

The investigation of diet recovery after distal gastrectomy

Tae-Han Kim, MD, PhD^a, Young-Joon Lee, MD, PhD^a, Kyungsoo Bae, MD, PhD^b, Ji-Ho Park, MD^a, Soon-Chan Hong, MD, PhD^a, Eun-Jung Jung, MD, PhD^a, Young-Tae Ju, MD, PhD^a, Chi-Young Jeong, MD, PhD^a, Tae-Jin Park, MD, PhD^a, Miyeong Park, MD, PhD^c, Ji Eun Kim, MD, PhD^b, Sang-Ho Jeong, MD, PhD^{a,*}

Abstract

This study aims to investigate the adaptation process of the alimentary tract after distal gastrectomy and understand the impact of remnant stomach volume (RSV) on diet recovery.

One year after gastrectomy, although patients' oral intake had increased, the RSV was decreased and small bowel motility was enhanced. Patients with a larger RSV showed no additional benefits regarding nutritional outcomes.

We prospectively enrolled patients who underwent distal gastrectomy with Billroth II reconstruction to treat gastric cancer at a tertiary hospital cancer center between September 2009 and February 2012. Demographic data, diet questionnaires, computed tomography (CT), and contrast fluoroscopy findings were collected. Patients were divided into 2 groups according to the RSV calculated using CT gastric volume measurements (large vs small). Dietary habits and nutritional status were compared between the groups.

Seventy-eight patients were enrolled. Diet volume recovered to 90% of baseline by the 36th postoperative month, and RSV was 70% of baseline at 6 months after surgery and gradually decreased over time. One year after surgery, small bowel transit time was 75% compared to the 1st postoperative month ($P < .05$); however, transit time in the esophagus and remnant stomach showed no change in any studied interval. Compared to patients with a small RSV, those with a large RSV showed no differences in diet volume, habits, or other nutritional benefits ($P > .05$).

Diet recovery for distal gastrectomy patients was achieved by increased small bowel motility. The size of the remnant stomach showed no positive impact on nutritional outcomes.

Abbreviations: AJCC = American Joint Committee on Cancer, BMI = body mass index, CT = computed tomography, EG = esophagogastric, GI study = gastrointestinal tract contrast fluoroscopy, GJ = gastrojejunostomy, PACS = Picture Archiving and Communication System, POM = postoperative month, RSV = remnant stomach volume.

Keywords: gastrectomy, gastric neoplasm, gastric stump, gastrointestinal motility

1. Introduction

Gastrectomy is the mainstay of treatment for gastric cancer.^[1,2] Curative distal gastrectomy includes resection of at least two-thirds of the stomach, involves the pylorus and distal antrum, and

is associated with lymph node dissection and division of the vagus nerve.^[2] Although small details might differ, all gastrectomized patients encounter anatomical rearrangement, an altered neural network and a shortened alimentary tract.^[3,4] In this process, patients suffer from symptoms related to eating restrictions (early satiety, pain, dysphagia, etc) and/or symptoms related to dumping syndrome (diarrhea, bloating, etc).^[5,6] These digestive symptoms affect insufficient food intake, resulting in malnutrition, a poor quality of life and possibly a poor oncologic outcome.^[7] From previous reports, the most severe forms of symptoms are experienced in the immediate postoperative phase and are slowly recovered over time, from 6 to 12 months after surgery.^[6,8] The restored diet volume has been limited to 67.5% to 80% of the preoperative diet volume in previous reports, and patients may not recover their normal diet volume at all.^[9]

The adaptation period after distal gastrectomy is time-consuming and inevitable; however, to date, its mechanism is poorly understood. This study is designed to investigate the adaptation process in patients who underwent distal gastrectomy and understand the impact of remnant stomach volume (RSV) on diet recovery after gastric resection.

2. Methods

A single arm, prospective observational study was designed and carried out according to the principles of the Declaration of

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THK and YJL contributed equally to the study.

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^a Department of Surgery, ^b Department of Radiology, ^c Department of Anesthesiology, Gyeongsang National University School of Medicine, Jinju, South Korea.

* Correspondence: Sang-Ho Jeong, Department of Surgery, Gyeongsang National University, Changwon Hospital, 11 Samjungja-ro, Sungsan-gu, Changwon-si, Gyeongsangnam-do 51472, South Korea (e-mail: jshgnu@gmail.com).

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Helsinki, 1989. Written consent was obtained from all participants before inclusion in the trial. This study was approved by the institutional review board (GNUH-IRB-5219).

2.1. Data collection

Consecutive patients who were diagnosed with gastric cancer and scheduled for a distal gastrectomy at Gyeongsang National University Hospital between September 2009 and February 2012 were enrolled in the study. Patients with the following factors were excluded from the study: additional cancer (including synchronous and metachronous double cancer); underwent total gastrectomy or partial gastrectomy other than distal gastrectomy; reconstruction method other than Billroth II anastomosis; severe peritoneal adhesion from previous abdominal surgery.

Demographic data (sex, age, body weight, operation methods, and pathologic reports) and nutritional outcomes (laboratory data included serum hemoglobin, albumin, and cholesterol tested at the 1st, 3rd, 6th, 12th, and 24th postoperative month [POM]) were collected from enrolled patients. Data were collected from an esophagogastroduodenoscopy, gastrointestinal tract contrast fluoroscopy (GI study), and abdominal computed tomography (CT) scans, which were performed before surgery and at the 6th, 12th, 24th, and 36th POM.

During the follow-up period, we dropped out patients who did not undergo CT scan or were lost to follow-up. Among the 78 patients, 15 dropped out at postoperative year 2 ($n=63$) and 7 at postoperative year 3 ($n=56$).

2.2. Questionnaire for diet configuration

To investigate diet patterns, a written questionnaire was collected from the participants. Variables regarding the diet configuration were studied, including oral intake volume, mealtime, homemade vs dine out, frequency, diet interval and exact length of time taken to consume each meal (minutes/meal). Diet volume was estimated in proportion to the preoperative intake volume (volume at the time of estimation/preoperative volume, %). The questionnaire was collected at the 1st, 3rd, 6th, 12th, 24th, and 36th POM, and each participant's diet recovery state was studied.

2.3. Motility study: gastrointestinal tract real-time contrast fluoroscopy

In our study, motility was reviewed by observing ingested barium contrast in the esophagus, remnant stomach, gastrojejunal anastomosis, and small bowel, including the terminal ileum (Fig. 1A). For the standardization of gastric distension, patients received a pack (4 g) of gas-producing granules (Robas granules; Dong In Dang, Gyeong-gido, Korea) with a small amount of water shortly before the study. After barium ingestion, the anteroposterior area and lateral area of the remnant stomach were calculated when contrast filling was observed in the remnant stomach (Fig. 1B–D), and the outcomes were compared between measurement times (6th, 12th, 24th, and 36th POM).

The transit time from the esophagogastric junction to the gastrojejunal junction site (EG to GJ transit time) was measured under fluoroscopic monitoring (Fig. 1A and B) in an upright

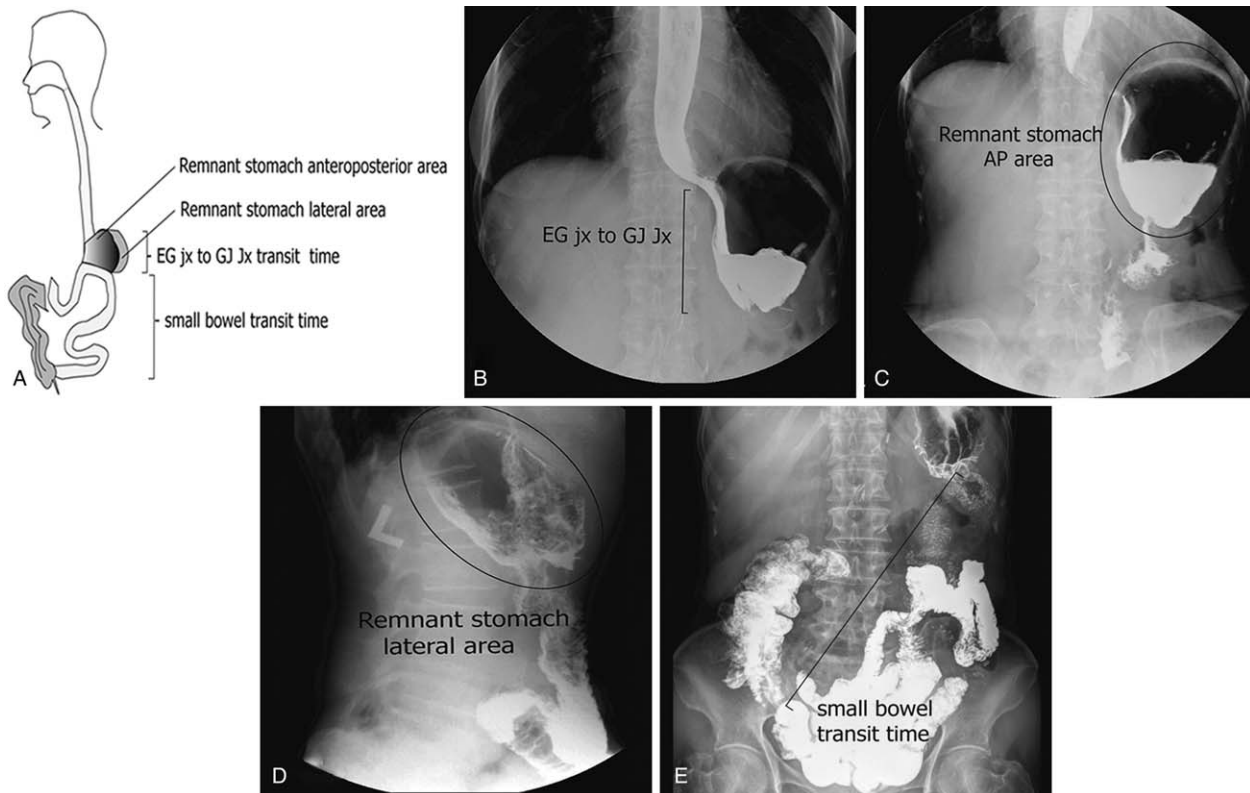


Figure 1. (A) Schematic of the measurement of remnant gastric volume and transit time using barium upper gastrointestinal and small bowel series (UGI & SBS). (B) After the patient ingested barium, transit time was measured from the esophagogastric junction (EG jx) to the gastrojejunal junction site (GJ jx). (C) Anteroposterior (AP) and (D) lateral areas after filling the remnant stomach. (E) Transit time was measured from the gastrojejunal junction to the terminal ileum (small bowel transit time).

position. The transit time from the gastrojejunal anastomosis to the ileocecal valve was measured by prone overhead imaging along the abdomen every 30 minutes (small bowel transit time) (Fig. 1A, B, and E). The transit times were compared over time.

2.4. Gastric volume study: computed tomography volumetry

The change in gastric volume after gastrectomy was reviewed using CT volumetry. For the preparation of the study, after 8 hours of prestudy fasting, 10 mg of scopolamine (Buscopan; Boehringer Ingelheim, Seoul, Korea) was administered via IV injection. Then, patients received the gas-producing granules (Robas granules, 4g/pack; Dong In Dang): 2 packs for the preoperative study and 1 pack for gastrectomized cases for standardized gastric distension before the CT scan.

After axial CT images were obtained in a 3-mm thickness, a 2-dimensional volumetric analysis was performed. The entire perimeter of the gastric image was outlined on each slice using a Picture Archiving and Communication System (PACS) workstation (Impax 5.3; Agfa, Mortsel, Belgium) (Fig. 2A–D). After integrating the area measured on each slice, gastric volume (cm^3) was calculated by multiplying the summed area (cm^2) by the slice thickness (3 mm). Gastric volume before the operation and at the 6th, 12th, 24th, and 36th POM was studied (Fig. 2E).

To investigate the nutritional benefits of a larger RSV, the patients were divided into 2 groups based on mean CT gastric volume of patients (CT gastric volumes at [POM 6 + 12 + 24 + 36]/4). The larger RSV half of the patients were allocated to the L group, and the smaller RSV half of the patients were allocated to the S group. Dietary habits, nutritional status, and reflux status were compared between the 2 groups.

2.5. Statistical analysis

A paired *t* test was used for the statistical analyses, conducted with SPSS version 24.0 (SPSS, Chicago, IL). A *P*-value of $<.05$ (2-sided) was considered statistically significant.

3. Results

3.1. Patient demographics

In total, 78 patients were enrolled in this study. The male to female ratio was 2:1, and the mean patient age was 62.1 ± 10.7 years. The majority of tumor locations were in the lower 3rd of the stomach (89.7%, $n=70$), and most of the patients were pathologic stage I according to the American Joint Committee on Cancer (AJCC) 7th staging system (73.1%, $n=50$). Regarding the surgical approach, laparoscopic surgery was performed in

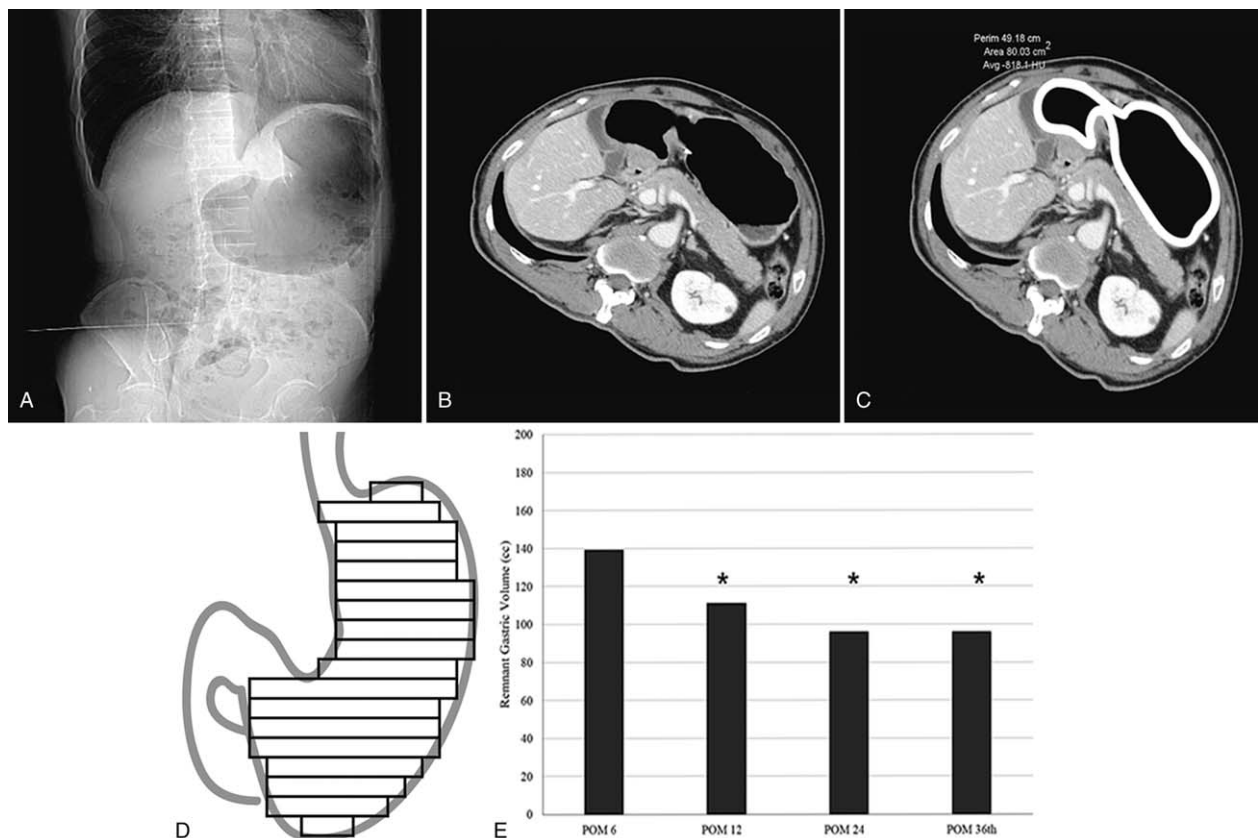


Figure 2. Schematic of the calculation of gastric volume using abdominal computed tomography (CT). (A) CT scout image of the abdomen. (B) Distension of the stomach using CT with gas-producing granules. (C) Gastric volume calculated using a PACS workstation (Impax 6; Agfa HealthCare, Canton, MA). (D) Summation of all measurements. (E) Bar chart showing the remnant gastric volume, which was calculated using 3-dimensional enhanced CT at postoperative months (POM) 1, 3, 6, 12, 24, and 36. $P > .05$.

Table 1	
Clinical and demographic characteristics.	
Variables	
Age	61.1 ± 10.7
Sex	
Male	52 (66.7%)
Female	26 (33.3%)
Body weight, kg	62.0 ± 11.4
BMI	22.8 ± 4.2
Tumor location	
Middle 3rd of stomach	8 (10.3%)
Lower 3rd of stomach	70 (89.7%)
Tumor size	3.0 ± 2.0
Retrieved nodes	26.9 ± 13.9
TNM stage	
I	57 (73.1%)
II	14 (17.9%)
III	7 (9%)
Surgical approach	
Open	14 (18%)
Laparoscopy	64 (82%)

BMI=body mass index, TNM stage (AJCC 7th edition).

82% (n = 64) of the patients and the open method was performed in 18% (n = 14) (Table 1).

3.2. Nutritional outcomes after gastrectomy

The patients' preoperative (initial) mean body weight was 61.9 ± 11.3 kg, and after a 10% decrease during the 1st POM (56.8 ± 9.9 kg, $P < .01$), weight loss was continued until 1 year after the operation (56.3 ± 9.4 kg, $P < .01$). Body weight gradually increased between the 1st and 2nd year after surgery (56.3 ± 9.4 kg vs 57 ± 9.4 kg, $P < .01$), and patients reached a plateau between the 2nd and 3rd year after surgery (57.2 ± 8.2 kg) (Fig. 3A).

The mean initial hemoglobin level was 12.2 ± 3.9 g/dL, and it decreased to 10.7 ± 3.7 g/dL 1 month after gastrectomy ($P < .01$). Recovery started at the 3rd POM (11.2 ± 3.8 g/dL) and was fully recovered by the 6th POM (12.5 ± 2.2 g/dL, $P < .01$) (Fig. 3B).

The mean initial albumin level was 4.1 ± 0.4 g/dL, which had a 10% decrease during the 1st POM (3.8 ± 0.4 g/dL, $P < .01$) and then recovered to baseline levels (4.1 ± 0.3 g/dL) by the 3rd POM (Fig. 3C). Regarding the cholesterol levels, there were no statistical changes during the study period (Fig. 3D).

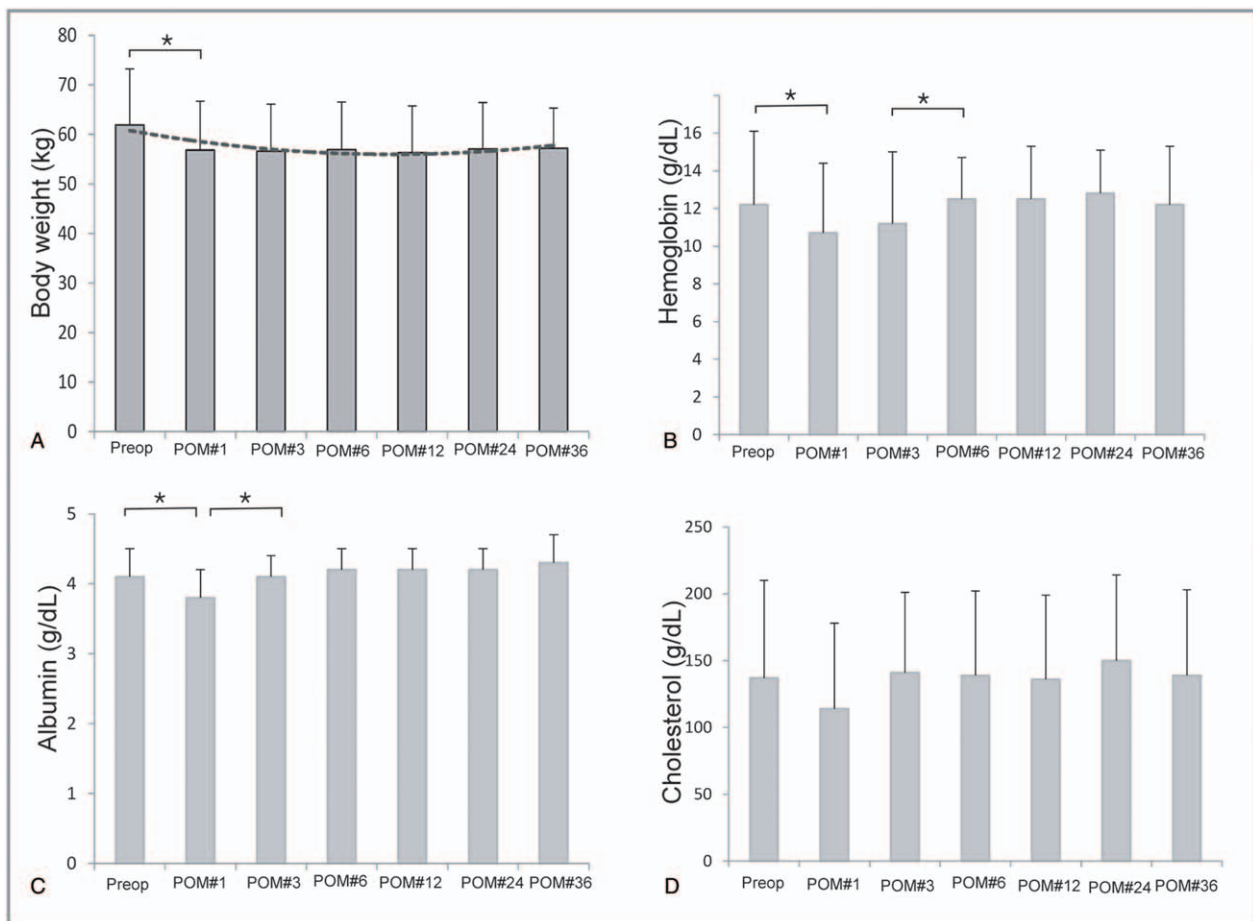


Figure 3. Assessment of nutritional status by (A) body weight (kg), (B) serum hemoglobin (g/dL), (C) albumin (g/dL), and (D) cholesterol (g/dL) at postoperative months (POM) 1, 3, 6, 12, 24, and 36.

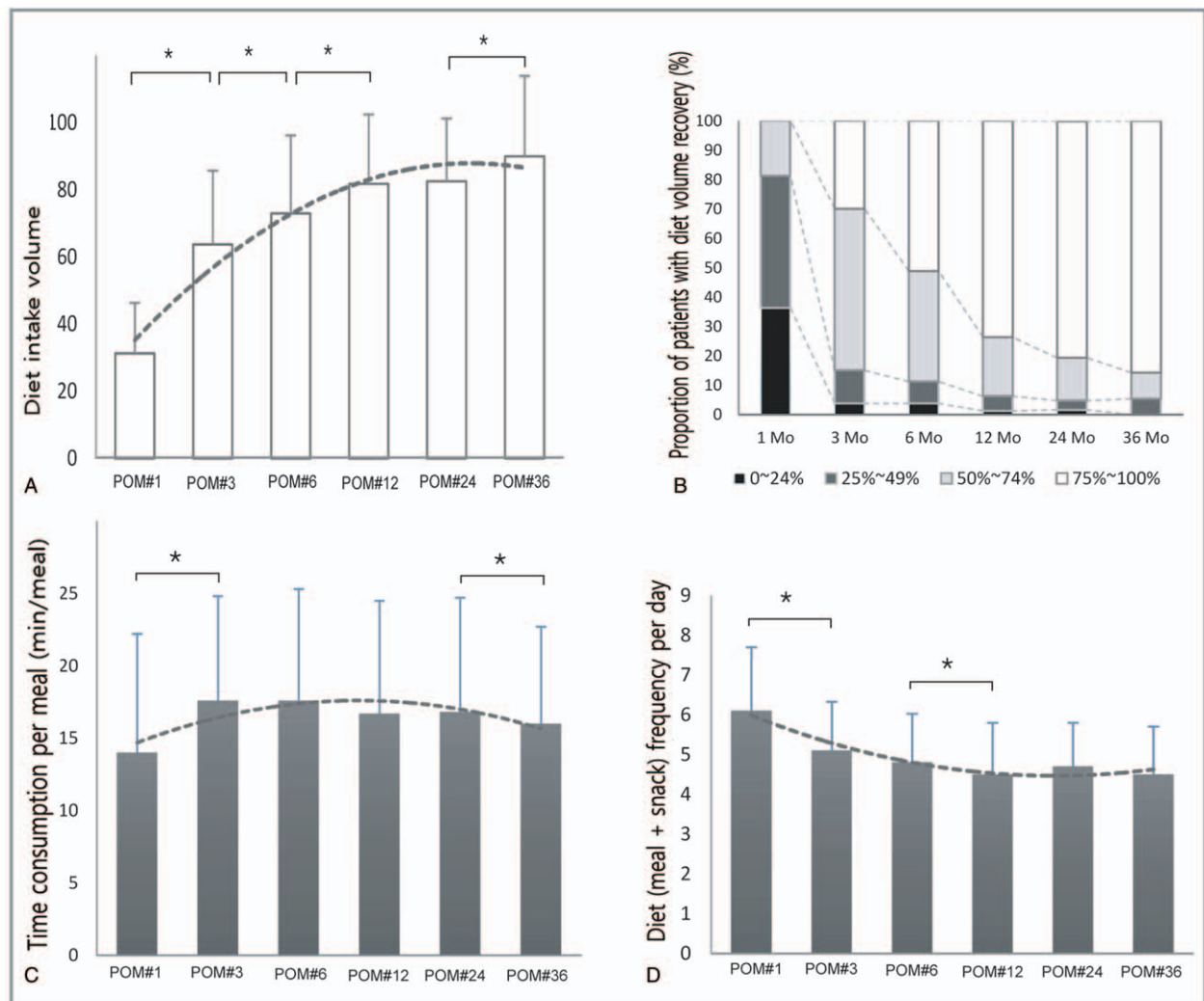


Figure 4. Analysis of dietary habits according to (A) diet amount, (B) proportion of patients per preoperative diet amount quartile (0–24%, 25–49%, 50–74%, 75–100%), (C) mealtime length (Min, min), (D) diet frequency (main meal + snack, number of times) at postoperative months (POM) 1, 3, 6, 12, 24, and 36. * $P > .05$.

3.3. Diet configuration

According to the diet questionnaire, considering the preoperative diet volume as 100%, the patients' diet intake volume decreased to 31.5% ($P < .05$) 1 month after surgery (Fig. 4A). Three months after surgery, the intake volume had increased to 63.7%, followed by 72.9% at the 6th POM and 81.7% at the 12th POM. The intake volume had recovered to 82.5% of the preoperative volume at the 24th POM and 90% at the 36th POM. The intake volume increased with statistical significance at all the studied intervals except one, between the 12th and 24th POM.

The proportion of patients with diet volume recovery is depicted for each quartile of preoperative diet volume in Figure 4B. Six months after gastrectomy, half of the patients were able to consume more than 75% of their preoperative volume. Two years after gastrectomy, 95% of the patients were able to consume more than 75% of their preoperative volume.

Time consumption per meal was 14.0 ± 8.2 minutes/meal at the 1st POM (Fig. 4C). The length of time increased and reached a plateau by the 3rd POM (17.6 ± 7.2 minutes/meal, $P < .05$),

which lasted until the 2nd year, and then decreased during the 3rd year after surgery to 16 ± 6.7 minutes/meal ($P < .05$).

Diet (meal + snack) frequency per day was 6.1 ± 1.6 times/d at the 1st POM. The diet frequency was decreased at the 3rd and 12th POM and reached a plateau over time, after the 2nd year (Fig. 4D).

3.4. Contrast real-time fluoroscopy

In the GI study, the mean anteroposterior surface area of the remnant stomach showed no difference between the 1st and 3rd POM (52.4 ± 29.2 vs 51.8 ± 27.2 cm², $P > .05$). Six months after surgery, this area had significantly decreased (43.9 ± 18.6 cm², $P < .05$), and it reached a plateau until 1 year after surgery (42.2 ± 14.5 cm², $P > .05$) (Fig. 5A). At the same time, the lateral surface area of the remnant stomach showed no difference in any studied period after gastrectomy ($P > .05$) (Fig. 5B).

There were no changes regarding barium transit time from the esophagus to the gastrojejunostomy site throughout the study (Fig. 5C). The small bowel transit time was 133.5 ± 61.7 minutes, 129.6 ± 49.5 minutes, and 126.3 ± 42.2 minutes at the 1st, 3rd

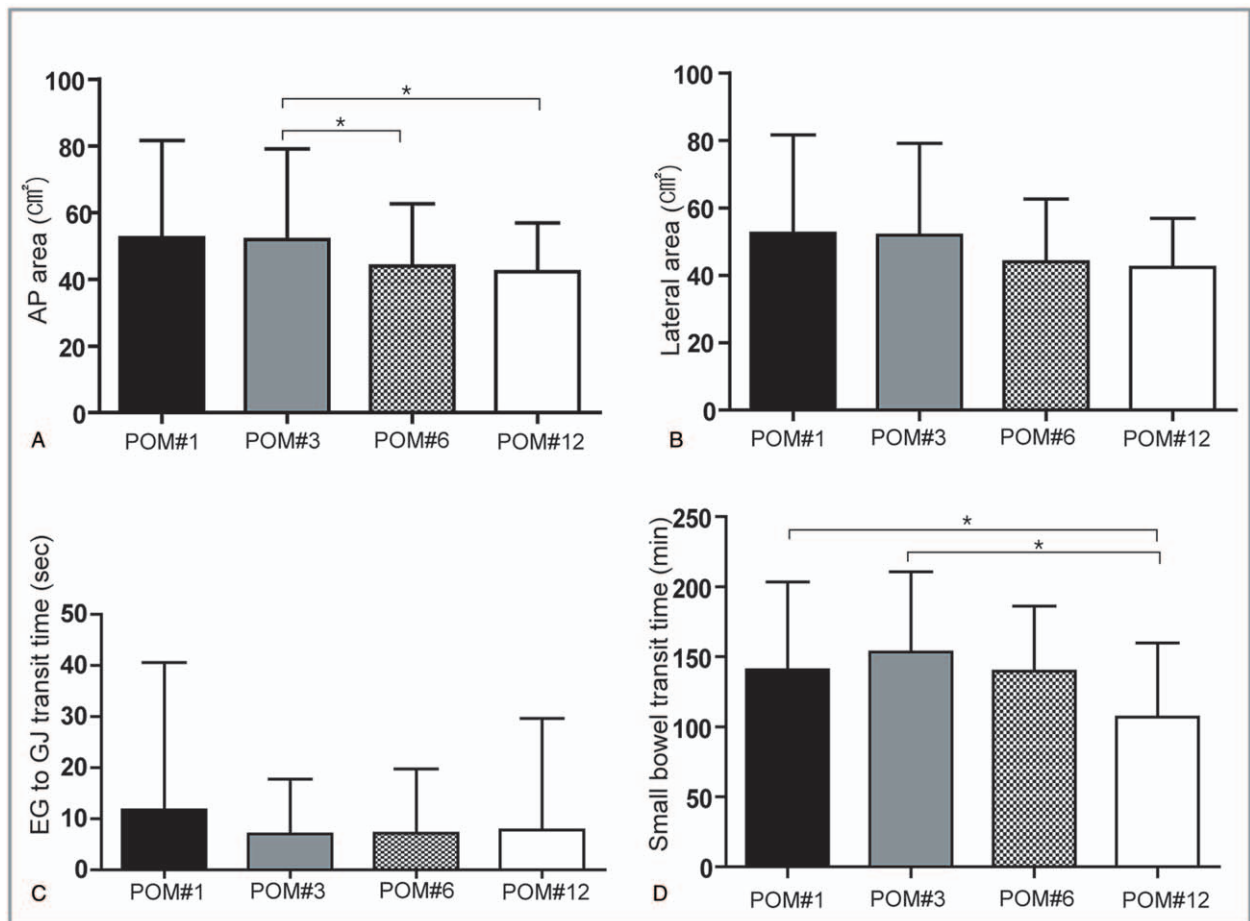


Figure 5. Serial changes in the remnant stomach area and transit time using barium upper gastrointestinal and small bowel series at postoperative months (POM) 1, 3, 6, and 12. (A) Serial changes in the anteroposterior (AP) area (cm²). (B) Serial changes in the lateral area (cm²). (C) Serial changes in transit time from the esophagogastric junction (EG jx) to the gastrojejunostomy site (GJ jx) (EG to GJ transit time, s). (D) Serial changes in transit time from the gastrojejunal junction to the terminal ileum (small bowel transit time, min).

and 6th month after gastrectomy, respectively, and showed no significant change during this period ($P > .05$). One year after surgery, the transit time had decreased to 105.1 ± 40.4 minutes, which was significant compared to other time points ($P < .05$, vs 1st and 3rd POM small bowel transit time) (Fig. 5D).

3.5. Changes in the remnant stomach volume after gastrectomy

From the CT volumetry, the mean baseline gastric volume was 605 ± 276 mL. Six months after surgery, the mean gastric volume was 139 ± 81 mL, which decreased to 111 ± 64 mL 1 year after surgery ($P < .01$) and to 96 ± 54 mL 2 years after surgery ($P = .07$). This decrease was maintained until the 3rd year after surgery (96 ± 55 mL, $P = .79$) (Fig. 2E).

3.6. Small vs large remnant stomach volume: diet configuration and nutrition status

According to the CT volumetric database, patients were divided into 2 groups (S group ≤ 110 mL vs L group > 110 mL) based on the median value of the RSV (110 mL). After allocation, the mean RSV was larger in the L group than in the S group (195 mL vs 90

mL, $P < .01$) (Fig. 6). Between the groups, there were no differences regarding nutritional outcomes (body weight change, hemoglobin, albumin, cholesterol) or diet configuration (diet volume, diet frequency, time consumption per meal).

4. Discussion

The present study was conducted to investigate the mechanism of diet recovery after distal gastrectomy and identify the influence of gastric volume on nutritional outcomes. We compared each step of the alimentary tract at different time intervals in regard to anatomical and functional aspects and included a patient-oriented survey. In our study, remnant gastric volume decreased over time and small bowel motility was enhanced after gastrectomy. Patients with a larger remnant gastric volume showed no additional benefits regarding nutritional outcomes. Based on these results, after gastrectomy, diet volume is recovered by the acceleration of small bowel motility, while the RSV has a limited effect.

Regarding food intake, increased food or volume tolerance is not due to an increase in gastric volume; however, the gastric emptying rate is associated with a decreased transit time of the small intestine.^[10,11]

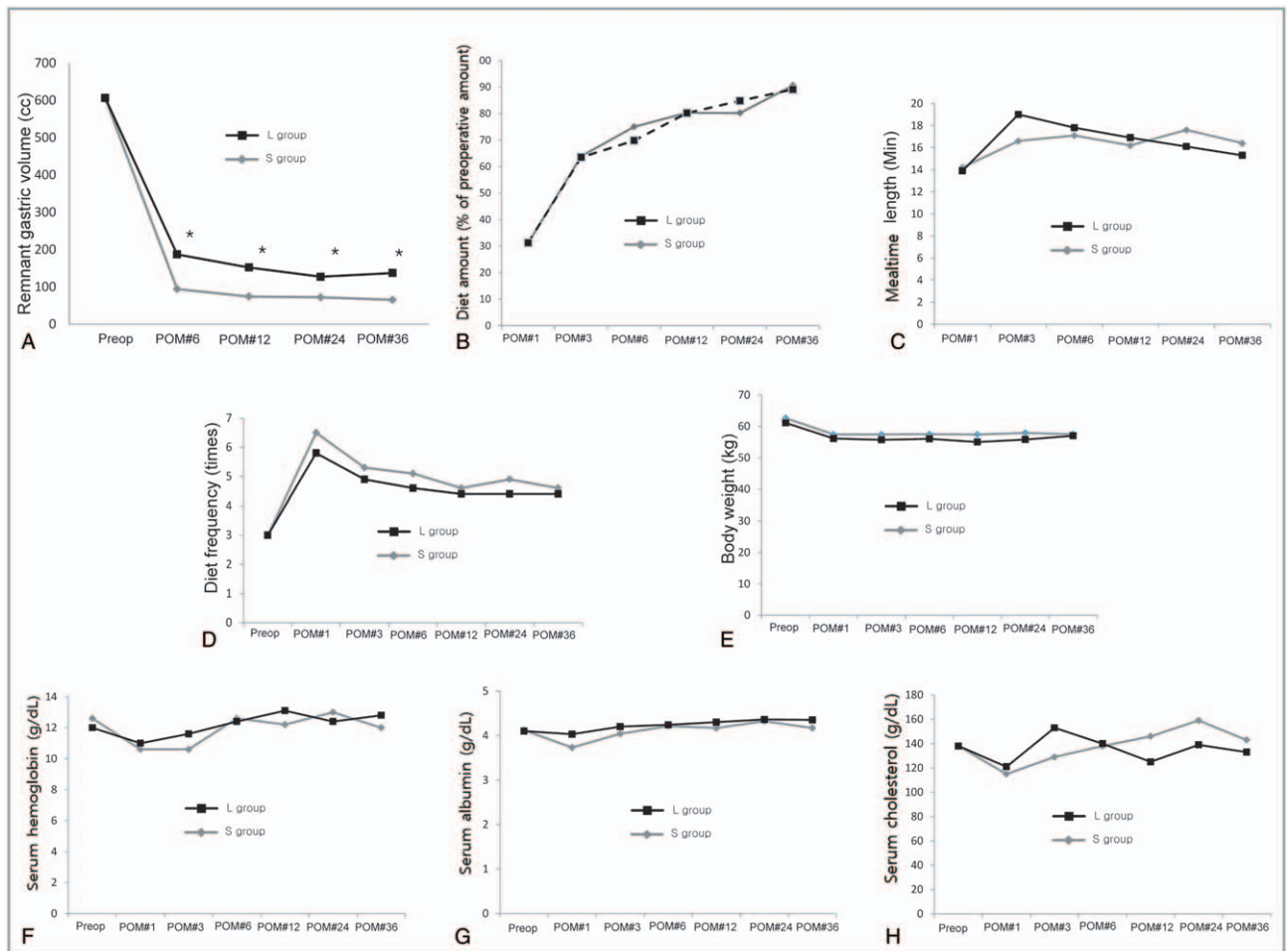


Figure 6. (A) Gastric volume was calculated using 3-dimensional enhanced computed tomography and compared to the remnant gastric volume for the S and L groups. We assessed dietary habits according to (B) diet amount, (C) mealtime length (Min, min), and (D) diet frequency (main meal + snack, number of times), and we assessed nutritional status according to (E) body weight (kg), (F) serum hemoglobin (g/dL), (G) serum albumin (g/dL), and (H) serum cholesterol (g/dL) at postoperative months (POM) 1, 3, 6, 12, 24, and 36. S group, small remnant stomach group, ≤110 mL; L group, large remnant stomach group, >110 mL. *P* > .05.

The gastrointestinal system plays a pivotal role in the control of food consumption, digestion, and nutrient absorption. The successful execution of these physiologic functions depends on intact coordination between neural innervation, intestinal receptors, and various gut hormones. Their integrated output regulates the rate at which nutrients are processed and participates in the control of appetite and satiety.^[12–14] Faster gastric emptying may lead to symptoms such as fullness, bloating, nausea, and pain secondary to distention, as well as increased or earlier secretion of gastrointestinal peptides, such as cholecystokinin and glucagon-like peptide 1, in response to the increased nutrient load to the small intestine.^[15] These peptides may increase symptom perception (satiety, hunger, nausea) through the activation of vagal afferents, which may partly explain the earlier satiation and increased symptoms after meals in patients with functional dyspepsia with/without increased gastric emptying.

Previous investigations regarding gastrointestinal motility after gastrectomy have shown that bowel motility is enhanced after gastrectomy.^[16,17] Under scintigraphic review, small bowel movement is increased after distal gastrectomy compared to the preoperative state, and this finding is more prominent in patients who undergo total gastrectomy.^[18–20]

Neural innervation is supplied by both the vagus nerve and the splanchnic nerves. The former provides sensory fibers exclusively to the gut, whereas the latter contain fibers originating from both the gut and the mesentery. The vagus nerve, especially the celiac branch, contains parasympathetic preganglionic fibers and controls alimentary tract movements and pancreatic endocrine secretion.^[21,22] Radical gastrectomy, performed for gastric cancer, usually involves a section of the vagus nerve and may require division from the jejunum and mesentery according to the type of reconstruction, followed by radical node dissection, which all together results in injury to the nerve endings of the vagus and/or splanchnic nerves.^[5] This surgical denervation results in a fast bowel transit time, which is considered a major determinant of postoperative diarrhea and alterations in serum glucose control.^[23] Likewise, patients who underwent vagus nerve preserved gastrectomy have shown less weight loss and shorter-term diarrhea than conventional gastrectomized groups in previous reports.^[15,24,25]

Since the ratio of vagal to splanchnic afferent fibers is typically lower in the jejunoileal region than in the gastroduodenal area, splanchnic nerve stimulation via the distal small bowel is considered to restore gastrointestinal motility.^[26] This is

mediated by chemoreceptors, osmoreceptors, and mechanoreceptors that are involved in tonic (maintaining smooth muscle tone) or phasic (facilitating the progression of peristaltic waves) motility actions of the small intestine.^[26] After the rapid introduction of fluids, electrolytes, or malabsorbed nutrients, these various receptors promote bowel motility via the splanchnic nerve pathway.^[26] In 1 study, small bowel motility 4 weeks after sleeve gastrectomy was compared to the preoperative small bowel transit time, and the results showed that gastric resection accelerated gastric emptying and small bowel transit in addition to causing a cecal filling delay.^[18] Food contact time with the area of the terminal ileum increases after sleeve gastrectomy due to neuronal, humoral, and local stimuli. This accelerated ileal action may be supported and accompanied by a change in bile metabolism, transport, and hepatic circulation after surgery.^[27]

The clinical impact of gastric fundus is beyond the reservoir function of the stomach.^[28] Growing evidence indicates that weight loss and nutritional changes after gastrectomy are not only caused by anatomical changes following gastric surgery but also occur in parallel with alterations in factors such as ghrelin, a gut hormone released from gastric fundus that is known to increase the appetite.^[29] Ghrelin results in weight gain via central nervous system stimulation by involving hypothalamic neuropeptides, which are associated with other metabolic functions, such as increased appetite, metabolic rate regulation, and growth hormone release.^[30] In previous reports, while no additional nutritional benefit has been reported with simple reservoir procedures such as pouch reconstruction after total gastrectomy, the extent of the resection and the length of the bypassed intestinal tract after gastric cancer surgery results in a worse quality of life and inferior nutritional outcomes.^[5,31–34] Similar results were shown in our study; in spite of a larger remnant stomach, the L group showed no nutritional benefit over the S group. The limited nutritional benefits despite a larger remnant stomach may be due to patients having undergone a similar type of distal gastrectomy, the degree of the vagotomy, or a random distribution of ghrelin-producing cells in the upper 3rd of the stomach that does not correlate with the removed area of the fundus.^[35,36]

With improvements in postgastrectomy symptoms, patients' diet intake volume slowly increases after gastrectomy.^[9] On the contrary, in the present study, the RSV was decreased by 30% after surgery and reached a plateau without recovery. This study is the 1st to report that the remnant stomach shows shrinkage over time, inverse to the patients' intake volume after gastrectomy. There are several explanations for this phenomenon. First, the vagotomy may have resulted in the atony of the remnant stomach and atrophy of the gastric structure. An increased prevalence of gastric atony was reported in a series of patients who underwent truncal vagotomy with a drainage procedure for peptic ulcers, where neural stimulation is required to maintain smooth muscle tone for remnant stomach tissue.^[37,38] Second, since the short gastric artery is the only feeding artery to the remnant stomach, a limited blood supply could have influenced the volume of the remnant stomach. Third, the functional role of the pylorus and the distal part of the stomach, which controls the gastric outlet and creates a reverse force of gastric content to inflate the fundus, is reduced after gastrectomy.

In 1 recent analysis, Furukawa et al compared patients who underwent subtotal gastrectomy with a very small remnant stomach to proximal gastrectomy and total gastrectomy patients, and showed that even a small remnant stomach results in lower

body weight, better albumin levels and less anemia.^[39] In our study, there were no differences in dietary configurations (diet intake volume, meal frequency per day, and time consumption per meal) or nutritional outcomes between patients with small RSV and patients with large RSV. Regardless of the RSV size, from our results, it is important to preserve the stomach as much as possible.

There are some issues to be addressed in our study. First, the study was based only on a Billroth II anastomosis. In addition to gastroduodenostomy, in distal gastrectomy, this method results in the least damage of the mesentery and jejunal limb; therefore, it was considered the most suitable model for investigating the influence of gastric resection, vagotomy, and node dissections alone. However, this implies that the scope of our study is limited, and an attempt to include additional procedures, such as a Braun anastomosis or Roux en Y reconstructions after distal gastrectomy, should be considered in future studies. Additional well-designed studies using various reconstruction methods are necessary.

Another limitation is that gut hormones were not studied in the current series. A comparison of the ghrelin levels between the large and small remnant stomach groups would have provided stronger evidence for this work. Since the patient questionnaire was obtained directly from a large number of patients over a considerable period of time, it was quite an effort to collect such a large volume of data. However, the questionnaire was mostly focused on the patient as an individual, and thus patients were eager to play the role of a "better patient." One possible method to overcome this problem is to collect photographs or footage of the meals, but this was not applied in our study. To add, there might be some association of immunopathologic conditions including gut flora change before and after gastrectomy that affect diet recovery, however, was not considered in our study.^[40,41]

A highlight of our study is that it is the 1st study to collect large-scale, long-term data on changes in the remnant stomach and to elucidate the mechanism of diet recovery in gastrectomy patients.

In conclusion, diet recovery in distal gastrectomy patients was achieved by increased small bowel motility. The size of the remnant stomach showed no positive nutritional effects.

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Author contributions

Conceptualization: Young-Joon Lee, Sang-Ho Jeong.

Data curation: Kyungsoo Bae, Ji-Ho Park, Eun-Jung Jung,

Young-Tae Ju, Chi-Young Jeong, Ji Eun Kim, Sang-Ho Jeong.

Formal analysis: Young-Joon Lee.

Funding acquisition: Soon-Chan Hong, Young-Tae Ju, Chi-Young Jeong.

Methodology: Kyungsoo Bae, Miyeong Park, Ji Eun Kim.

Software: Tae-Jin Park.

Supervision: Soon-Chan Hong.

Validation: Tae-Jin Park, Miyeong Park.

Writing – original draft: Tae-Han Kim, Sang-Ho Jeong.

Writing – review & editing: Ji-Ho Park, Eun-Jung Jung, Sang-Ho Jeong.

Sang-Ho Jeong orcid: 0000-0001-9061-6236.

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