient composition of the items on the FFQW82.

Statistical analyses. The decrease in DI was determined as the DI loss rate (%)=(1 month and three months postoperative DI-preoperative DI)×100/preoperative DI. Categorical values are expressed as numbers and percentages, while continuous values are expressed as medians and ranges. Student's *t*-test and the chi-square test were used to compare the continuous and categorical variables between the two groups, respectively. All statistical analyses were performed using the JMP PRO software program, version 16.0 (SAS Institute Inc., Cary, NC, USA), and *p*-values of <0.05 were considered statistically significant.

Ethics. This study was approved by the Institutional Review Board of Kanagawa Cancer Center (2023-eki-29).

Results

Background patient characteristics. The patient characteristics and comparison of the characteristics between male and female patients are presented in Table I. Surgical and pathological outcomes are listed in Table II. A total of 154 patients were enrolled in this study. The median age was 65.5 (27-86) years. Of these, 97 (63.0%) were men, and 57 (37.0%) were women. The male patients had a significantly higher height, BW, and body mass index (BMI). The male patients also had a significantly higher rate of total gastrectomy (28.9% *vs*. 14.0%, $p=0.036$) and a significantly longer operative time (median: 277 min *vs*. 261 min, $p=0.013$), compared to the female patients. However, the other characteristics, surgical outcomes, pathological outcomes, and frequency of postoperative complications were not significantly different between the groups.

Comparison of dietary intake changes. Changes in the DI are shown in Table III. The median preoperative DI of the entire study population was 1,856.3 kcal/day (1,379.5-2,330 kcal/day), while the DI at 1 and 3 months were 1,532.5 kcal/day (986-2,195 kcal/day) and 1,637 kcal/day (816-2,443 kcal/day), respectively. The median preoperative DI was 1,805 kcal/day (1,300-2,330 kcal/day) in male patients and 1481 kcal/day (1,126-1,957 kcal/day) in female patients ($p<0.0001$). In the male patients, the median DI at 1 month was 1,627 (1,101-–2,195) kcal/day, whereas it was 1308 (986–1,915) kcal/day ($p<0.0001$) in the female patients. At 3 months postoperatively, the median DI in the male patients was 1,737 (1,130-2,443) kcal/day, while it was 1,428 (816-2,005) kcal/day ($p<0.0001$) in the female patients. The male patients had a significantly higher DI volume preoperatively,

Table I. *A comparison of the patients' background characteristics.*

	All cases	Male Number of patients (%)	Female Number of patients (%)	
	N=154	N=97 (63.0%)	N=57 (37.0%)	*p*-Value
Age, years*	65.5 (27-86)	67 (27-86)	66 (36-81)	0.217
ASA-PS				0.507
1	48 (31.2)	27 (27.8)	21 (36.8)	
2	103 (66.9)	68 (70.1)	35 (61.4)	
3	3 (1.9)	2 (2.1)	1 (1.8)	
Height cm	162.1 (132.8-182.8)	165.2 (151.9-182.8)	153 (132.8-166.5)	<0.001
Total body weight, kg*	59.2 (35.3-88.2)	63.0 (45.7-88.2)	49.4 (35.3-69)	<0.001
Lean body mass, kg*	46.5 (30.2-67)	50.5 (32.7-67)	37.0 (29.8-44.3)	<0.001
Body mass index*	22.3 (15.6-31.8)	22.9 (16.5-31.8)	21.5 (15.6-29.5)	0.002
Tumor site				0.069
EGJ or Upper third	34 (22.1)	27 (27.8)	7 (12.3)	
Middle third	71 (46.1)	40 (41.2)	31 (54.4)	
Lower third	49 (31.8)	30 (30.9)	19 (33.3)	
Clinical T factor				0.382
T1-T2	139 (90.3)	86 (88.7)	53 (93.0)	
T3-T4	15 (9.7)	11 (11.3)	4 (7.0)	
Clinical N factor				0.502
Negative	93 (60.4)	94 (96.9)	54 (94.7)	
Positive	61 (39.6)	3 (3.1)	3 (5.3)	
Co-morbidity				
Hypertension	61 (39.6)	39 (40.2)	22 (38.6)	0.844
Diabetes mellitus	16 (10.4)	13 (13.4)	3 (5.3)	0.110
COPD	10 (6.5)	8 (8.3)	2 (3.5)	0.249

ASA PS: ASA physical status; COPD: chronic obstructive pulmonary disease; EGJ: esophagogastric junction. *Median (range).

at 1 month, and 3 months than the female patients. The median DI loss at 1 month postoperatively was –180 (–751-610) kcal/day in the male patients, and –133 (–878-454) kcal/day in the female patients (p=0.815). The median DI loss at 3 months postoperatively was –67 (–587-858) kcal/day in the male patients, and –75 (–842-544) kcal/day in the female patients (p=0.181). In addition, there was no significant difference in the DI loss rate at 1 month (median: –9.7% *vs*. –9.3%, p=0.765) and 3 months (median: –3.5% *vs*. –4.8%, p=0.137) between the male and female patients.

Comparison of surgical stress. The postoperative surgical stress was assessed by the white blood cell (WBC) count and serum C-reactive protein (CRP) level. Changes in these parameters induced by systemic surgical stress are shown in Table IV. The preoperative median WBC count was 5,700/μl (3,100-10,200) and 5,100/μl (2,800-9,900) in the male and female patients, respectively (p=0.003). The preoperative median CRP levels were 0.06 mg/dl in male patients and 0.07 mg/dl in female patients (p=0.072). The median WBC count on POD1 was 8,500/μl and 7,900/μl in the male and female patients, respectively (p=0.892). The median WBC count on POD7 in male patients was significantly higher (6,000/μl *vs*. 4,800/μl, p=0.0002). However, the median CRP levels in the male and female patients were not significantly different (1.88 mg/dl *vs*. 1.36 mg/dl, p=0.188). Similarly, the median WBC count at 1 month postoperatively in male patients was significantly higher (5,600/μl *vs*. 4,600/μl, p=0.0007) compared to female patients. The median CRP levels at 1 month postoperatively were 0.10 mg/dl in male patients *vs*. 0.07 mg/dl in female patients and were not significantly different (p=0.570).

Discussion

The aim of the present study was to clarify the differences in the postoperative DI change between male and female patients after gastrectomy for GC. Although several studies have explored the risk factors for DI loss after gastrectomy (20-22), this is the first study to investigate the DI changes quantitatively according to the sex. The major finding of this study is that postoperative DI and DI loss were significantly different between men and women. In contrast, the DI loss rates at 1 month and 3 months after gastrectomy were almost similar between the two groups. Therefore, physicians need to consider the differences in the DI change between male and female patients for optimal postoperative nutritional support and management.

Table II. *Surgical and pathological outcomes.*

	All cases (N=154)	Male (N=97)	Female (N=57)	*p*-Value
		Number of patients (%)	Number of patients (%)	
Type of gastrectomy				0.036
Distal gastrectomy	118 (76.6)	69 (71.1)	49 (86.0)	
Total gastrectomy	36 (23.4)	28 (28.9)	8 (14.0)	
Lymph node dissection				0.447
D1+ dissection	125 (81.7)	81 (83.5)	44 (78.6)	
D2 dissection	28 (18.3)	16 (16.5)	12 (21.4)	
Type of reconstruction				0.150
Billroth-I	94 (61.0)	55 (56.7)	39 (68.4)	
Roux-en-Y	60 (39.0)	42 (43.3)	18 (31.6)	
Type of approach				0.636
Conventional	55 (35.7)	36 (37.1)	19 (33.3)	
Laparoscopic	99 (64.3)	61 (62.9)	38 (66.7)	
Bleeding, g (median)	70	80	50	0.058
(range)	0-1165	5-1165	0-950	
Operation time, min (median)	270	277	261	0.013
(range)	85-512	95-512	85-360	
Time to first dietary intake	2	2	2	0.257
(range)	2-49	2-15	2-49	
Postoperative hospital stay	8.5	8	9	0.290
(range)	6-58	6-25	7-58	
Pathological T factor				0.966
T0-T1	138 (89.6)	87 (89.7)	51 (89.5)	
T2	16 (10.4)	10 (10.3)	6 (10.5)	
Pathological N factor				0.057
N0	143 (92.9)	93 (95.9)	50 (87.7)	
N1	11 (7.1)	4 (4.1)	7 (12.3)	
pStage				0.187
1A	127 (82.5)	83 (85.6)	44 (77.2)	
1B	27 (17.5)	14 (14.4)	13 (22.8)	
Complication CD				
≥2	21 (13.6)	16 (16.5)	4 (8.8)	0.178
≥3	3 (1.9)	2 (2.1)	1 (1.8)	0.894

First, regarding the DI in male and female patients, we found that the DI was greater in male patients than in female patients. Previously, a large cohort study by Bennett *et al.* characterized the sex differences in dietary behaviors at baseline between men and women aged 40-69 years from the UK Biobank. This prospective cohort study enrolled 210,106 participants, with a mean age of 56 years and 55% women. Information about dietary behavior was collected using 24-hour recall questionnaires on the amounts and items from over 200 food and beverages, as in the FFQW82. The results showed that men consumed 9,525.1 kJ/day, while women consumed 8,168.0 kJ/day. Men had a significantly higher energy intake than women, with a mean difference in total energy intake of 1,358 kJ per day (about 325 kcal/day) (23). The most likely reason for this result was the difference in the energy metabolism between men and women. It is well known that energy metabolism depends on the body composition (24). In the present study, there were significantly differences in preoperative body composition parameters, such as the BW and height, between male and female patients. Therefore, the baseline DI required to maintain the BW may be different between male and female patients.

Second, we investigated the rate of decrease of DI between male and female patients. Initially, we hypothesized that the rate of decrease in DI was greater in men than in women because previous studies have demonstrated that perioperative surgical stress was greater in male than in female patients. Ono *et al.* reported differences in the postoperative inflammatory response between men and women. A total of 25 patients who underwent gastrectomy for GC were enrolled in the study, comprising 16 men and nine women. They measured and compared the inflammatory cytokines such as TNF-α on the day before surgery and on POD1, and measured serum CRP on POD3 to assess the systemic inflammatory response.

Table III. *Rate of decrease in the dietary intake and body weight.*

	All cases	Male	Female	
	Median, (range)	Median, (range)	Median, (range)	*p*-Value
	N=154	N=97	N=57	
Preoperative term				
Dietary intake, kcal/day	1,856.3 (1,379.5-2,330)	1,805 (1,300-2,330)	1,481 (1,126-1,957)	<0.001
1 month postoperatively				
Dietary intake, kcal/day	1,532.5 (986-2,195)	1,627 (1,101-2,195)	1,308 (986-1,915)	<0.001
Decrease dietary intake kcal/day	–165.5 (–878-610)	–180 (–751–610)	–133 (–878-454)	0.815
Decrease dietary intake rate %	–9.5 (–46.3-38.5)	–9.7 (–39.4-38.5)	–9.3 (–46.3-31.1)	0.765
3 months postoperatively				
Dietary intake, kcal/day	1,637 (816-2,443)	1,737 (1,130-2443)	1428 (816-2,005)	<0.001
Decrease dietary intake kcal/day	–70 (–842-858)	–67 (–587-858)	–75 (–842-544)	0.181
Decrease dietary intake rate %	–3.9 (–50.8-54.1)	–3.5 (–26.0-54.1)	–4.8 (–50.8-37.2)	0.137

Table IV. *Comparison of surgical stress.*

	Male (N=97)	Female (N=57)	*p*-Value
Preoperative WBC (/μl)	5,700 (3,100-10,200)	5,100 (2,800-9,900)	0.003
Preoperative CRP (mg/dl)	0.06 (0.02-3.22)	0.07 (0.01-3.99)	0.072
WBC POD 1 (/μl)	8,500 (2,700-15,900)	7,900 (3,600-15,300)	0.089
WBC POD 7 (/μl)	6,000 (3,100-16,800)	4,800 (3,000-14,800)	0.0002
CRP POD 7 (mg/dl)	1.88 (0.03-18.29)	1.36 (0.2-39.16)	0.188
WBC 1 month postoperatively (/μl)	5,600 (2,900-10,100)	4,600 (2,200-10,600)	0.0007
CRP 1 month postoperatively (mg/dl)	0.10 (0.01-16.43)	0.07 (0.01-3.94)	0.570

WBC: White blood cell; CRP: C-reactive protein; POD: postoperative day.

They found that excessive TNF-α occurred more often in men and CRP levels on POD3 were significantly higher in men than in women (25). However, in the present study, surgical stress one week after surgery and one month after surgery was almost similar between men and women Therefore, although the inflammatory response in the acute phase may differ between men and women, it is almost similar between men and women at one week after surgery, and the rate of DI loss due to surgical stress might also be similar between the two groups.

Our study results have important clinical implications. Several randomized studies have evaluated ONSs for patients with GC who received gastrectomy to prevent body composition changes due to DI loss after surgery (12-14). However, these studies could not show the clinical usefulness of ONS for preventing body composition changes after gastrectomy. One of the possible reasons is that men and women were administered the same dose and calories of ONS, ranging from 300 to 600 calories/day. Thus, the ONS dose may have been less than the requirement for men and more than the requirement for women, and not the optimal dose for both sexes. Therefore, future studies need to consider the optimal dose of ONS and differences in the amount of DI loss between men and women.

Study limitations. First, this study was conducted at a single institution. Second, our patients did not receive perioperative adjuvant treatment. The standard treatment for locally advanced GC is perioperative adjuvant therapy. However, in the perioperative adjuvant treatment period, the patients may experience adverse events, such as nausea and vomiting, due to the adjuvant treatment. These adverse events might affect the DI loss after gastrectomy. Considering these issues, our findings need to be confirmed in future large studies.

Conclusion

Although the DI loss rate between men and women after gastrectomy for GC was not significantly different, the postoperative DI and DI loss differed significantly. Therefore, when conducting clinical trials to evaluate the efficacy of adding nutritional support such as ONS after gastrectomy, the clinical management and study design should be based on the differences in the DI loss between men and women.

Conflicts of Interest

The Authors declare no conflicts of interest in association with the present study.

Authors' Contributions

JM, TA, and AK contributed substantially to the concept and design. JM, TA, MT, KO, SO, IH, KH, KK1 (Keisuke Kazama), KK2 (Keisuke Komori), KK3 (Kyohei Kanematsu), SN, YM, MN, SK, TY, and HC substantially contributed to data acquisition, analysis, and interpretation. TA, MN, SS, AT, TO1 (Takashi Ogata), NY, AS, YR, and TO2 (Takashi Oshima) were involved in drafting and critically revising the manuscript for important intellectual content. TA and AK approved the final version of the manuscript.

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