



Original Article

Development and Internal/External Validation of a Prediction Model for Weight Loss Following Gastric Cancer Surgery: A Multicenter Retrospective Study

Ji-Hyeon Park^{1,2}, Seong-Ho Kong^{1,3}, Do Joong Park^{1,3}, Han-Kwang Yang^{1,3}, Jong Won Kim⁴, Ki Bum Park⁵, In Cho⁶, Sun-Hwi Hwang⁷, Dong-Wook Kim⁸, Su Mi Kim⁹, Seung-Wan Ryu¹⁰, Seong Chan Gong¹¹, Pil Young Jung¹¹, Hoon Ryu¹¹, Sung Geun Kim¹², Chang In Choi¹³, Dae-Hwan Kim¹³, Sung-IL Choi¹⁴, Ji-Ho Park¹⁵, Dong Jin Park¹⁶, Gyu-Yeol Kim¹⁶, Yunhee Choi¹⁷, Hyuk-Joon Lee^{1,3}

¹Department of Surgery, Seoul National University Hospital, Seoul, ²Department of Surgery, Gachon University Gil Medical Center, Incheon, ³Department of Surgery and Cancer Research Institute, Seoul National University College of Medicine, Seoul, ⁴Department of Surgery, Chung-Ang University Hospital, Seoul, ⁵Department of Surgery, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Seoul, ⁶Department of Surgery, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, Bucheon, ⁷Department of Surgery, Pusan National University Yangsan Hospital, Yangsan, ⁸Department of Surgery, Dankook University College of Medicine, Cheonan, ⁹Department of Surgery, CHA Bundang Medical Center, CHA University, Seongnam, ¹⁰Department of Surgery, Keimyung University School of Medicine, Daegu, ¹¹Department of Surgery, Yonsei University Wonju College of Medicine, Wonju, ¹²Department of Surgery, The Catholic University of Korea Yeouido St. Mary's Hospital, Seoul, ¹³Department of Surgery, Pusan National University College of Medicine, Busan, ¹⁴Department of Surgery, Kyung Hee University Hospital at Gangdong, Seoul, ¹⁵Department of Surgery, Gyeongsang National University College of Medicine, Jinju, ¹⁶Department of Surgery, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, ¹⁷Department of Medical Research Collaborating Center, Seoul National University Hospital, Seoul, Korea

ABSTRACT

Purpose: To develop an individualized model for predicting the extent of unintentional weight loss following gastrectomy in patients with gastric cancer based on related risk factors and to externally validate this model using multicenter clinical data in Korea.

Materials and Methods: Among gastric cancer patients who underwent curative gastrectomy at 14 different gastric cancer centers, clinical data from patients with more than one weight measurement during the three-year follow-up period were retrospectively collected. Risk factors associated with weight loss in gastric cancer patients after gastrectomy were analyzed, and a predictive model was developed. Internal and external validation were performed.

Results: The data from 2,649 patients were divided into a derivation set (n=1,420 from Seoul National University Hospital) and validation set (n=1,229 from 13 different gastric cancers). Postoperative duration (six vs. 12, 24, or 36 months), sex (female vs. male), age, preoperative body mass index, type of surgery (pylorus-preserving vs. total, distal or proximal gastrectomy), and cancer stage (I vs. II or III) were included in the final prediction model. The model showed approximately 20% accuracy in predicting weight loss at each period: R2 at six, 12, 24 and 36 months after gastrectomy in internal validation=0.20, 0.21, 0.17, and 0.18, respectively, and in external validation=0.20, 0.22, 0.18, and 0.18, respectively. Calibration slopes of internal and external validation were 0.95 and 1.0, respectively.

Conclusion: Although predictive accuracy of the model did not reach an acceptable level, repeated external validation measurements showed high reliability. The model may serve as a basic reference in clinical practice.

Keywords: Gastrectomy; Risk factors; Stomach neoplasms; Validation study; Weight loss

Received October 11, 2022; Revised November 12, 2022; Accepted November 15, 2022

Corresponding author: Hyuk-Joon Lee

E-mail appe98@snu.ac.kr ORCID <https://orcid.org/0000-0002-9530-647X>



This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Copyright © The Korean Society of Surgical Metabolism and Nutrition · The Korean Society for Parenteral and Enteral Nutrition.

INTRODUCTION

The diagnosis rate of early gastric cancer has increased remarkably, and radical gastrectomy is the most effective treatment for gastric cancer [1]. Although there are patients with gastric cancer who complain of significant weight loss due to the gastric cancer before surgery, the anatomical changes of the stomach and small bowel after gastrectomy create a higher possibility of weight loss in the short- or long-term post-surgically [2-4]. While mild weight loss is associated only with decreased quality of life (QoL) [5,6], postoperative unintentional severe weight loss may lead to shorter survival [7-9].

As minimally invasive surgery, surgeons' skill levels and pre- and post-operative nutritional supplementation management have improved, the rate of significant weight loss after surgery for gastric cancer is gradually decreasing. However, in 10%~20% of patients, significant unintentional weight loss after gastrectomy has been reported in recent studies [10,11]. The risk of unintended post-surgical weight loss is a common pre-surgical concern of gastric cancer patients, and gastric cancer surgeons have become increasingly aware of the importance of postoperative nutritional management.

Postoperative nutritional supplementation to support malnourished patients after gastrectomy has been a topic of research [12,13], and we sought to develop a tool to allow for screening of patients who may become malnourished after gastrectomy to ensure active nutritional support before and after surgery. We recently studied the pattern of body mass index (BMI) loss over time after gastrectomy using a group-based trajectory model and developed a prediction model for screening patients at risk of malnutrition six months post-gastrectomy [11,14]. During this process, we identified the need for a tool for predicting the extent of weight loss in each patient after gastrectomy. A few studies that identify risk factors for weight loss after gastrectomy in patients with gastric cancer have been conducted [15-17]. However, externally verified models for predicting the magnitude of weight loss at specific time points after gastrectomy based on these independent risk factors are lacking.

The purposes of this study were to develop a predictive model for percentage (%) weight loss after gastrectomy and to perform external validation of this model using multicenter clinical data. Through the external validation process, our goal was to develop a clinically applicable model.

MATERIALS AND METHODS

1. Study design and ethical statement

This was a retrospective multicenter study in Korea. All participating institutions have received research approval for this study from their Institutional Review Boards: Seoul National University Hospital (SNUH, H-2101-007-1184), Chung-Ang University Hospital (2110-036-19390), The Catholic University of Korea St. Vincent's Hospital (XC21RCDI0003V), Soon-

chunhyang University Bucheon Hospital (2021-02-027-001), Pusan National University Yangsan Hospital (05-2021-055), Dankook University Hospital (2020-12-026), CHA Bundang Medical Center (2020-12-052), Keimyung University Dong-san Medical Center (2021-01-053), Yonsei University Wonju Severance Christian Hospital (CR320169), The Catholic University of Korea Yeouido St. Mary's Hospital (020-4467-0001), Pusan National University Hospital (2102-001-099), Kyung Hee University Hospital at Gangdong (2021-06-003), Gyeongsang National University Hospital (2021-01-015-001), and Ulsan University Hospital (2021-01-033). The requirement for informed consent was waived because of the retrospective study design. All procedures followed were in accordance with the institutional and national ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964 and later versions.

2. Inclusion criteria

Clinical data from patients with stage I~III gastric cancer who underwent curative gastrectomy (R0 resection with either D1+ or D2 lymph node dissection) between January 2014 and January 2019 at 14 different gastric cancer centers and who met study inclusion criteria were retrospectively collected. These inclusion criteria were patients with data on measurement of preoperative height and body weight and patients with more than one body weight measurement at six, 12, 24, and 36 months after gastrectomy (Fig. 1).

3. Definition of malnutrition

The same definition of malnutrition used in our previous study was applied in this study: BMI <18.5 kg/m² [11]. This definition meets the criteria for being 'at nutritional risk' in the Malnutrition Universal Screening Tool [18] and the criteria for malnutrition in the European Society of Clinical Nutrition and Metabolism guidelines [19].

4. Predictor candidates

Our study group has used a group-based trajectory model to evaluate weight loss pattern after gastric cancer surgery [11]. The factors that were highly associated with post-gastrectomy weight loss in our previous study were the factors we primarily considered in the development of our prediction model. These factors were age, sex, preoperative BMI, preoperative nutrition state, cancer stage (I~III), surgical approach (open, laparoscopic or robotic), operation type (total gastrectomy [TG], proximal gastrectomy [PG], distal gastrectomy [DG], or pylorus-preserving gastrectomy [PPG]), reconstruction (Roux-en-Y esophago-jejunostomy, esophago-gastrostomy, double tract, Billroth I, Billroth II, Roux-en-Y gastro-jejunostomy or gastro-gastrostomy), use of adjuvant chemotherapy and postoperative complications (Clavien-Dindo grade). Based on clinician input, nutritional laboratory indicators, such as preoperative hemoglobin, protein, albumin, and cholesterol levels, were also included as predictor candidates.

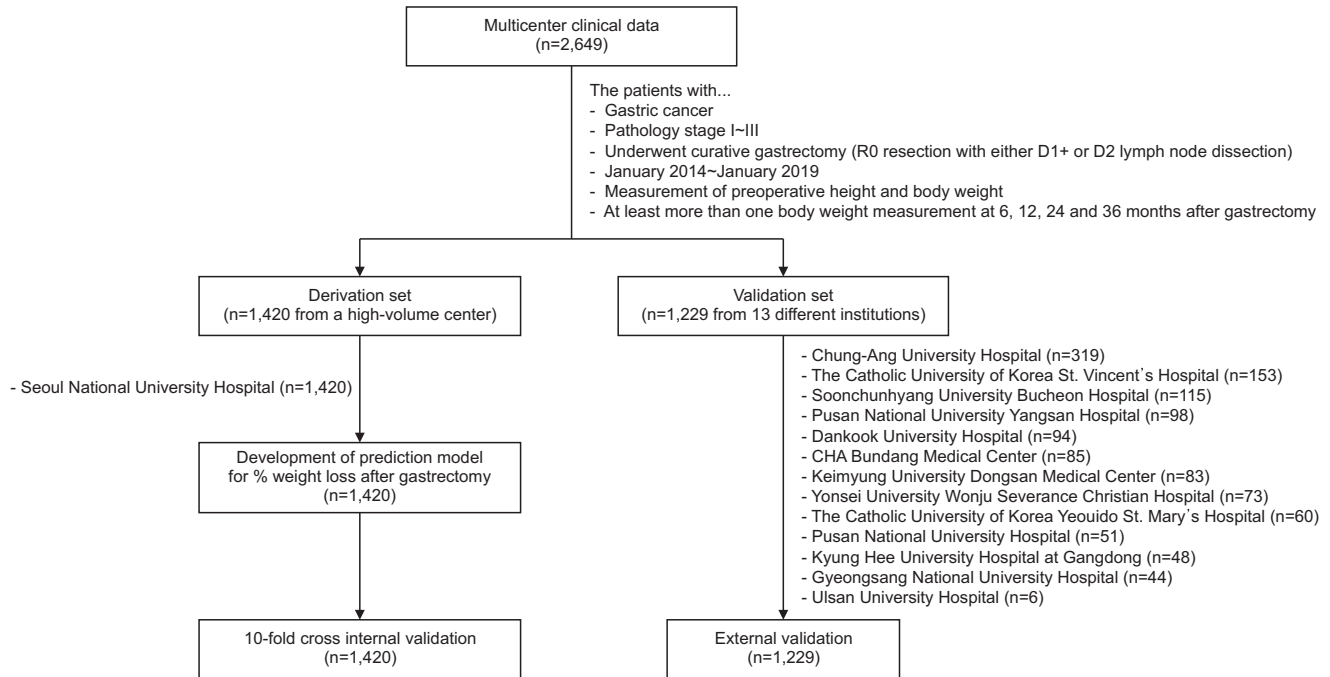


Fig. 1. Flowchart of the data collection.

5. Dataset assignment

Data from SNUH, a tertiary referral center in Korea, were used as a derivation set to develop the post-gastrectomy weight loss prediction model. The same SNUH data were used for internal validation (homogeneous setting) using tenfold cross-validation. The internally validated prediction model developed was externally validated with data collected from 13 different gastric cancer centers (a heterogeneous setting).

6. Statistical analysis

Characteristics of subjects are summarized and were compared using mean (standard deviation) and independent t-test for continuous variables and frequency (proportion) and chi-square test for categorical variables. A prediction model that accounts for individual patient % weight loss over time after gastrectomy was developed using a linear mixed effect model. The fixed effects were the predictors, time and interaction between time and predictors; the random effect was the subject. The estimated effect of each predictor was adjusted by time period after gastrectomy, and the statistically significant predictors were used for multivariable analysis. The prediction model was determined by the stepwise variable selection method. The adjusted mean difference per unit change in each predictor and its 95% confidence interval (CI) were calculated. The prediction model is presented using a prediction scoring table and nomogram. The prediction model was internally validated using tenfold cross-validation. The model performance was evaluated internally

and externally using R^2 , the distribution of the difference between observed and predicted % weight loss and calibration slope. All statistical analyses were conducted by professional statisticians using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

1. Patients

Clinical data from 2,649 patients who met all inclusion criteria were collected from 14 participating institutions. Data from 1,420 SNUH patients (derivative set) were used for development and internal validation of the weight loss prediction model, and data from 1,229 patients collected from the remaining 13 hospitals (validation set) were used for external validation. Fig. 1 details the number of patients from each institution.

2. Baseline characteristics between the derivative and validation sets

As shown in Table 1, the predominant characteristics at the baseline for each variable in both sets were similar; but there was a statistically significant difference in the proportion of some variables. In both sets, approximately 60-year-old male patients with stage I gastric cancer who underwent laparoscopic DG with Billroth I or II reconstruction were predominant. However, significant differences between the derivative set and validation set were demonstrated for these characteristics: age (60.1 ± 11.3 years vs. 62.4 ± 11.5 years, $P < 0.0001$), sex (61.83% males vs. 70.63% males, $P < 0.0001$), use of

Table 1. Distribution of patient characteristics between derivation and validation sets

Variables		Derivation set (n=1,420)	Validation set (n=1,229)	P-value ^a
Age, yr		60.1±11.3	62.4±11.5	<0.0001
Sex	Male	878 (61.83)	868 (70.63)	<0.0001
	Female	542 (38.17)	361 (29.37)	
Preop BMI, kg/m ²		24.0±3.2	23.9±3.4	0.4364
Preop malnutrition, BMI <18.5 kg/m ²	No	1,376 (96.90)	1,178 (95.85)	0.1468
	Yes	44 (3.10)	51 (4.15)	
Surgical approach	Open	392 (27.61)	335 (27.26)	<0.0001
	Laparoscopy	914 (64.37)	846 (68.84)	
	Robot	114 (8.03)	48 (3.91)	
Operation type	TG	308 (21.69)	245 (19.93)	<0.0001
	PG	17 (1.20)	18 (1.46)	
	DG	834 (58.73)	952 (77.46)	
	PPG	261 (18.38)	14 (1.14)	
Reconstruction	RY (E-J)	308 (21.69)	245 (19.93)	<0.0001
	E-G	5 (0.35)	2 (0.16)	
	DT	12 (0.85)	16 (1.30)	
	B I	559 (39.37)	198 (16.11)	
	B II	180 (12.68)	672 (54.68)	
	RY (G-J)	95 (6.69)	82 (6.67)	
Gastric cancer stage	G-G	261 (18.38)	14 (1.14)	0.0396
	I	1,022 (71.97)	863 (70.22)	
	II	173 (12.18)	190 (15.46)	
	III	225 (15.85)	176 (14.32)	
Adjuvant chemotherapy	No	1,058 (74.51)	866 (70.46)	0.0199
	Yes	362 (25.49)	363 (29.54)	
Complication	No	1,059 (74.58)	1,079 (87.79)	<0.0001
	Yes	361 (25.42)	150 (12.21)	
Surgical mortality (within 30 days)	No	1,420 (100)	1,229 (100)	
	Yes	0	0	
Preop hemoglobin (11.5~15.5 g/dL)		13.5±1.8	13.4±2.1	0.0546
Preop protein (6.0~8.2 g/dL)		7.1±0.6	7.0±0.7	0.0015
Preop albumin (3.5~5.2 g/dL)		4.2±0.4	4.3±0.6	0.0011
Preop cholesterol (120~220 mg/dL)		185.5±39.4	176.9±40.9	<0.0001

Values are presented as mean±standard deviation or number (%).

Preop = preoperative; BMI = body mass index; TG = total gastrectomy; PG = proximal gastrectomy; DG = distal gastrectomy; PPG = pylorus-preserving gastrectomy; RY (E-J) = Roux-en-Y (esophago-jejunostomy); E-G = esophago-gastrostomy; DT = double tract; B = Billroth; RY (G-J) = Roux-en-Y (gastro-jejunostomy); G-G = gastro-gastrostomy.

^aP-value calculated by chi-squared test for categorical variables and independent t-test for continuous variables.

robotic surgery (8.03% vs. 3.91%, $P<0.0001$), use of PPG (18.38% vs. 1.14%, $P<0.0001$), use of Billroth I and gastro-gastrostomy reconstruction (Billroth I, 39.37% vs. 16.11%; gastro-gastrostomy, 18.38% vs. 1.14%; $P<0.0001$ for both) and complication rate (25.42% vs. 12.21%, $P<0.0001$). All preoperative nutritional laboratory indicators were in normal range in both sets.

3. Development of the percentage weight loss prediction model at six, 12, 24, and 36 months after gastrectomy

In the derivation set ($n=1,420$), nine candidate predictors were sufficiently associated with % weight loss over time after gastrectomy: age, sex, preoperative BMI, presence of preoperative malnutrition, surgical approach, operation type, reconstruction procedure, cancer stage and use

of adjuvant chemotherapy (Table 2). In the multivariable analysis by stepwise selection, postoperative duration (six months after gastrectomy vs. 12 months, 24 months or 36 months, $P=0.0004$); age ($P=0.0053$); sex (male vs. female, $P<0.0001$); preoperative BMI ($P<0.0001$); operation type (PPG vs. TG, PG, or DG, $P<0.0001$); and cancer stage (I vs. II or III, $P=0.0159$) were independently associated with postoperative weight loss. The prediction model for % weight loss at six, 12, 24, and 36 months after gastrectomy is shown in Table 3: weight loss (%) = $-14.8 + (0.412 \times 12 \text{ months after gastrectomy}) + (0.077 \times 24 \text{ months after gastrectomy}) + (-0.087 \times 36 \text{ months after gastrectomy}) + (0.04 \times \text{age}) + (2.069 \times \text{female}) + (0.782 \times \text{preoperative BMI}) + (5.275 \times \text{TG}) + (2.599 \times \text{PG}) + (0.755 \times \text{DG}) + (1.374 \times \text{cancer stage II}) + (0.663 \times \text{cancer stage III})$.

A nomogram and scoring table were developed based on the equation (Fig. 2).

4. Internal and external validation of the percentage weight loss prediction model at six, 12, 24, and 36 months after gastrectomy

The developed prediction model for the % weight loss at six, 12, 24, and 36 months after gastrectomy was internally validated in the same derivation set using tenfold cross-validation ($n=1,420$): R^2 (95% CI)=0.20 (0.20~0.21), 0.21 (0.20~0.21), 0.17 (0.17~0.17), and 0.18 (0.18~0.18), respectively, and calibration slope (95% CI)=0.95 (0.85~1.05) (Fig. 3A).

The model was also validated externally in the validation set ($n=1,229$): R^2 (95% CI)=0.20 (0.20~0.20), 0.22 (0.22~0.23), 0.18 (0.18~0.18), and 0.18 (0.18~0.19), respectively, and calibration slope (95% CI)=1.00 (0.89~1.12). Even though the calibration slope and plot of external validation tended to slightly overestimate the % of weight loss after gastrectomy in the interval of 4%, 8%, and 13%, the slope showed acceptable calibration overall (Fig. 3B).

Table 2. The effect of predictor on percentage (%) weight loss adjusted by time period after gastrectomy in the derivation set ($n=1,420$)

Variables		Beta	95% CI	P-value	P-value ^a
Age		0.047	0.016, 0.079	0.0033	
Sex	Female vs. Male	1.071	0.343, 1.798	0.0039	
Preop BMI		0.744	0.640, 0.849	<0.0001	
Preop malnutrition (BMI <18.5 kg/m ²)	No vs. Yes	7.724	5.689, 9.760	<0.0001	
Surgical approach	Open vs. Robot	2.150	0.738, 3.562	0.0029	0.0008
	Laparoscopy vs. Robot	0.788	-0.528, 2.104	0.2407	
Operation type	TG vs. PPG	5.520	4.443, 6.598	<0.0001	<0.0001
	PG vs. PPG	3.151	-0.048, 6.349	0.0535	
	DG vs. PPG	1.277	0.370, 2.183	0.0058	
Reconstruction	RY (E-J) vs. G-G	5.521	4.449, 6.593	<0.0001	<0.0001
	E-G vs. G-G	3.683	-2.123, 9.488	0.2137	
	DT vs. G-G	2.937	-0.800, 6.673	0.1235	
	B I vs. G-G	0.634	-0.320, 1.587	0.1928	
	B II vs. G-G	2.807	1.572, 4.042	<0.0001	
Gastric cancer stage	RY (G-J) vs. G-G	2.175	0.647, 3.703	0.0053	
	II vs. I	2.191	1.101, 3.281	<0.0001	<0.0001
	III vs. I	1.522	0.540, 2.504	0.0024	
Adjuvant chemotherapy	Yes vs. No	1.640	0.829, 2.450	<0.0001	
Complication	Yes vs. No	0.520	-0.294, 1.334	0.2107	
Preop hemoglobin		-0.078	-0.275, 0.120	0.4392	
Preop protein		0.137	-0.429, 0.703	0.6346	
Preop albumin		-0.064	-0.931, 0.802	0.8844	
Preop cholesterol		0.001	-0.008, 0.010	0.8710	

CI = confidence interval; Preop = preoperative; BMI = body mass index; TG = total gastrectomy; PPG = pylorus-preserving gastrectomy; PG = proximal gastrectomy; DG = distal gastrectomy; RY (E-J) = Roux-en-Y (Esophago-jejunosotomy); G-G = Gastro-gastrostomy; E-G = esophago-gastrostomy; DT = double tract; B = Billroth; RY (G-J) = Roux-en-Y (Gastro-jejunosotomy).

^aOverall significance of the predictor.

Table 3. Development of the percentage (%) weight loss prediction model at six, 12, 24, 36 months after gastrectomy

Predictive factors		Estimate	95% CI	P-value	P-value ^a
Time period after gastrectomy (mo)	6 (ref)				0.0004
	12	0.412	0.170, 0.654	0.0009	
	24	0.077	-0.174, 0.327	0.5483	
	36	-0.087	-0.350, 0.177	0.5196	
Age		0.040	0.012, 0.068	0.0053	
Sex	Male (ref)				
	Female	2.069	1.416, 2.721	<0.0001	
Preop BMI		0.782	0.683, 0.881	<0.0001	
Operation type	PPG (ref)				<0.0001
	TG	5.275	4.230, 6.321	<0.0001	
	PG	2.599	-0.336, 5.533	0.0826	
	DG	0.755	-0.106, 1.616	0.0855	
Gastric cancer stage	I (ref)				0.0159
	II	1.374	0.390, 2.358	0.0062	
	III	0.663	-0.241, 1.568	0.1506	
Equation of prediction model	Weight loss (%) = -14.8 + (0.412 × 12 months after gastrectomy) + (0.077 × 24 months after gastrectomy) + (-0.087 × 36 months after gastrectomy) + (0.04 × age) + (2.069 × female) + (0.782 × preop BMI) + (5.275 × TG) + (2.599 × PG) + (0.755 × DG) + (1.374 × cancer stage II) + (0.663 × cancer stage III)				

CI = confidence interval; ref = reference; Preop = preoperative; BMI = body mass index; PPG = pylorus-preserving gastrectomy; TG = total gastrectomy; PG = proximal gastrectomy; DG = distal gastrectomy.

^aOverall significance of the predictor.

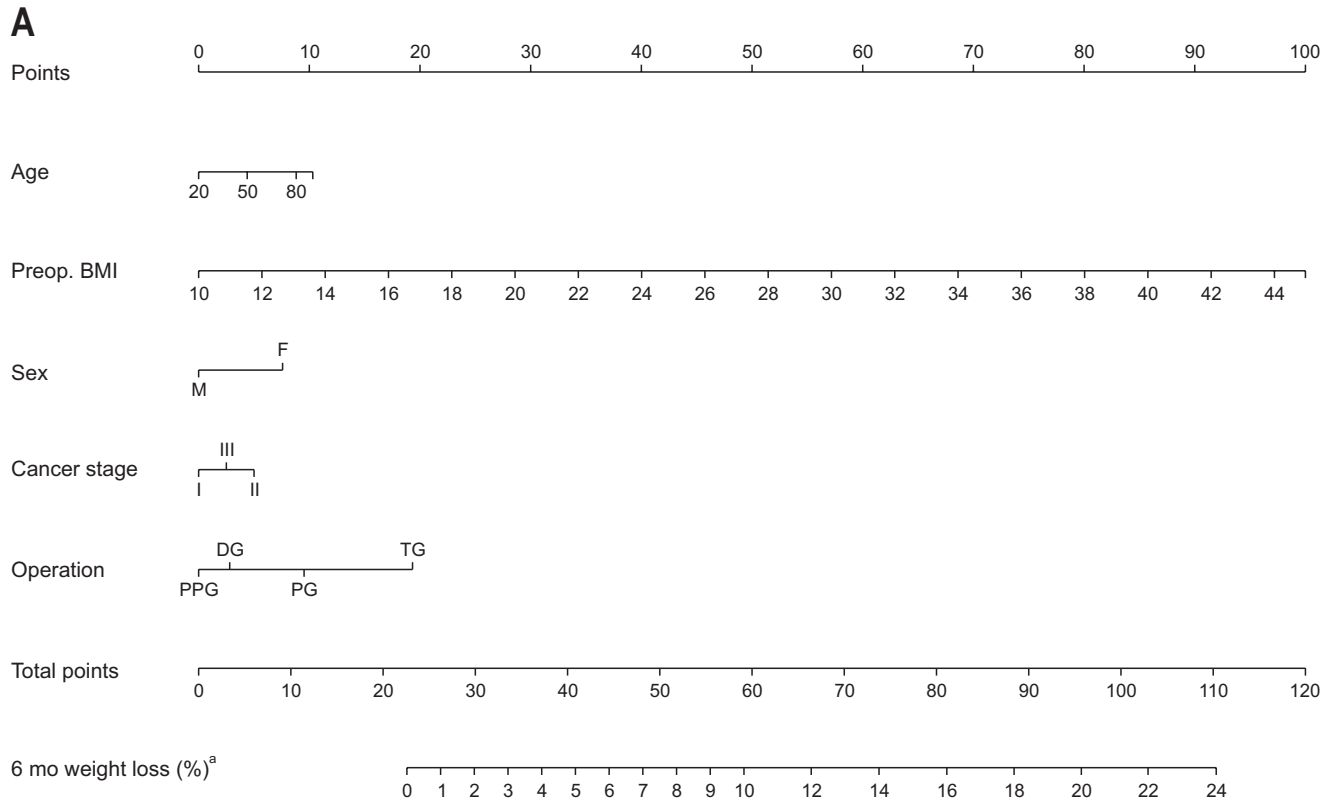
DISCUSSION

The area in which research on predictive models of weight loss has been most active is bariatric surgery [20-23]. Predicting postoperative weight loss is also an important subject in other fields of gastrointestinal surgery, but only a few relevant studies have been conducted [24,25]. Postoperative nutrition status is closely related to postoperative recovery and postoperative QoL improvement [5,16]. Because unintentional rapid weight loss after gastrectomy may lead to postoperative malnutrition [26,27], a tool to predict the extent of postoperative weight loss is necessary for both gastrointestinal surgeons and patients. In this study, we have developed a prediction model for % weight loss after gastrectomy and validated its accuracy and utility.

In our previous study, the BMI-loss trajectory model of patients with gastric cancer showed that severe BMI loss (approximately 21.5% reduction from preoperative BMI) at six months after gastrectomy was significantly associated with being elderly, being female, having higher preoperative BMI, being at an advanced cancer stage, having had open surgery, having had a TG performed, having had a Roux-en-Y reconstruction, having had chemotherapy and having had postoperative complications [11]. Among those factors, specific time point after gastrectomy, age, sex, preoperative BMI, surgical approach, and cancer stage were determined to be predic-

tors of % weight loss after gastrectomy in this study. Older age, being female, having a higher preoperative BMI, having had a TG performed, being at cancer stage II and being at one year after gastrectomy increased % of post-gastrectomy weight loss significantly. Risk factors independently associated with weight loss after gastrectomy for gastric cancer in other studies were not entirely consistent with our results, but higher operative BMI and TG were risk factors identified in many studies [15,17].

Higher preoperative BMI was associated with greater postoperative BMI loss in the prediction model for % weight loss. Davis et al. [17] conducted a similar study in the Western population and reported that preoperative BMI and procedure type were the independent post-gastrectomy risk factors. In their study, even though patients with higher preoperative BMI had significantly greater weight loss than patients with lower preoperative BMI, the higher preoperative BMI patients maintained normal or overweight BMI throughout [17]. A similar Asian study also identified higher BMI as the most influential factor affecting postoperative weight loss. Moreover, the patients with baseline obesity (BMI >25 kg/m², according to Asia BMI criteria) [28] exhibited the largest postoperative weight loss compared to normal BMI and underweight patients [15]. In our previous study, the BMI-loss trajectory model demonstrated a significant association between high preoperative BMI and severe weight loss



B

	Age	20	30	40	50	60	70	80	90							
	Point	0	1	3	4	6	7	9	10							
	Preop. BMI	10	15	20	25	30	35	40	45							
	Point	0	14	29	43	57	71	86	100							
	Sex	M	F													
	Point	0	8													
	Gastric cancer stage	I	II	III												
	Point	0	5	2												
	Operation type	PPG	DG	PG	TG											
	Point	0	3	9	19											
	Total points	23	30	38	45	52	59	67	74	81	89	96	103	111		
(%) Weight loss after 6 mo gastrectomy		0	2	4	6	8	10	12	14	16	18	20	22	24		

Fig. 2. Nomogram and scoring table for the percentage (%) weight loss prediction model at six, 12, 24, 36 months after gastrectomy. (A) Preoperative predictable nomogram. (B) Preoperative predictable scoring table.

Preop = preoperative; BMI = body mass index; M = male; F = female; PPG = pylorus-preserving gastrectomy; DG = distal gastrectomy; PG = proximal gastrectomy; TG = total gastrectomy.

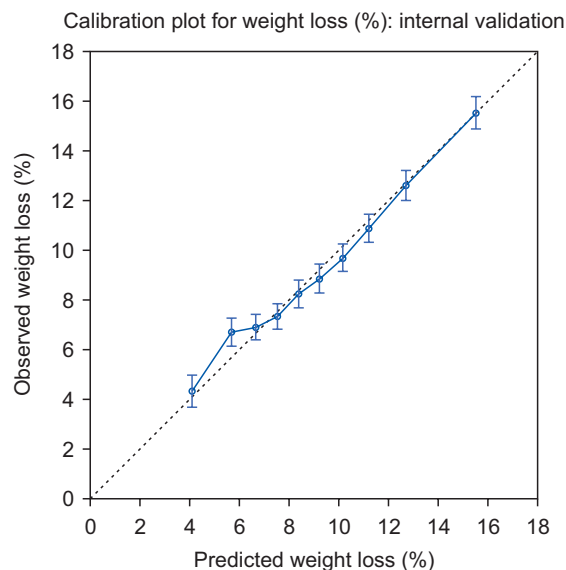
^a12 mo weight loss (%) = 6 mo weight loss + 0.412; 24 mo weight loss (%) = 6 mo weight loss + 0.077; 36 mo weight loss (%) = 6 mo weight loss - 0.087.

after gastrectomy. However, low, not high, preoperative BMI was one of the risk factors of post-gastrectomy malnutrition [11,29]. As we discussed in the previous study, patients with high preoperative BMI may lose more weight; but those with lower preoperative BMI are at greater risk for malnutrition after gastrectomy.

Consistent with our previous BMI-loss trajectory model and other studies, TG surgeries were associated with greater

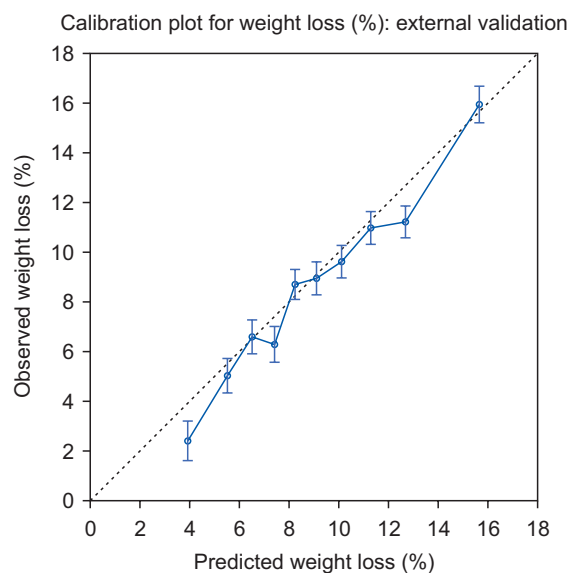
weight loss than the other operation types (PPG, DG and PG) [25]. Davis et al. [17] also reported that patients who underwent TG lost significantly more weight across all time points than patients who underwent subtotal gastrectomy regardless of reconstruction procedure ($P < 0.01$). One possible reason is the loss of storage volume after TG. In the patients who undergo DG, a portion of the stomach is retained and is usable as a reservoir; but patients who undergo TG have no

A



Statistics	Time period after gastrectomy			
	6 mo (n=1,280)	12 mo (n=1,361)	24 mo (n=1,232)	36 mo (n=1,051)
R ² (95% CI)	0.204 (0.203, 0.205)	0.205 (0.204, 0.206)	0.168 (0.167, 0.169)	0.179 (0.178, 0.180)
d (p25, p75) ^a	-4.03, 3.66	-4.03, 3.66	-4.34, 4.14	-4.29, 4.2
d (p5, p95) ^b	-9.49, 10.01	-10.05, 9.74	-10.92, 10.84	-11.18, 11.19
Calibration slope (95% CI)	0.951 (0.852, 1.050)			

B



Statistics	Time period after gastrectomy			
	6 mo (n=1,117)	12 mo (n=1,082)	24 mo (n=1,040)	36 mo (n=1,005)
R ² (95% CI)	0.196 (0.195, 0.198)	0.224 (0.223, 0.225)	0.179 (0.178, 0.180)	0.183 (0.182, 0.185)
d (p25, p75) ^a	-4.38, 4.019	-4.818, 3.729	-4.633, 4.258	-4.809, 4.327
d (p5, p95) ^b	-11.208, 10.65	-12.806, 10.44	-12.979, 11.181	-12.905, 11.424
Calibration slope (95% CI)	1.004 (0.893, 1.116)			

Fig. 3. Internal and external validation of the percentage (%) weight loss prediction model at six, 12, 24, 36 months after gastrectomy. (A) Internal validation using derivation set (tenfold cross validation). (B) External validation using validation set (n=1,229). CI = confidence interval.

^aLimit of the middle half of the distribution of the difference between observed and predicted percentage weight loss. ^bLimit of the middle 90% of the distribution of the difference between observed and predicted percentage weight loss.

remaining stomach. A second possible reason for the TG-associated body weight loss is the loss of ghrelin, which works as the promotion of the appetite signal in the hypothalamus and the stimulation of gastrointestinal activity. Previous studies demonstrated that persistent decline of serum ghrelin and body weight was observed commonly after TG, and short-term administration of synthetic ghrelin successfully lessened postoperative body weight loss after TG [30,31].

External validation procedures showed that our model was only able to predict weight loss at each follow-up mark with an accuracy of $R^2=0.20$ at six months, 0.22 at 12 months, 0.18 at 24 months and 0.18 at 36 months (Fig. 3B). Postoperative weight loss prediction models have been developed for bariatric surgeries and have been able to predict weight loss with an accuracy of R^2 ranging from 0.24 to 0.75 [20-23]. Even though the R^2 values in these studies were higher than ours, R^2 in these studies was still low. Livingston et al. [32] concluded that accurate prediction of weight loss depends on the initial fat and lean compartment mass since weight is lost from these at different rates and to different extents. Development of a predictive model with high accuracy is difficult even in weight loss predictive models after bariatric surgery calculated only using factors such as preoperative BMI, age, and sex. For patients with gastric cancer, development of a prediction model with high accuracy is more difficult because there are more factors, such as cancer stage, operation type, reconstruction method and use of chemotherapy for which to account.

This is a limitation of our study. Ideally, in order to develop a prediction model, data representative of all gastric cancer patients, a development set, should be used. However, predictive models are usually developed using data from one institution or one country; and we have also developed the predictive models using data from a single institution. Therefore, in our prediction model, there were some differences in baseline characteristics of the derivative and validation sets. SNUH used robotic surgery, PPG, Billroth I and gastrogastrostomy reconstruction more frequently and had a higher complication rate than the other institutions. These differences may be due to the location of the center, case volume, surgeons' technical preference and available surgical equipment. Differences in the complication rates may have been affected because each institution had different methods of collecting data on complications. However, there was no "within 30-day postoperative mortality" in the entire cohort. To overcome this limitation, we evaluated the predictive power of the model through external validation in a slightly heterogeneous group of gastric cancer patients. Another limitation is that we could not include other variables which may affect weight loss after gastrectomy such as modification in physical activity or dietary behavior, psychological profiles, genetic background and support group participation. Because our research design was that of a multi-center and retrospective study, missing data was an issue; collecting and

standardizing such data from all participating centers was difficult. These variables should be included in a future prospective multicenter study.

CONCLUSION

While we developed a model for predicting weight loss after gastrectomy, its prediction accuracy was only about 20%. This did not meet our expectations. However, since similar predicted values were shown in internal and external validation, we expect that the model can be used as a reliable reference material in actual clinical practice. The % weight loss prediction model may be helpful to facilitate appropriate preoperative consultation with patients regarding individualized postoperative weight changes, nutritional supplementation strategies and follow-up.

AUTHOR CONTRIBUTIONS

Conceptualization: JHP, HJL. Data curation: JHP, JWK, KBP, IC, SHH, DWK, SMK, SWR, SCG, PYJ, HR, SGK, CIC, DHK, SIC, JHP, DJP, GYK, SHK, DJP, HKY, YC, HJL. Formal analysis: JHP, YC, HJL. Funding acquisition: JHP, HJL. Investigation: JHP, HJL. Methodology: JHP, YC, HJL. Project administration: JHP, HJL. Resources: JHP, JWK, KBP, IC, SHH, DWK, SMK, SWR, SCG, PYJ, HR, SGK, CIC, DHK, SIC, JHP, DJP, GYK, SHK, DJP, HKY, YC, HJL. Software: JHP, YC, HJL. Supervision: YC, HJL. Validation: JHP, YC, HJL. Visualization: JHP, YC. Writing – original draft: JHP. Writing – review & editing: JHP, JWK, KBP, IC, SHH, DWK, SMK, SWR, SCG, PYJ, HR, SGK, CIC, DHK, SIC, JHP, DJP, GYK, SHK, DJP, HKY, YC, HJL.

CONFLICTS OF INTEREST

The authors of this manuscript have no conflicts of interest to disclose.

FUNDING

This study was supported by Seoul National University College of Medicine and by a research grant (no. 0431-20200021) from Korean Society of Surgical Metabolism and Nutrition.

ORCID

Ji-Hyeon Park, <https://orcid.org/0000-0002-6811-8895>
 Seong-Ho Kong, <https://orcid.org/0000-0002-3929-796X>
 Do Joong Park, <https://orcid.org/0000-0001-9644-6127>
 Han-Kwang Yang, <https://orcid.org/0000-0003-3495-3048>
 Jong Won Kim, <https://orcid.org/0000-0002-9556-7143>
 Ki Bum Park, <https://orcid.org/0000-0001-6035-6584>
 In Cho, <https://orcid.org/0000-0002-8568-0679>
 Sun-Hwi Hwang, <https://orcid.org/0000-0001-8058-0524>

Dong-Wook Kim, <https://orcid.org/0000-0002-3552-5988>
 Su Mi Kim, <https://orcid.org/0000-0003-0272-4662>
 Seung-Wan Ryu, <https://orcid.org/0000-0003-0374-5748>
 Seong Chan Gong, <https://orcid.org/0000-0001-9685-5924>
 Pil Young Jung, <https://orcid.org/0000-0001-6460-8072>
 Hoon Ryu, <https://orcid.org/0000-0002-7161-7644>
 Sung Geun Kim, <https://orcid.org/0000-0002-3087-9728>
 Chang In Choi, <https://orcid.org/0000-0002-1920-1879>
 Dae Hwan Kim, <https://orcid.org/0000-0002-0045-5692>
 Sung-IL Choi, <https://orcid.org/0000-0002-0662-0951>
 Ji-Ho Park, <https://orcid.org/0000-0002-2751-7320>
 Dong Jin Park, <https://orcid.org/0000-0001-7820-9179>
 Gyu-Yeol Kim, <https://orcid.org/0000-0001-5389-160X>
 Yunhee Choi, <https://orcid.org/0000-0002-7422-0466>
 Hyuk-Joon Lee, <https://orcid.org/0000-0002-9530-647X>

REFERENCES

- Ning FL, Zhang CD, Wang P, Shao S, Dai DQ. Endoscopic resection versus radical gastrectomy for early gastric cancer in Asia: a meta-analysis. *Int J Surg* 2017;48:45-52.
- Tian Q, Qin L, Zhu W, Xiong S, Wu B. Analysis of factors contributing to postoperative body weight change in patients with gastric cancer: based on generalized estimation equation. *PeerJ* 2020;8:e9390.
- Kim YN, Choi YY, An JY, Choi MG, Lee JH, Sohn TS, et al. Comparison of postoperative nutritional status after distal gastrectomy for gastric cancer using three reconstructive methods: a multicenter study of over 1300 patients. *J Gastrointest Surg* 2020;24:1482-8.
- Kim KH, Yoon JH, Song GJ, Son MW, Kim SY, Baek MJ, et al. Comparison of post-operative nutritional status according to the extent of gastrectomy and the reconstruction method in patients with gastric cancer. *Ann Clin Nutr Metab* 2021;13:34-42.
- Climent M, Munarriz M, Blazeby JM, Dorcaratto D, Ramón JM, Carrera MJ, et al. Weight loss and quality of life in patients surviving 2 years after gastric cancer resection. *Eur J Surg Oncol* 2017;43:1337-43.
- Wang CJ, Suh YS, Lee HJ, Park JH, Park SH, Choi JH, et al. Postoperative quality of life after gastrectomy in gastric cancer patients: a prospective longitudinal observation study. *Ann Surg Treat Res* 2022;103:19-31.
- Park YS, Park DJ, Lee Y, Park KB, Min SH, Ahn SH, et al. Prognostic roles of perioperative body mass index and weight loss in the long-term survival of gastric cancer patients. *Cancer Epidemiol Biomarkers Prev* 2018;27:955-62.
- Lee HH, Park JM, Song KY, Choi MG, Park CH. Survival impact of postoperative body mass index in gastric cancer patients undergoing gastrectomy. *Eur J Cancer* 2016;52:129-37.
- Kubo H, Komatsu S, Ichikawa D, Kawaguchi T, Kosuga T, Okamoto K, et al. Impact of body weight loss on recurrence after curative gastrectomy for gastric cancer. *Anticancer Res* 2016;36:807-13.
- Lim HS, Lee B, Cho I, Cho GS. Nutritional and clinical factors affecting weight and fat-free mass loss after gastrectomy in patients with gastric cancer. *Nutrients* 2020;12:1905.
- Park JH, Kim E, Seol EM, Kong SH, Park DJ, Yang HK, et al. Prediction model for screening patients at risk of malnutrition after gastric cancer surgery. *Ann Surg Oncol* 2021;28:4471-81.
- Kong SH, Park JS, Lee IK, Ryu SW, Park YK, Yang HK, et al. Postoperative oral nutritional supplementation after major gastrointestinal surgery: a randomized controlled clinical trial. *Asia Pac J Clin Nutr* 2017;26:811-9.
- Kong SH, Lee HJ, Na JR, Kim WC, Han DS, Park SH, et al. Effect of perioperative oral nutritional supplementation in malnourished patients who undergo gastrectomy: a prospective randomized trial. *Surgery* 2018;164:1263-70.
- Park JH, Kim E, Lee HJ. ASO author reflections: how can we accurately predict patients expected to be malnourished after gastrectomy? *Ann Surg Oncol* 2021;28:4482-3.
- Segami K, Aoyama T, Kano K, Maezawa Y, Nakajima T, Ikeda K, et al. Risk factors for severe weight loss at 1 month after gastrectomy for gastric cancer. *Asian J Surg* 2018;41:349-55.
- Tanabe K, Takahashi M, Urushihara T, Nakamura Y, Yamada M, Lee SW, et al. Predictive factors for body weight loss and its impact on quality of life following gastrectomy. *World J Gastroenterol* 2017;23:4823-30.
- Davis JL, Selby LV, Chou JF, Schattner M, Ilson DH, Capanu M, et al. Patterns and predictors of weight loss after gastrectomy for cancer. *Ann Surg Oncol* 2016;23:1639-45.
- Todorovic V, Russell C, Elia M, eds. The 'MUST' explanatory booklet. A guide to the 'malnutrition universal screening tool' ('MUST') for adults. Redditch: BAPEN, 2011.
- Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition - an ESPEN consensus statement. *Clin Nutr* 2015;34:335-40.
- Goulart A, Leão P, Costa P, Pereira M, Fernandes A, Manso F, et al. Doctor, how much weight will I lose?-a new individualized predictive model for weight loss. *Obes Surg* 2016;26:1357-9.
- Cottam S, Cottam D, Cottam A, Zaveri H, Surve A, Richards C. The use of predictive markers for the development of a model to predict weight loss following vertical sleeve gastrectomy. *Obes Surg* 2018;28:3769-74.
- Seyssel K, Suter M, Pattou F, Caiazzo R, Verkindt H, Raverdy V, et al. A predictive model of weight loss after Roux-en-Y gastric bypass up to 5 years after surgery: a useful tool to select and manage candidates to bariatric surgery. *Obes Surg* 2018;28:3393-9.
- Karpińska IA, Kulawik J, Pisarska-Adamczyk M, Wysocki M, Pędzwiatr M, Major P. Is it possible to predict weight loss after bariatric surgery?-external validation of predictive models. *Obes Surg* 2021;31:2994-3004.
- Schandl A, Kauppila JH, Anandavadivelan P, Johar A, Lagergren P. Predicting the risk of weight loss after esophageal cancer surgery. *Ann Surg Oncol* 2019;26:2385-91.
- Aoyama T, Sato T, Segami K, Maezawa Y, Kano K, Kawabe T, et al. Risk factors for the loss of lean body mass after gastrectomy for gastric cancer. *Ann Surg Oncol* 2016;23:1963-70.

26. Fujiya K, Kawamura T, Omae K, Makuuchi R, Irino T, Tokunaga M, et al. Impact of malnutrition after gastrectomy for gastric cancer on long-term survival. *Ann Surg Oncol* 2018;25:974-83.
27. Loh KW, Vriens MR, Gerritsen A, Borel Rinkes IH, van Hillegersberg R, Schippers C, et al. Unintentional weight loss is the most important indicator of malnutrition among surgical cancer patients. *Neth J Med* 2012;70:365-9.
28. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363:157-63. Erratum in: *Lancet* 2004;363:902.
29. Komatsu S, Kosuga T, Kubota T, Okamoto K, Konishi H, Shiozaki A, et al. Preoperative low weight affects long-term outcomes following curative gastrectomy for gastric cancer. *Anticancer Res* 2018;38:5331-7.
30. Takachi K, Doki Y, Ishikawa O, Miyashiro I, Sasaki Y, Ohigashi H, et al. Postoperative ghrelin levels and delayed recovery from body weight loss after distal or total gastrectomy. *J Surg Res* 2006;130:1-7.
31. Adachi S, Takiguchi S, Okada K, Yamamoto K, Yamasaki M, Miyata H, et al. Effects of ghrelin administration after total gastrectomy: a prospective, randomized, placebo-controlled phase II study. *Gastroenterology* 2010;138:1312-20.
32. Livingston EH, Sebastian JL, Huerta S, Yip I, Heber D. Bi-exponential model for predicting weight loss after gastric surgery for obesity. *J Surg Res* 2001;101:216-24.