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Effect of Preoperative Gastric Shape on Loss of Lean Body Mass After Distal Gastrectomy

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Abstract. *Background/Aim: Based on gastric shape, patients with gastric cancer can be divided into storage (hook-shaped and ptotic stomach) and reverse outflow (steer-horn and cascade stomach) groups. In patients with gastric cancer, postoperative loss of lean body mass (LBM) is associated with a poor prognosis. This study investigated the influence of preoperative gastric shape on LBM loss 1 month after curative distal gastrectomy. Patients and Methods: Between May 2011 and May 2019, we enrolled 487 patients with pathological stage IA/IB/IIA gastric cancer who underwent curative distal gastrectomy and did not receive adjuvant chemotherapy. Patients were divided into storage (n=370) and outflow (n=117) groups according to whether barium was stored in the stomach during the preoperative fluoroscopic examination. Clinicopathological features, LBM 1 month after gastrectomy, and predictors of postoperative LBM loss were compared between the groups using multivariable logistic regression. Results: The incidence of >5% LBM loss and >7.5% body weight loss 1 month postoperatively were significantly higher in the storage group than in the outflow group (p=0.003 and p=0.009, respectively). Multivariable analysis revealed that gastric shape [odds ratio (OR)=3.30, 95% confidence interval (CI)=1.95-5.59, p<0.001], male sex (OR=3.20, 95% CI=2.07-4.96, p<0.001), and Roux-en-Y reconstruction (OR=1.69, 95% CI=1.08-2.64, p=0.02) were independent predictors of LBM loss. Postoperative dietary problems, especially dumping syndrome, diarrhea, and reflux were more common in the storage group (p<0.001). Conclusion: Gastric shape may be a useful independent predictor of postoperative LBM loss in patients with gastric cancer undergoing distal gastrectomy.*

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Key Words: Distal gastrectomy, gastric cancer, lean body mass, preoperative gastric shape.

Gastric cancer is the fifth most diagnosed cancer and the third most common cause of cancer-related deaths worldwide (1). However, the outcome of resectable locally advanced gastric cancer has improved owing to the establishment of lymph node dissection and development of postoperative chemotherapy. Specifically, postoperative adjuvant chemotherapy improves the prognosis of patients with locally advanced gastric cancer by approximately 10% (2-8). Furthermore, continued adjuvant chemotherapy is important for improving prognosis (9, 10). In patients undergoing surgery for gastric cancer, postoperative weight loss and loss of lean body mass (LBM) have a strong influence on decisions to discontinue adjuvant chemotherapy, particularly if LBM decreases by ≤5% in the first month after surgery (11-13). Thus, a decrease in LBM after gastric cancer surgery may prevent the continuation of adjuvant chemotherapy and thus contribute to poor survival in patients with locally advanced gastric cancer. However, it is difficult to predict which patients with locally advanced gastric cancer will have decreased LBM preoperatively.

The stomach differs in tonicity and emptying capacity depending on its shape. Gastric wall tonicity and tension affect eating behavior, hormone secretion, and blood sugar regulation (14). The speed of gastric emptying varies by sex, body weight, degree of tension, and gastric shape (15, 16). Thin women tend to have hypotonic J-shaped stomachs that are slower to empty. In contrast, overweight individuals and men tend to have hypertonic steer-horn-shaped stomachs that empty faster.

We hypothesized that postoperative changes in gastric emptying may vary according to the preoperative shape of the stomach. We further hypothesized that changes in the rate of gastric emptying after gastrectomy may cause postoperative disorders, such as dumping syndrome, diarrhea, and vomiting, and that the preoperative gastric shape may play a role in the decrease in LBM after distal gastrectomy.

Therefore, this study aimed to clarify the relationship between the shape of the stomach, as classified by preoperative barium examination, and changes in LBM 1 month after distal gastrectomy.

Patients and Methods

Patients. Patients were retrospectively selected from the medical database of the Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan, according to the following criteria: 1) histologically proven adenocarcinoma, in accordance with the Japanese Classification of Gastric Carcinoma (17); 2) pathological (p) stage I or IIA (pT1pN2 or pT3pN0) disease in accordance with the Union for International Cancer Control TNM 8th edition (18); 3) patients who underwent curative resection (R0 resection) between May 2011 and May 2019 and who had not received adjuvant chemotherapy; and 4) body composition analysis performed within 1 week before surgery and 1 month after surgery. However, patients who had postoperative complications of grade 3a or higher or that required ≥8 days without oral intake of food or drinks, or those who had undergone subtotal gastrectomy were excluded from the study. This study was approved by the Institutional Review Board of Kanagawa Cancer Center (2022-epidemiology-79). Informed consent was obtained in the form of opt-out on the website.

Definition of preoperative gastric shape. Patients with gastric cancer scheduled for pyloric gastrectomy were administered 200 ml of 220 w/v% barium sulfate and 20 mg of scopolamine butyl bromide intramuscularly preoperatively to stop gastric peristalsis and confirm tumor location, and fluoroscopy was performed to classify the gastric shape using standing full-face images. The gastric shape was classified as follows (Figure 1): 1) Hooked stomach: vertical, J-shaped, with a gastric angle. 2) Ptotic: vertical, J-shaped, with a gastric angle below Jacoby's line. 3) Steer-horn: horizontal; no gastric horns were observed. 4) Cascade: barium accumulates in the fundus and drains. Because shapes 1) and 2) allow barium to remain in the stomach and shapes 3) and 4) allow barium to flow out of the stomach, we classified patients with shapes 1) and 2) as the storage group, and those with shapes 3) and 4) as the outflow group.

Surgical procedure and perioperative care. Surgery was performed by R0 distal gastrectomy with lymph node dissection and reconstruction using the Billroth-I or Roux-en-Y method according to the Japanese guidelines for the treatment of gastric cancer (19). After gastrectomy, patients were managed using the Enhanced Recovery After Surgery protocol (20). During the preoperative period, patients were allowed to eat until midnight the day before surgery and were given two 500 ml plastic bottles containing oral rehydration solution which they were allowed to drink until 3 h before surgery. Postoperatively, oral drinking water intake was started on the second postoperative day and solid food was started on the third postoperative day. Both the main and side meals were soft foods, and by the seventh postoperative day, most patients resumed a normal diet. Patients were generally discharged from the hospital on the seventh postoperative day after confirming that their laboratory data were normal.

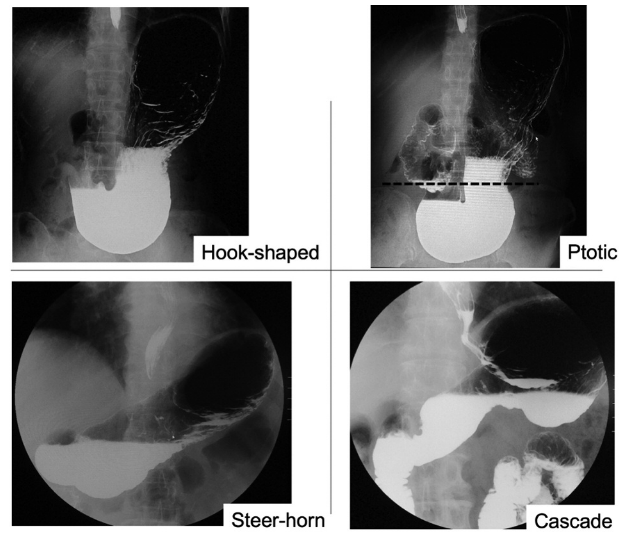


Figure 1. *Definition of preoperative gastric shape. Preoperative gastrofluoroscopy was performed by administering 200 ml of 220 w/v% barium sulfate. In the upright position filled with barium, the shape of the stomach was defined as follows: 1) Ptotic stomach: gastric angle below Jacoby's line; 2) steer-horn stomach: no gastric angle; 3) cascade stomach: barium accumulated in the fundus and drained out; and 4) ptotic stomach: barium was in the fundus and drained out.*

Pathological diagnosis, postoperative complications. The depth of invasion, lymph node metastasis, and gastric cancer stage were determined according to the TNM 8th edition (18). Postoperative complications were defined as complications of Clavien-Dindo grade ≥3a occurring within 30 days after surgery (21).

Measurement of lean body mass (LBM). One week before surgery, and 1 and 3 months after surgery, the segmental composition of the trunk and limbs was analyzed using an MC-190EM bioelectrical impedance analyzer (Tanita, Tokyo, Japan), and the LBM was calculated for each time period.

Definition of rate of LBM loss, cutoff value for body weight decrease, and assessment of postoperative dietary disturbances. The rate of LBM loss was defined as: LBM loss rate=(preoperative LBM−1-month postoperative LBM)×100/preoperative LBM; Preoperative LBM was measured within 1 week before surgery. The cutoff value for LBM loss 1 month postoperatively was defined as 5% (12). Because body weight (BW) reduction 1 month after distal end gastrectomy has been reported to be 8.8% for open surgery and 6.4% for laparoscopic surgery (22), these averages were taken, and the cutoff value for BW reduction 1 month postoperatively was set at 7.5%.

Postoperative dietary disturbances 1 month after distal gastrectomy were assessed using a questionnaire administered by a dietitian. Five disorders associated with weight loss were evaluated: dumping syndrome, diarrhea, reflux, nausea and vomiting, and taste disorder (dysgeusia).

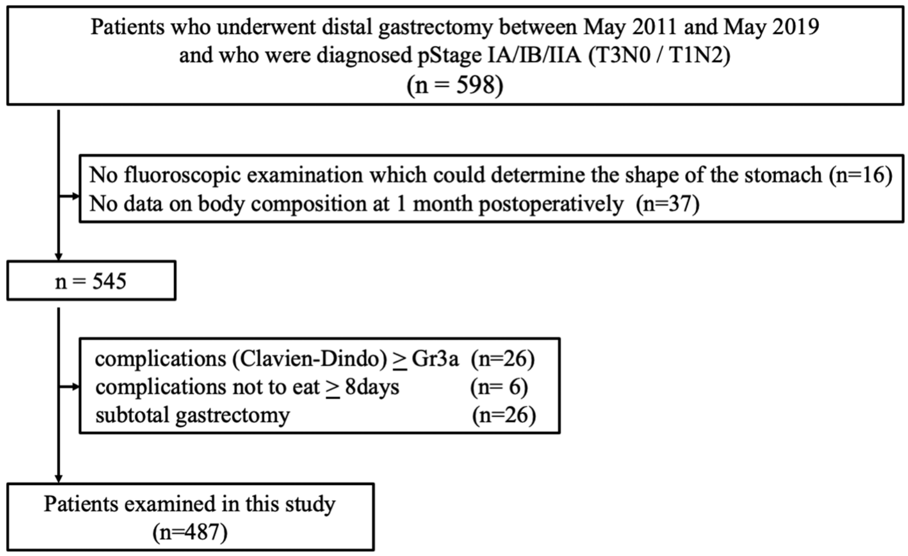


Figure 2. *Patient flow diagram. A total of 598 patients who underwent distal gastrectomy at our Institution between May 2011 and May 2019 were diagnosed with pStage IA/IB/IIA (pT1/N2 or pT3/N0) and did not receive adjuvant chemotherapy. Of these, 16 patients who had no preoperative fluoroscopic examination that could determine the shape of the stomach, 37 patients who had no data on body composition 1 month after surgery, 26 patients who had postoperative complications of grade 3a or higher, six patients who had postoperative complications that required ≥8 days of no intake of food or drinks, and 26 patients who had undergone subtotal gastrectomy were excluded from the study, and the remaining 487 patients were included.*

Statistical analysis. Fisher's exact test was used to compare the clinicopathological characteristics of the storage and outflow groups. Unadjusted and adjusted logistic regression analyses were performed to identify risk factors for LBM loss. The logistic regression analysis considered patient background, including loss of LBM 1 month after surgery, surgical background, and pathological factors. The multivariable analysis included clinically important factors that may affect LBM loss. In this analysis, we used the forced entry method to select the variables to include in the multivariable model.

Two-sided *p*-values <0.05 were considered statistically significant. Statistical analyses were performed using SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics. A total of 598 patients who underwent distal gastrectomy at our hospital between May 2011 and May 2019 without adjuvant chemotherapy and were diagnosed with pStage I, IIA (pT1pN2, or pT3pN0) were included in the analysis. Of these, 16 patients who had no preoperative fluoroscopic examination that could determine the shape of the stomach, 37 patients who had no data on body composition 1 month after surgery, 26 patients who had postoperative complications of grade 3a or higher, six patients who had postoperative complications that required ≥8 days of no intake of food or drinks, and 26 patients who had undergone subtotal gastrectomy were excluded from this study, and the remaining 487 patients were included in the analysis (Figure 2).

Preoperative, intraoperative, and postoperative clinicopathologic characteristics of the storage and outflow groups. Table I shows the association between patient characteristics, gastric shape, and clinicopathological features, including pathological and surgical findings. Compared to the storage group, the outflow group had a significantly higher percentage of males and higher body mass index and incidence of bleeding (p<0.001). In contrast, the proportion of patients requiring D2 lymph node dissection was higher in the outflow group than in the storage group (p=0.048). Postoperatively, the percentage of patients with decreased BW and LBM 1 month postoperatively was significantly higher in the storage group than in the outflow group (p=0.009 and p=0.003, respectively).

Unadjusted and adjusted logistic regression analysis of predictors of postoperative LBM loss. The unadjusted and adjusted logistic regression analyses of predictors of LBM loss are shown in Table II. The unadjusted analysis showed that male sex, Roux-en-Y reconstruction, and being in the storage group were significant risk factors for ≥5% LBM loss. Similarly, the adjusted analysis showed that male sex [odds ratio (OR)=2.47, 95% confidence interval (CI)=1.65-3.70, p<0.001), Roux-en Y reconstruction (OR=1.65, 95% CI=1.09-2.49, p=0.017), and being in the storage group (OR=2.00, 95% CI=1.25-3.20, p=0.003) were independent predictors of LBM loss.

Table I. *Patient characteristics and association between gastric shape and clinicopathological features.*

		Storage n=370 (%)	Outflow n=117 (%)	*p*-Value
Sex				<0.001
	Male	198 (53.5)	98 (83.8)	
	Female	172 (46.5)	19 (16.2)	
Age (years)	Median (IQR)	68.0 (60.0-74.0)	67.0 (59.0-73.0)	0.42
	>70	150 (40.5)	46 (39.3)	0.83
	<70	220 (59.5)	71 (60.3)	
BMI (kg/m^2)	Median (IQR)	22.0 (19.9-24.1)	24.2 (22.4-25.9)	<0.001
ASA score				0.13
	1	101 (27.3)	22 (18.8)	
	2	266 (71.9)	94 (80.3)	
	3	3 (0.8)	1 (0.9)	
Preoperative albumin (g/dl)	Median (IQR)	4.25 (4.0-4.5)	4.20 (4.0-4.4)	0.45
Loss of BW 1 month				0.009
postoperatively (%)	>7.5	69 (18.6)	10 (8.5)	
	<7.5	301 (81.4)	107 (91.5)	
Loss of LBM 1 month				0.003
postoperatively (%)	>5.0	147 (39.7)	29 (24.8)	
	<5.0	223 (60.3)	88 (75.2)	
pT				0.51
	T1	311 (84.1)	94 (80.3)	
	T2	37 (10.0)	16 (13.7)	
	T3	22 (5.9)	7 (6.0)	
pN				0.12
	N0	333 (90.0)	112 (95.7)	
	N1	29 (7.8)	5 (4.3)	
	N2	8 (2.2)	0 (0.0)	
pTMN stage				0.79
	IA	278 (75.1)	90 (76.9)	
	IB	58 (15.7)	19 (16.2)	
	IIA	34 (9.2)	8 (6.8)	
Histological type				0.11
	Intestinal	118 (31.9)	48 (41.0)	
	Diffuse	174 (47.0)	41 (35.0)	
	Mixed	70 (18.9)	24 (20.5)	
	Indeterminate	8 (2.2)	4 (3.4)	
Postoperative stay (day)	Median (IQR)	8.0 (7.0-9.0)	8.0 (7.0-8.0)	0.53
Operation Time (min)				0.09
	>252	177 (47.8)	67 (57.3)	
	<252	193 (52.2)	50 (42.7)	
Bleeding				<0.001
	>50 (ml)	166 (44.9)	80 (68.4)	
	<50	204 (55.1)	37 (31.6)	
LN dissection				0.048
	D1	2 (0.5)	3 (2.6)	
	D1+/D1β	268 (72.4)	91 (77.8)	
	D2	100 (27.1)	23 (19.7)	
Reconstruction				0.71
	Billroth-I	275 (74.3)	85 (72.6)	
	Roux-en Y	95 (25.7)	32 (27.4)	
Procedure				0.47
	Laparoscopic	272 (73.5)	82 (70.1)	
	Laparotomy	98 (26.5)	35 (29.9)	

ASA score, American Society of Anesthesiologists score; BMI, body mass index; BW, body weight; LBM, lean body mass; pN, pathological lymph node metastasis; pT, pathological tumor depth; pTNM classification, pathological TNM classification.

Comparison of postoperative LBM change between the storage and outflow groups. The median of LBM reduction 1 and 3 months postoperatively was 3.9% (1.5-6.1%) and 3.3% (1.1-5.9%), respectively, in the storage group, and 3.6% (1.9-4.9%) and 3.0% (1.1-5.3%), respectively, in the outflow group (Figure 3). The reduction in LBM in the

Table II. *Unadjusted and adjusted logistic regression analyses of predictors of postoperative LBM loss.*

		Unadjusted analysis of loss of LBM			Adjusted analysis of loss of LBM		
Factor (category)	Number	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
Age (years)				0.32			
<70	291	1.00			1.00		0.38
≥70	196	1.21	0.83-1.76		1.19	0.80-1.77	
Sex				<0.001			<0.001
Female	191	1.00			1.00		
Male	296	2.47	1.65-3.70		3.20	2.07-4.96	
BMI (kg/m^2)				0.33			0.13
<25	377	1.00			1.00		
≥25	110	1.24	0.80-1.91		1.46	0.88-2.38	
Procedure				0.21			0.10
Laparoscopic	354	1.00			1.00		
Open	133	1.30	0.86-1.96		1.51	0.91-2.51	
Reconstruction				0.017			0.02
Billroth-I	360	1.00			1.00		
Roux-en-Y	127	1.65	1.09-2.49		1.69	1.08-2.64	
Operation time (min)				0.36			0.6
<252	243	1.00			1.00		
≥252	244	1.19	0.82-1.72		1.13	0.71-1.80	
pT				0.55			0.47
T1a, T1b	405	1.00			1.00		
T2, T3	82	1.16	0.71-1.89		1.21	0.71-2.07	
pN				0.11			0.23
N0	445	1.00			1.00		
≥N1	42	1.68	0.89-3.18		1.52	0.76-3.02	
Gastric shape				0.003			<0.001
Outflow	117	1.00			1.00		
Storage	370	2.00	1.25-3.20		3.30	1.95-5.59	

BMI, Body mass index; LBM, lean body mass; pN, pathological lymph node metastasis; pT, pathological tumor depth; pTNM, pathological TNM.

retention group at 1 month postoperatively was significantly greater than that in the outflow group (*p*=0.049).

Dietary disturbances 1 month after gastrectomy. The dietary disturbances in the storage and outflow groups 1 month after gastrectomy are shown in Table III. Dietary disturbances that may be related to weight loss, such as dumping, diarrhea, regurgitation, nausea/vomiting, and dysgeusia, were compared between the storage and outflow groups. Postoperative dietary disturbances, including dumping syndrome, diarrhea, and reflux were significantly more common in the storage group than in the outflow group (*p*=0.001, *p*=0.05, and *p*=0.04, respectively).

The dietary disturbances 1 month postoperatively in the groups with LBM reductions of ≥5% and <5% are shown in Table IV. Postoperative dietary disturbances were more likely to occur in the group with ≥5% LBM reduction than in the group with <5% LBM reduction (*p*<0.001). Diarrhea and nausea/vomiting were also significantly more likely to occur in the group with ≥5% LBM reduction than in the group with <5% LBM reduction (*p*=0.003 and *p*=0.04, respectively).

Discussion

In this study, we examined the effect of preoperative gastric shape on the reduction in LBM 1 month after distal gastrectomy. The study revealed two important clinical findings. First, a significantly higher percentage of patients in the storage group (hook and ptotic stomach shapes) had at least a 5% reduction in LBM 1 month after surgery compared with the outflow group (steer-horn and cascade stomach shapes). In addition, a significantly higher proportion of patients in the storage group had problems with eating and voiding 1 month after distal gastrectomy than those in the outflow group.

Most patients experience weight loss after gastrectomy, with a reported average weight loss of 8.8% 1 month after surgery for distal gastrectomy and 10.7% after total gastrectomy (22). Furthermore, the reported average decrease in LBM is approximately 4.1% 1 month after distal gastrectomy (13).

Table III. *Comparison of dietary problems 1 month after surgery between the storage group and outflow group.*

		Storage n=370 n (%)	Outflow n=117 n (%)	*p*-Value
Dietary problems	No	222 (60.0)	95 (81.2)	<0.001
	Yes	148 (40.0)	22 (18.8)	
Type of problem	Dumping	49 (13.2)	4 (3.4)	0.001
	Diarrhea	51 (13.8)	8 (6.8)	0.05
	Reflux	47 (12.7)	7 (6.0)	0.04
	Nausea/vomiting	31 (8.4)	5 (4.3)	0.16
	Dysgeusia	3 (0.8)	1 (0.9)	>0.99

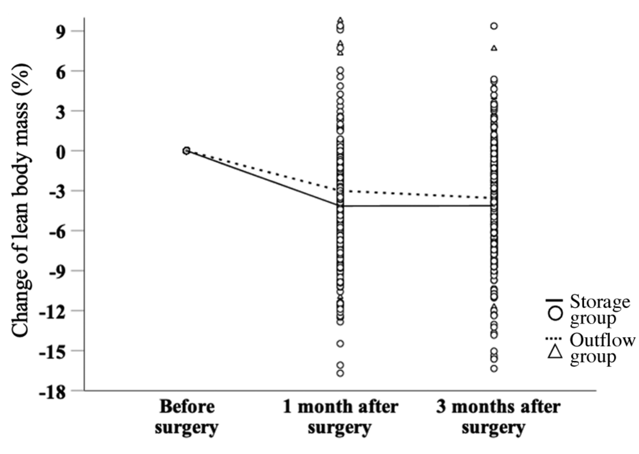
BMI, Body mass index.

Table IV. *Comparison of dietary problems 1 month after surgery according to extent of LBM loss.*

		Loss of LBM >5% n=176 n (%)	Loss of LBM <5% n=311 n (%)	*p*-Value
Dietary problems	No	97 (55.1)	220 (70.7)	<0.001
	Yes	79 (44.9)	91 (29.3)	
Type of problems	Dumping	16 (9.1)	37 (11.9)	0.36
	Diarrhea	32 (18.2)	27 (8.7)	0.003
	Reflux	25 (14.2)	29 (9.3)	0.13
	Nausea/vomiting	19 (10.8)	17 (5.5)	0.04
	Dysgeusia	3 (1.7)	1 (0.3)	0.13

LBM, Lean body mass.

We hypothesized that although the speed of food flow from the residual stomach to the small intestine after gastrectomy did not differ between the storage and outflow groups, but preoperatively, the rate of food flow might be much slower in the storage group than in the outflow group. Therefore, the change in the rate of food flow was greater in the storage group than in the outflow group, and this is why the percentage of patients with feeding and voiding disorders at 1 month after gastrectomy We speculated that the proportion of patients with eating and voiding disorders at 1 month after gastrectomy was higher in the storage group. Since ingested food always flowed from the stomach to the intestines in a relatively short time in the outflow group, they were physically accustomed to this condition before surgery and were therefore less affected by the surgery than the retention group. On the other hand, the peristalsis of the stomach and pylorus in the reservoir group may have allowed sufficient time for food to flow from the stomach to the small intestine prior to surgery. After distal gastrectomy with loss of the pylorus, the flow from the stomach to the intestine may have increased, leading to an increased frequency of disorders, such as dumping, diarrhea, and reflux.



		Storage group	Outflow group	*p*-value
1 month after surgery	Median (IQR)	-3.9% (-6.1 to -1.5)	-3.6% (-4.9 to -1.9)	0.061
3 months after surgery	Median(IQR)	-3.3% (-5.9 to -1.1)	-3.0% (-5.3 to -1.1)	0.35

Figure 3. *Changes in the percent (%) LBM in the storage and outflow groups. The median rate of LBM reduction was 3.9% (1.5-6.1%) 1 month postoperatively and 3.3% (1.1-5.9%) 3 months postoperatively in the storage group and 3.6% (1.9-4.9%) 1 month postoperatively and 3.0% (1.1-5.3%) 3 months postoperatively in the outflow group. LBM: Lean body mass; IQR: interquartile range.*

A decreased LBM 1 month after gastrectomy has been reported to be a possible risk factor for discontinuation of adjuvant chemotherapy (12). Weight loss and skeletal muscle loss have also been reported to worsen the prognosis of various cancers (23-28). Although this study did not examine the effect of preoperative gastric shape on long-term prognosis, these findings suggest that preoperative gastric shape may be associated with long-term prognosis.

This study has certain limitations. First, it was a retrospective, single-center cohort study. The results of this study need to be validated in a large multicenter prospective study using standardized assessments of gastric geometry. Second, there is no strict morphological definition of gastric shape, and this study used its own definition for classification purposes. Although classification by physiological tonus of the gastric wall may be appropriate and other classifications may be more appropriate, we believe that our classification scheme reflects the consensus use of the terms gastric shape and tonus as closely as possible. Third, we used a bioelectrical impedance analyzer to perform a segmental analysis of body composition, including liver, kidney, and muscle mass. Visceral mass does not change after surgery, and it is likely that muscle is the major contributor to changes in LBM. However, the bioelectrical impedance analyzer could not directly measure muscle mass.

In conclusion, preoperative gastric shape is a useful predictor of decreased LBM 1 month after distal gastrectomy. The results of this study suggest that patients with a preoperative storage shape may be more prone to feeding and voiding disorders than those with a preoperative outflow shape. In patients with a preoperative storage shape, appropriate nutritional guidance and drug prescription after surgery may reduce early postoperative LBM loss, which may facilitate continuation of adjuvant chemotherapy and improve the long-term prognosis.

Conflicts of Interest

The Authors have no conflicts of interest or financial ties to disclose.

Authors' Contributions

SN designed the study. Data collection and literature search were performed by SN, MT, SO, JM, IH and TO. Data analysis and interpretation were performed by SN. Data interpretation was performed by all researchers. The paper and figures were drafted by SN and TO. Finally, the paper was revised and approved by all researchers. Thus, all Authors actively participated in this study.

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References

1 Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68(6): 394-424, 2018. DOI: 10.3322/caac.21492

2 Sasako M, Sakuramoto S, Katai H, Kinoshita T, Furukawa H, Yamaguchi T, Nashimoto A, Fujii M, Nakajima T, Ohashi Y: Five-year outcomes of a randomized phase III trial comparing adjuvant chemotherapy with S-1 *versus* surgery alone in stage II or III gastric cancer. J Clin Oncol 29(33): 4387-4393, 2011. DOI: 10.1200/JCO.2011.36.5908

3 Noh SH, Park SR, Yang HK, Chung HC, Chung IJ, Kim SW, Kim HH, Choi JH, Kim HK, Yu W, Lee JI, Shin DB, Ji J, Chen JS, Lim Y, Ha S, Bang YJ, CLASSIC trial investigators: Adjuvant capecitabine plus oxaliplatin for gastric cancer after D2 gastrectomy (Classic): 5-year follow-up of an open-label, randomized phase 3 trial. Lancet Oncol 15(12): 1389-1396, 2014. DOI: 10.1016/S1470-2045(14)70473-5

4 Park SH, Lim DH, Sohn TS, Lee J, Zang DY, Kim ST, Kang JH, Oh SY, Hwang IG, Ji JH, Shin DB, Yu JI, Kim KM, An JY, Choi MG, Lee JH, Kim S, Hong JY, Park JO, Park YS, Lim HY, Bae JM, Kang WK, ARTIST 2 investigators: A randomized phase III trial comparing adjuvant single-agent S1, S-1 with oxaliplatin, and postoperative chemoradiation with S-1 and oxaliplatin in patients with node-positive gastric cancer after D2 resection: the ARTIST 2 trial. Ann Oncol 32(3): 368-374, 2021. DOI: 10.1016/j.annonc.2020.11.017

5 Yoshida K, Kodera Y, Kochi M, Ichikawa W, Kakeji Y, Sano T, Nagao N, Takahashi M, Takagane A, Watanabe T, Kaji M, Okitsu H, Nomura T, Matsui T, Yoshikawa T, Matsuyama J, Yamada M, Ito S, Takeuchi M, Fujii M: Addition of docetaxel to oral fluoropyrimidine improves efficacy in patients with Stage III gastric cancer: Interim analysis of JACCRO GC-07, a randomized controlled trial. J Clin Oncol 37(15): 1296-1304, 2019. DOI: 10.1200/JCO.18.01138

6 Toyokawa T, Ohira M, Sakurai K, Kubo N, Tanaka H, Muguruma K, Hirakawa K: The role of adjuvant chemotherapy for patients with Stage IB gastric cancer. Anticancer Res 35(7): 4091-4097, 2015.

7 Moon JH, Fujiwara Y, Hirao M, Imamura H, Kimura Y, Fujitani K, Fujita J, Tamura S and Takiguchi S, Yano M, Mori M, Doki Y: Randomized controlled trial of adjuvant chemotherapy with fluoropyrimidines *versus* surgery-alone for gastric cancer. Anticancer Res 37(6): 3061-3067, 2017. DOI: 10.21873/anticanres.11661

8 Morino K, Yamamoto M, Yamanaka R, Iwasaki Y, Nakanishi N, Goto T, Tanaka H, Matsusue R, Machimoto T: Clinical impact of laparoscopic surgery on the long-term survival of advanced gastric cancer patients with regard to facilitating doublet adjuvant chemotherapy. Anticancer Res 43(5): 2203-2209, 2023. DOI: 10.21873/anticanres.16383

9 Fujitani K, Kurokawa Y, Takeno A, Endoh S, Ohmori T, Fujita J, Yamasaki M, Takiguchi S, Mori M, Doki Y, Osaka University Clinical Research Group for Gastroenterological Surgery: Time to initiation or duration of S-1 adjuvant chemotherapy; which really impacts on survival in stage II and III gastric cancer? Gastric Cancer 21(3): 446-452, 2018. DOI: 10.1007/s10120-017-0767-9

10 Yoshikawa T, Terashima M, Mizusawa J, Nunobe S, Nishida Y, Yamada T, Kaji M, Fukushima N, Hato S, Choda Y, Yabusaki H, Yoshida K, Ito S, Takeno A, Yasuda T, Kawachi Y, Katayama H, Fukuda H, Boku N, Sano T, Sasako M: Four courses *versus* eight courses of adjuvant S-1 for patients with stage II gastric cancer (JCOG1104 [OPAS-1]): an open-label, phase 3, non-inferiority, randomised trial. Lancet Gastroenterol Hepatol 4(3): 208-216, 2019. DOI: 10.1016/S2468-1253(18)30383-2

11 Aoyama T, Yoshikawa T, Shirai J, Hayashi T, Yamada T, Tsuchida K, Hasegawa S, Cho H, Yukawa N, Oshima T, Rino Y, Masuda M, Tsuburaya A: Body weight loss after surgery is an independent risk factor for continuation of S-1 adjuvant chemotherapy for gastric cancer. Ann Surg Oncol 20(6): 2000-2006, 2013. DOI: 10.1245/s10434-012-2776-6

12 Aoyama T, Kawabe T, Fujikawa H, Hayashi T, Yamada T, Tsuchida K, Yukawa N, Oshima T, Rino Y, Masuda M, Ogata T, Cho H, Yoshikawa T: Loss of lean body mass as an independent risk factor for continuation of S-1 adjuvant chemotherapy for gastric cancer. Ann Surg Oncol 22(8): 2560-2566, 2015. DOI: 10.1245/s10434-014-4296-z

13 Aoyama T, Yoshikawa T, Maezawa Y, Segami K, Kano K, Numata M, Yamada T, Tamagawa H, Fujikawa H, Komori K, Hayashi T, Sato T, Yukawa N, Rino Y, Masuda M, Ogata T, Cho H, Oshima T: Influence of postoperative surgical complications after gastrectomy on body weight and body composition changes in patients with gastric cancer. Anticancer Res 39(2): 1073-1078, 2019. DOI: 10.21873/anticanres.13215

14 Camilleri M: Peripheral mechanisms in appetite regulation. Gastroenterology 148(6): 1219-1233, 2015. DOI: 10.1053/j.gastro.2014.09.016

15 Wang YJ, Hung KL, Yang JN, Wang TC, Chin CH: Gastric anatomic type is associated with obesity and gender. Obes Facts 9(3): 221-229, 2016. DOI: 10.1159/000445062

16 Keet AD: The Pyloric sphincteric cylinder in health and disease. Berlin Heidelberg, Springer, 2012.

17 Sano T, Aiko T: New Japanese classifications and treatment guidelines for gastric cancer: revision concepts and major revised points. Gastric Cancer 14(2): 97-100, 2011. DOI: 10.1007/s10120-011-0040-6

18 Sobin LH, Gospodarowicz MK, Wittekind C: TNM Classification of Malignant Tumours, 8^{th} edn. John Wiley & Sons, 2017.

19 Japanese Gastric Cancer Association: Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer 24(1): 1-21, 2021. DOI: 10.1007/s10120-020-01042-y

20 Yamada T, Hayashi T, Cho H, Yoshikawa T, Taniguchi H, Fukushima R, Tsuburaya A: Usefulness of enhanced recovery after surgery protocol as compared with conventional perioperative care in gastric surgery. Gastric Cancer 15(1): 34-41, 2012. DOI: 10.1007/s10120-011-0057-x

21 Dindo D, Demartines N, Clavien PA: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240(2): 205-213, 2004. DOI: 10.1097/01.sla.0000133083.54934.ae

22 Abdiev S, Kodera Y, Fujiwara M, Koike M, Nakayama G, Ohashi N, Tanaka C, Sakamoto J, Nakao A: Nutritional recovery after open and laparoscopic gastrectomies. Gastric Cancer 14(2): 144-149, 2011. DOI: 10.1007/s10120-011-0021-9

23 Kugimiya N, Harada E, Oka K, Kawamura D, Suehiro Y, Takemoto Y, Hamano K: Loss of skeletal muscle mass after curative gastrectomy is a poor prognostic factor. Oncol Lett 16(1): 1341-1347, 2018. DOI: 10.3892/ol.2018.8747

24 Maréchal R, Demols A, Gay F, De Maertelaere V, Arvanitaki M, Hendlisz A, Van Laethem J: Prognostic factors and prognostic index for chemonaïve and gemcitabine-refractory patients with advanced pancreatic cancer. Oncology 73(1-2): 41-51, 2007. DOI: 10.1159/000120627

25 Iritani S, Imai K, Takai K, Hanai T, Ideta T, Miyazaki T, Suetsugu A, Shiraki M, Shimizu M, Moriwaki H: Skeletal muscle depletion is an independent prognostic factor for hepatocellular carcinoma. J Gastroenterol 50(3): 323-332, 2015. DOI: 10.1007/s00535-014-0964-9

26 Kuwada K, Kikuchi S, Kuroda S, Yoshida R, Takagi K, Noma K, Nishizaki M, Kagawa S, Umeda Y, Fujiwara T: Survival impact of postoperative skeletal muscle loss in gastric cancer patients who underwent gastrectomy. Anticancer Res 43(1): 223-230, 2023. DOI: 10.21873/anticanres.16153

27 Tanaka Y, Aoyagi K, Umetani Y, Tanaka Y, Kaku H, Minami T, Isobe T, Murakami N, Fujita F, Akagi Y: Impact of skeletal muscle mass reduction on long-term survival after radical resection of gastric cancer. Anticancer Res 43(8): 3779-3786, 2023. DOI: 10.21873/anticanres.16563

28 Buentzel J, Heinz J, Bleckmann A, Bauer C, Röver C, Bohnenberger H, Saha S, Hinterthaner M, Baraki H, Kutschka I, Emmert A: Sarcopenia as prognostic factor in lung cancer patients: a systematic review and meta-analysis. Anticancer Res 39(9): 4603-4612, 2019. DOI: 10.21873/anticanres.13640

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