J Gastric Cancer. 2022 Apr;22(2):145-155
https://doi.org/10.5230/jgc.2022.22.e15
pISSN 2093-582X·eISSN 2093-5641

Journal of Gastric Cancer

Original Article

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Larger Remaining Stomach Volume Is Associated With Better Nutrition and Muscle Preservation in Patients With Gastric Cancer Receiving Distal Gastrectomy With Gastroduodenostomy

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OPEN ACCESS

Received: Mar 18, 2022
Revised: Apr 25, 2022
Accepted: Apr 26, 2022
Published online: Apr 30, 2022

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ABSTRACT

Purpose: Weight loss and deterioration in body composition are observed in patients with gastric cancer (GC) following gastrectomy. This study aimed to investigate the impact of residual stomach volume (RSV) on the nutritional status and body composition of patients with GC treated with distal gastrectomy.
Materials and Methods: In total, 227 patients who underwent minimally invasive distal gastrectomy with Billroth 1 anastomosis for stage I GC between February 2015 and May 2018 were enrolled. Clinicodemographic and laboratory data were collected from the GC registry. The RSV, abdominal muscle area, and subcutaneous/visceral fat areas were measured using computed tomography data.
Results: A larger RSV was associated with a lower decrease in the nutritional risk index (P=0.004) and hemoglobin level (P=0.003) during the first 3 months after surgery, and better recovery at 12 months. A larger RSV demonstrated an advantage in the preservation of abdominal muscle area (P=0.02) and visceral fat (P=0.04) after surgery, as well as less reduction in weight (P=0.02) and body mass index (P=0.03).
Conclusions: Larger RSV was associated with improved nutritional status and better preservation of muscle and fat after distal gastrectomy.

Keywords: Gastric cancer; Gastrectomy; Remnant stomach; Body composition; Nutritional status; Skeletal muscle

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Funding
This study was supported by a grant from Asan Institute for Life Sciences and Corporate Relations of Asan Medical Center, Seoul, Korea (2017IT0216), the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (No. HI18C1216), and the National Research Foundation of Korea (NRF) grand funded by the Korea government (MSIT) (No. NRF-2020R1F1A1048267). The authors declare that they have no conflicts of interest.

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
Conceptualization: L.I.S., K.A., K.K.W., L.J.B. Data curation: L.I.S., K.A., K.Y., L.K. Formal analysis: L.J.B., K.Y., L.I.S. Funding acquisition: L.I.S., K.K.W. Investigation: K.Y., P.T., J.H., J.J.K., L.K., K.K.W. Methodology: L.I.S., K.A., L.J.B., K.K.W. Project administration: L.I.S. Resources: L.I.S., K.K.W., K.S., L.K. Supervision: L.I.S. Writing - original draft: K.A. Writing - review & editing: L.I.S., K.A.

INTRODUCTION

Gastric cancer (GC) is one of the most common malignancies [1], and surgery is the mainstay of curative treatment [2]. Patients undergoing gastrectomy experience metabolic and physiologic derangements, such as anemia, altered gastrointestinal function, significant loss of body weight and muscle, and worsened nutritional status. Although several factors are responsible for these postoperative changes, the absence or restricted volume of the remaining stomach is regarded as a major cause [3,4].

According to the current treatment guidelines for GC, standard gastrectomy requires resection of at least two-thirds of the stomach to obtain optimal oncological outcomes [5]. As the procedure includes ablation of a large part of the stomach, GC surgery mimics gastric restrictive surgery in the treatment of morbid obesity or metabolic disorders. Indeed, the influence of residual stomach volume (RSV) on changes in body weight and metabolic profiles, which is known to be closely associated with a significant reduction and stabilization of body weight [6-8], has been proposed in the field of bariatric surgery. In addition, remarkable differences in weight change and metabolic profiles have been noted in patients receiving distal and total gastrectomy [9,10]. These results suggest that RSV might affect postoperative changes in nutritional and anthropometric values, even in patients with GC receiving distal gastrectomy. However, the impact of RSV on postoperative nutritional and/or body composition-related parameters in patients with GC remains unclear.

Over the last two decades, the establishment of an endoscopic surveillance program that enables early detection of GC and the introduction of perioperative chemotherapy has improved the overall prognosis of patients [11-14]. Owing to the growing number of survivors and their prolonged life expectancy, more attention has been paid to postoperative nutrition and quality of life in patients with this malignancy [15]. Postoperative deterioration of physiological or metabolic parameters is remarkable in the first year after gastrectomy [10,16]. A few studies have also demonstrated that the extent of gastric resection is associated with postoperative quality of life in terms of post-gastrectomy syndrome [17-19].

Based on these findings, we hypothesized that RSV is associated with patients' nutritional status and muscle/fat-related variables. Our previous results revealed that the measurement of RSV is feasible using computed tomography (CT) for follow-up with 3-dimensional (3D) reconstruction, and a larger RSV might have a protective effect on nutritional parameters in GC patients receiving distal gastrectomy [20,21]. However, certain shortcomings, including inadequate patient cohort size and the confounding effect of the anastomosing method on variables, have alleviated the clinical implications of the study. We addressed these limitations and aimed to determine the impact of RSV by investigating a group of patients with stage I GC treated with distal gastrectomy with gastroduodenostomy (Billroth 1 anastomosis), which is similar to normal gastrointestinal continuity. We also analyzed the follow-up parameters during the first postoperative year.

MATERIALS AND METHODS

Patients

This study was based on a retrospective review of a prospectively built comprehensive GC surgery registry. The medical records of patients who underwent minimally invasive

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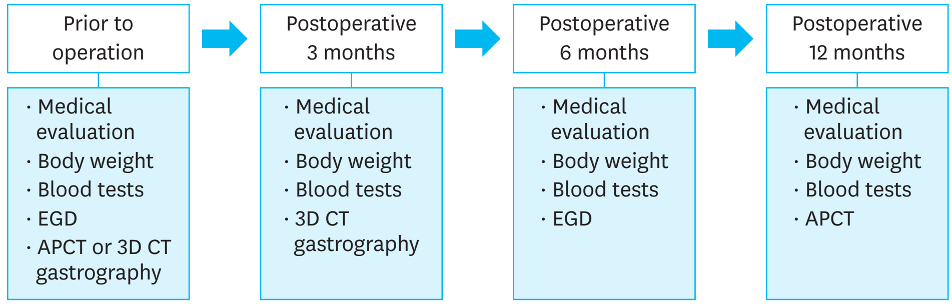

Fig. 1. Diagram showing the regular follow-up protocol of patients who underwent laparoscopic distal gastrectomy for early gastric cancer during the first year after surgery.
EGD = esophagogastroduodenoscopy; APCT = abdominopelvic computed tomography; 3D = 3-dimensional; CT = computed tomography.

(laparoscopic or robotic) distal gastrectomy with Billroth 1 anastomosis for stage I GC at the Asan Medical Center, Seoul, Korea between February 2015 and May 2018 were analyzed. The registry includes information on patient demographics, preoperative examination results, surgical procedure-related data, postoperative outcomes, and follow-up examination results. This study was approved by the Institutional Review Board (IRB) of Asan Medical Center, Seoul, Korea (IRB No. 2019-1159). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all subjects and/or their legal guardians.

The patients were treated and followed up according to the Japanese Gastric Cancer Treatment Guidelines [5] (**Fig. 1**). 3D CT was performed 3 months after surgery for RSV measurement as well as for detection of tumor relapse. Abdominopelvic CT was performed 1 year postoperatively for the surveillance of tumor recurrence.

Among the 393 patients who underwent minimally invasive distal gastrectomy with Billroth 1 anastomosis for stage I GC, (a) patients without 3D CT at 3 months after surgery (n=160), (b) those who received neoadjuvant chemotherapy (n=2), (c) those diagnosed with other synchronous malignancies (n=2), and (d) patients who received adjuvant chemotherapy (n=2) were excluded from the study.

Medical data collection

Patient demographics included age at surgery, sex, height, preoperative weight, and body mass index (BMI). Postoperative outcomes included the pathological stage according to the American Joint Committee on Cancer (AJCC) Staging Manual 8th edition [22], proximal resection margin, and RSV.

Follow-up examinations included laboratory results related to nutrition and CT-based anthropometric data. Data on nutritional index factors, including protein, albumin, cholesterol, and hemoglobin as anemia-related parameters, were collected before surgery and at 3, 6, and 12 months after surgery. The nutritional risk index (NRI) was calculated according to the following formula developed by the Veterans Affairs Total Parental Nutrition Cooperative Study Group (1991) [23]: $\text{NRI}=1.519\times\text{serum albumin level (in grams per liter)}+0.417\times(\text{current weight}/\text{usual weight})\times 100$. We used preoperative weight for the usual weight and weight measured at postoperative 3, 6, and 12 months for the current weight to compare the NRI at each time point.

For evaluation of body composition, preoperative CT scans and those taken at 3 and 12 months postoperatively were used. Body composition on CT was evaluated with an artificial intelligence software (AID-U™, iAID Inc., Seoul, Korea), which was developed using a fully convolutional network segmentation technique [24,25]. Experienced operators (Y. K and K. W. K), who were blinded to clinical information, selected axial CT slices at the L3 inferior endplate level in a semi-automatic manner with the aid of coronal reconstructed images. Selected CT images were automatically segmented to generate the boundary of the total abdominal muscles, and the abdominal muscle and fat areas were measured (**Fig. 2**). Thereafter, 2 operators (Y. K. and K. W. K.) checked the quality of the muscle segmentation in all images. The skeletal muscle area (SMA), including all muscles on the selected axial images, that is, psoas, paraspinal, transversus abdominis, rectus abdominis, quadratus lumborum, and internal and external obliques, was demarcated using predetermined thresholds of −29 to +150 Hounsfield units. The visceral fat area (VFA) and subcutaneous fat area (SFA) were also demarcated using fat tissue thresholds of −190 to −30 Hounsfield units.

RSV was estimated using 3D CT gastrography performed 3 months postoperatively. The details of the techniques used for the estimation of RSV are described in our previous report [21]. The estimation was performed by a medical researcher in the radiology department (Y. K.) and a surgeon (A. K.), and all estimated values were double-checked by an expert radiologist (K. W. K.). The included patients were dichotomized according to a median RSV value of 275.2 cm^2: the RSV_{small} ($RSV \leq 275$ cm^2) and RSV_{large} ($RSV > 275$ cm^2) groups.

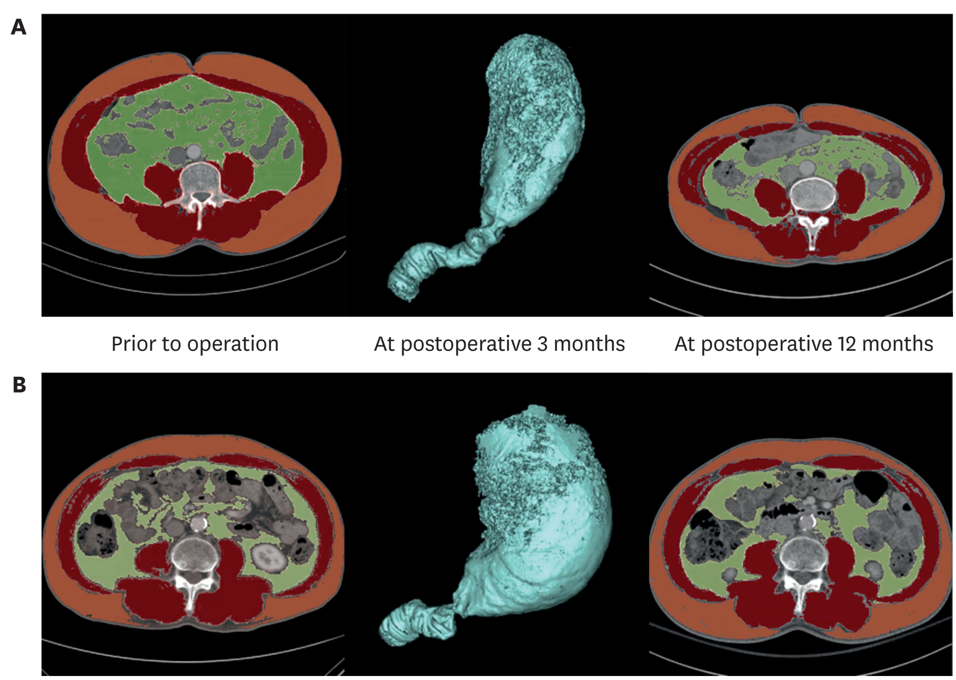

Fig. 2. Representative cases from different RSV groups. (A) A 50-year-old man with stage I gastric cancer underwent laparoscopic distal gastrectomy with Billroth 1 (delta) anastomosis. The RSV measured at 3 months was 254.40 cm^3. The SMA, VFA, and SFA decreased from 182.12 to 145.08 cm^2, 225.9 to 90.5 cm^2, and 192.24 to 124.29 cm^2, respectively. (B) A 55-year-old man with stage I gastric cancer underwent laparoscopic distal gastrectomy with Billroth 1 (delta) anastomosis. The RSV measured at 3 months was 565.85 cm^3. The SMA, VFA, and SFA decreased from 185.52 to 177.96 cm^2, 113.99 to 98.93 cm^2, and 126.75 to 120.13 cm^2, respectively.
RSV = residual stomach volume; SMA = skeletal muscle area; VFA = visceral fat area; SFA = superficial fat area.

https://doi.org/10.5230/jgc.2022.22.e15

BMI, weight at each time point over the preoperative weight, SMA, SFA, VFA, and SMA index defined as SMA adjusted by the square of the height, were assessed as indicators of body composition.

Statistical analyses

For the analysis of the baseline characteristics and surgical outcomes between the 2 RSV groups, the dependent t-test and chi-square test were performed for continuous and categorical variables, respectively. The linear mixed model was used to evaluate the influence of RSV on between-group differences (RSV_{small} vs. RSV_{large}) in the longitudinal changes in nutritional factors, anemia, and body composition. Pearson's correlation analysis was performed to determine the correlation between RSV (cm^2) and nutritional factors 12 months postoperatively. SPSS version 20.0 (SPSS, Inc., Chicago, IL, USA) was used for all statistical analyses, and a P-value less than 0.05 was considered statistically significant.

RESULTS

Patient demographics and clinicopathologic outcomes

In total, 227 patients were included in this study. The median age at operation was 57 (range: 23–82) years, and the median BMI before surgery was 24.5 (range: 16.0–32.0). The median residual volumes of the RSV_{small} and RSV_{large} groups were 175.1 (range: 27.3–273.2) and 423.4 (range: 275.2–995.9) mm^3, respectively. The distribution of RSV is shown in **Figure 3**. Most patients (98.2%) had stage IA tumors. No significant differences were found in the baseline characteristics and clinicopathological outcomes between the 2 groups in addition to RSV (P<0.001) (**Table 1**). There were no anastomosis-related complications or mortalities within the 1-year follow-up period.

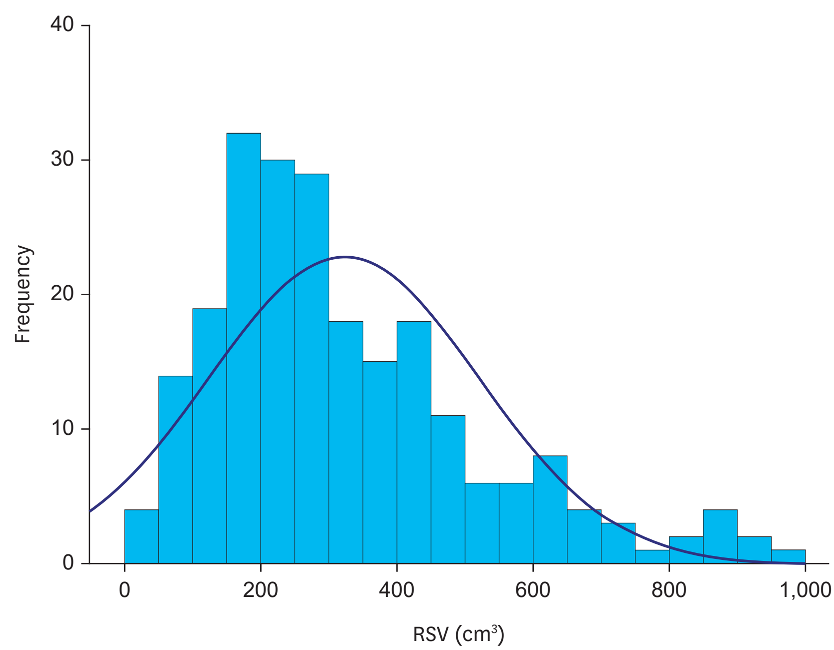

Fig. 3. The distribution of RSV at 3 months postoperatively in patients who underwent laparoscopic distal gastrectomy for early gastric cancer.
RSV = residual stomach volume.

https://doi.org/10.5230/jgc.2022.22.e15

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Table 1. Baseline characteristics and early surgical outcomes of the patients with small and large remnant gastric volume

Variables	Groups		P-value
	RSV_{small} (n=113)	RSV_{large} (n=114)	
Baseline characteristics			
Age at operation (yr)	57 (35–82)	57 (23–80)	0.19
Sex			0.47
Male	73 (64.6)	71 (62.3)	
Female	40 (35.4)	43 (37.7)	
Height (cm)	163.6 (143.0–181.5)	163.6 (142.0–178.6)	0.44
Preoperative body weight (kg)*	65 (40.9–92.4)	65.2 (43.0–91.3)	0.07
Preoperative BMI	24.7 (17.7–31.0)	24.3 (16.0–31.9)	0.10
Clinicopathologic outcomes			
Pathologic stage*			0.99
IA	111 (98.2)	112 (98.2)	
IB	2 (1.8)	2 (1.8)	
PRM (cm)	4.5 (0.6–11.5)	4.5 (1.0–12.0)	0.15
RSV (cm^3)	175.1 (27.3–273.2)	423.4 (275.2–995.9)	<0.001

Values are presented as median (range) or number (%).
RSV = residual stomach volume; BMI = body mass index; PRM = proximal resection margin.
*Pathologic stage was recorded according to the American Joint Committee on Cancer (AJCC) Staging Manual, 8th edition.

Influence of RSV on nutrition and anemia

In both groups, serum albumin, total protein, and cholesterol levels showed a similar decreasing trend during the first 3 months after surgery and gradual recovery during the next 9 months. There were no significant differences in the 3 parameters between the 2 groups. However, the patient group with larger RSV demonstrated a smaller decrease in the first 3 months and a larger increase in the following 9 months in NRI, with a significant time-group interaction (P=0.04) (**Fig. 4**). Pearson's correlation analysis also revealed a statistically significant positive linear relationship between RSV and NRI (Pearson's coefficient=0.13, P=0.03) (**Fig. 5**).

Hemoglobin levels decreased at 3 months postoperatively and recovered at 6 months in both the groups (**Fig. 4**). However, the RSV_{small} group had a larger decline in hemoglobin level and remained lower than the RSV_{large} group during the entire postoperative period with a statistical significance (P=0.003).

Influence of RSV on change in abdominal muscle and fat-related parameters

BMI decreased gradually during the 12-month follow-up period in both patient groups; however, the RSV_{large} group demonstrated a statistically smaller decrease (P=0.03) than the RSV_{small} group, (**Fig. 6A**). A significant difference in body weight reduction during the year was also observed between the 2 groups. Furthermore, the RSV_{large} group showed a protective effect in terms of body weight (P=0.02) (**Fig. 6B**).

In addition to weight loss, 1-year change in body composition was more remarkable in the RSV_{small} group. Skeletal muscle mass, indicated by SMA, continuously decreased after surgery, and this decrease was significant in the RSV_{small} group (P=0.02) (**Fig. 6C**). The decrease in SMI was also more prominent in the RSV_{small} group (P=0.04), lining the SMA (**Fig. 6D**). Interestingly, the SMA and SMI values recovered 3 months postoperatively in the RSV_{large} group, contrary to the RSV_{small} group exhibiting a continuous decrease in these parameters.

The amount of visceral fat was significantly better preserved in the RSV_{large} group (P=0.04); however, no difference was found in the change in SFA (**Fig. 6E and F**).

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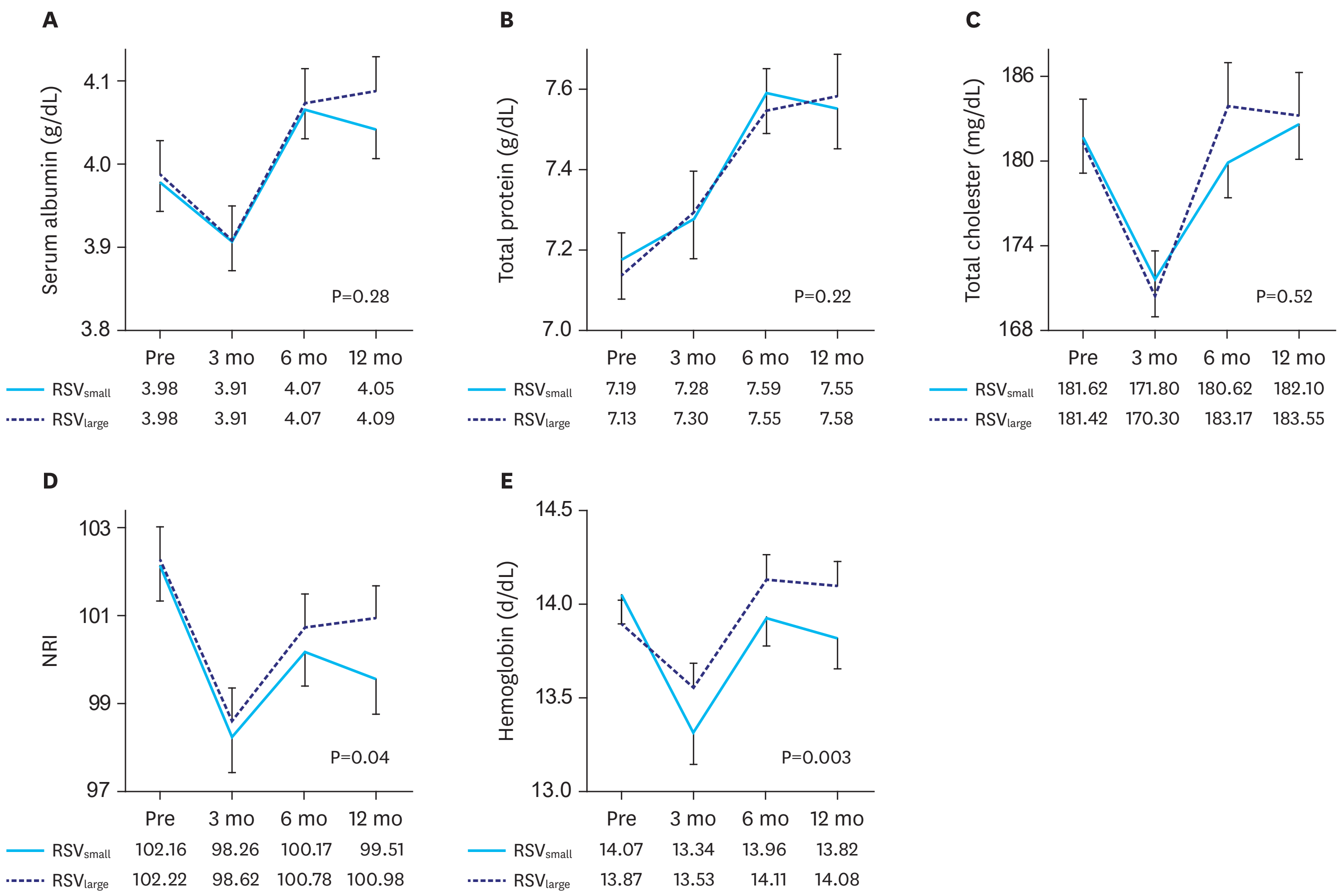

Fig. 4. Influence of RSV on nutrition- and anemia-related factors. RSV$_{small}$ group: RSV≤275 mm^3, RSV$_{large}$ group: RSV>275 mm^3. The RSV$_{large}$ group demonstrated a less decrease in NRI and hemoglobin over the year after surgery compared to the RSV$_{small}$ group.
RSV = residual stomach volume; NRI = nutritional risk index.

DISCUSSION

Gastrectomy is often followed by tormenting sequelae directly related to one of the most important functions of humans: eating [26]. It manifests as early satiety, dumping syndrome, reflux gastritis/esophagitis, and many other miscellaneous symptoms, leading to nutritional deficiency and significant weight loss [3,27,28].

The role of weight loss and sarcopenia in deteriorating surgical outcomes and quality of life after surgery has been extensively investigated across various fields of oncologic surgery over the past few years [29-35]. The results of previous studies affirmed the importance of nutritional assessment in patients undergoing cancer treatment.

Our previous study investigated the differences in nutritional parameters and body composition after gastrectomy according to anastomosis method and RSV. However, owing to the small patient cohort, adjustment for the anastomosis method to verify the impact of RSV was not possible. We performed the current study with a cohort of patients with stage I GC who underwent distal gastrectomy with Billroth 1 anastomosis to demonstrate the impact of RSV on postoperative nutrition and body composition.

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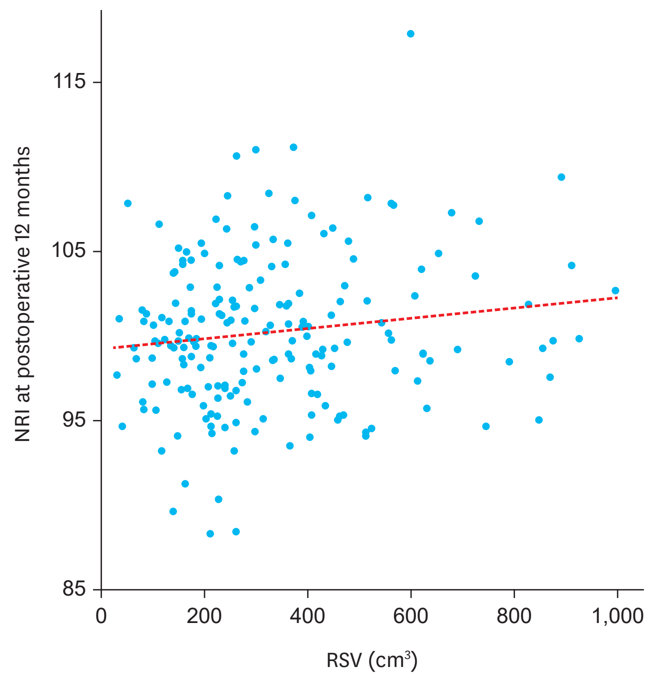

Fig. 5. Graph indicating the correlation between the RSV and NRI. A positive linear relationship with Pearson's coefficient of 0.134 was observed between the RSV (cm^3) and NRI at 12 months post-operatively (P=0.03).
RSV = residual stomach volume; NRI = nutritional risk index.

The RSV_{large} group showed less decrease and better recovery of hemoglobin levels and NRI after surgery, and less decrease in BMI relative to the RSV_{small} group. Moreover, a larger RSV demonstrated an advantage in the preservation and earlier recovery of muscles and adipose tissue after surgery. A larger RSV may be associated with delayed satiety and increased food intake, yielding better nutrition and metabolism. However, the amount of food intake in the patient group was not investigated in this analysis, and further studies are required to confirm this assumption.

Only patients diagnosed with stage I GC were included in the study for several reasons. Favorable long-term survival is expected for patients with stage I GC; therefore, postoperative nutrition and quality of life are considered more important in this cohort. In addition, an implicit bias according to chemotherapy, which is known to have a major impact on nutritional status [36,37], was eliminated. For this early stage patient group, surgeons also consider function preservation rather than standard radical gastrectomy while taking less risk of compromising imperative oncologic safety.

To the best of our knowledge, this is the first study to provide a quantified measurement of RSV after a specified operative method and to establish the association between RSV and various nutrition- and body composition-related parameters. The current findings suggest that the nutritional status and quality of life of patients after gastrectomy can be improved by maximizing the RSV while ensuring oncologic safety.

Our study had some limitations. We did not implement a quality-of-life questionnaire for this study and could not investigate whether the protective effect of preserving RSV led to an actual improvement in the quality of life that patients could perceive. Furthermore, we could not analyze the impact of RSV on postoperative complications and mortality as there was no

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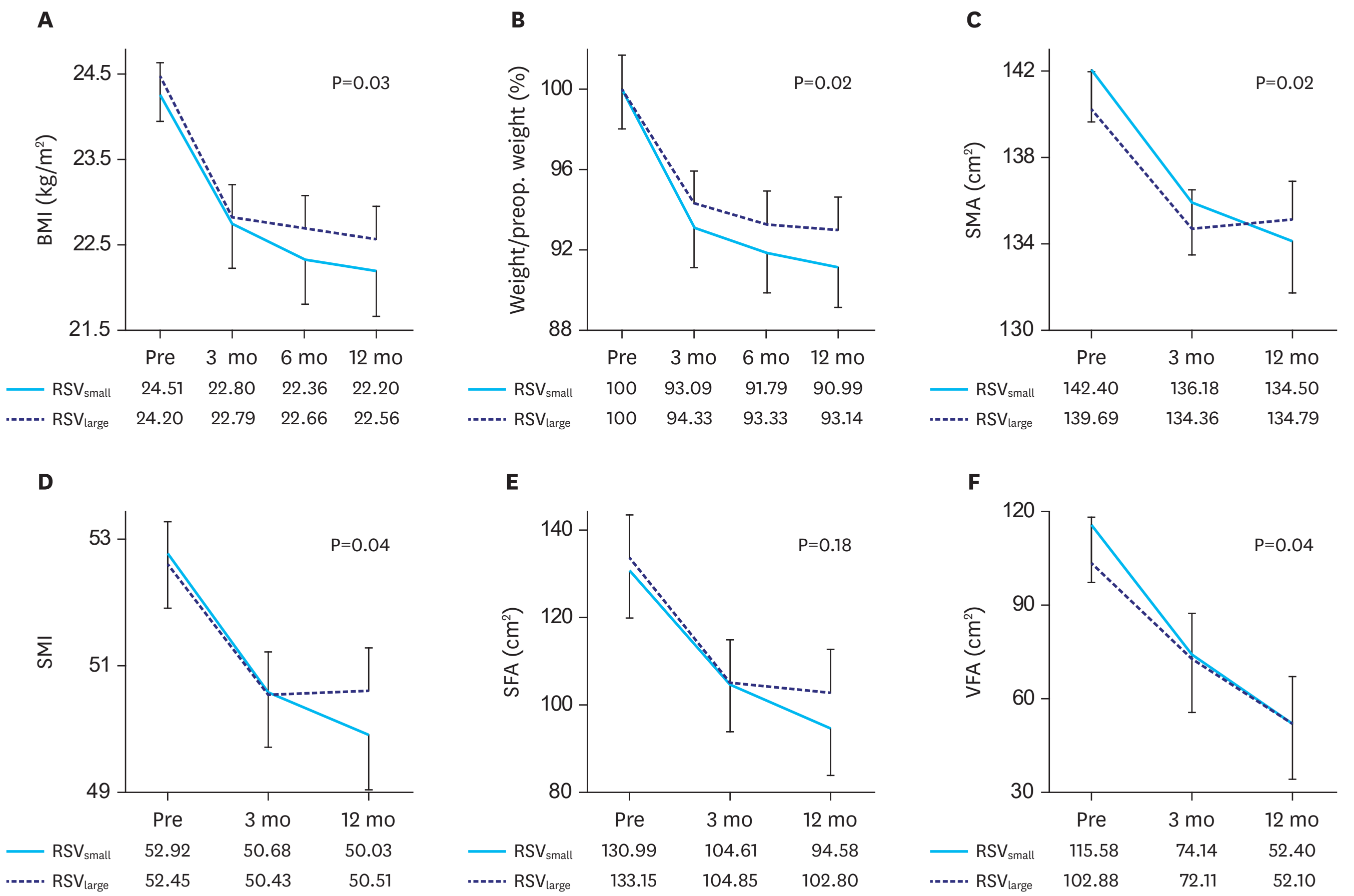

Fig. 6. Influence of RSV on body composition. RSV_{small} group: RSV≤275 mm³, RSV_{large} group: RSV>275 mm³. BMI and the proportion of postoperative weight over preoperative weight showed less decrease in the RSV_{large} group than in the RSV_{small} group. VFA, SMA, and SMI were better preserved in the RSV_{large} group.
BMI = body mass index; RSV = residual stomach volume; SMA = skeletal muscle area; SMI = skeletal muscle index; SFA = subcutaneous fat area; VFA = visceral fat area.

incidence among the included patients. Nevertheless, this is a preliminary small-scale study, and we are currently collecting extensive ongoing data for further research that will provide better insight into the significance of RSV from both nutritional and oncological standpoints.

In conclusion, a larger RSV was associated with improved nutritional status and preservation of visceral fat after distal gastrectomy with Billroth 1 anastomosis. Moreover, it promoted earlier recovery and preservation of skeletal muscle. Thus, we cautiously suggest that efforts should be made to secure maximum RSV while ensuring oncologic safety when distal gastrectomy is performed for patients with stage I GC.

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