

Risk factors and clinical outcomes of postgastrectomy sarcopenia newly developed after curative resection for gastric cancer

Hye Jin Kim, MD^a, Eun Sun Lee, MD, PhD^b, Beom Jin Kim, MD, PhD^{a,*} , Won-Seok Kim, MD^a, Jae Yong Park, MD^a, Jae Gyu Kim, MD, PhD^a, Joong-Min Park, MD, PhD^c, Jong Won Kim, MD, PhD^c, Kyong-Choun Chi, MD, PhD^c, Hyung Kang, MD, PhD, MPH^d

Abstract

This study aimed to investigate the risk factors and clinical impact of newly developed sarcopenia after surgical resection on the prognosis of patients undergoing curative gastrectomy for gastric cancer (GC).

The clinicopathological data of 573 consecutive patients with GC who underwent curative gastrectomy were reviewed. Their skeletal muscle mass and abdominal fat volume were measured using abdominal computed tomography.

Forty six of them (8.0%) were diagnosed with preoperative sarcopenia. Among the 527 patients without sarcopenia, 57 (10.8%) were diagnosed with postgastrectomy sarcopenia newly developed 1 year after curative gastrectomy. Female sex, weight loss, proximal location of the tumor and differentiated tumor were significant risk factors of postgastrectomy sarcopenia newly developed after curative gastrectomy. There was a significant difference in the 5-year overall survival among the preoperative sarcopenic, nonsarcopenic, and postgastrectomy sarcopenic groups ($P=.017$). Especially, there was a significant difference between nonsarcopenic and postgastrectomy sarcopenic groups ($P=.009$). However, there was no significant difference in the 5-year disease-free survival among the groups ($P=.49$).

Since newly developed sarcopenia after surgical resection had an influence on the overall survival, patients with high sarcopenia risks after curative gastrectomy may require early nutritional support.

Abbreviations: CT = computed tomography, DFS = disease-free survival, GC = gastric cancer, OS = overall survival, SFA = subcutaneous fat area, VFA = visceral fat area.

Keywords: gastric cancer, nutrition, sarcopenia, surgical resection

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HJK and ESL contributed equally to this work.

The authors alone are responsible for the content and writing of the manuscript.

The guarantor for this article was Beom Jin Kim, M.D., Ph.D. Beom Jin Kim conceived and designed the study. Eun Sun Lee, Won-Seok Kim, Jae Yong Park, Jae Gyu Kim, Joong-Min Park, Jong-Won Kim, and Kyung Chun Chi collected the data. Hyung Kang analyzed the data. Hye Jin Kim and Eun Sun Lee wrote the manuscript. All authors have approved the final version of this article and its list of authors.

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^a Department of Internal Medicine, College of Medicine, Chung-Ang University, Seoul, Korea, ^b Department of Radiology, College of Medicine, Chung-Ang University, Seoul, Korea, ^c Department of Surgery, College of Medicine, Chung-Ang University, Seoul, Korea, ^d Department of Anesthesiology and Pain Medicine, College of Medicine, Chung-Ang University, Seoul, Korea.

* Correspondence: Beom Jin Kim, Department of Internal Medicine, College of Medicine, Chung-Ang University, 102 Heukseok-ro, Dongjak-gu, Seoul 06973, Korea (e-mail: kimbj@cau.ac.kr).

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1. Introduction

Gastric cancer (GC) is the fifth most common cancer and third leading cause of cancer-related death worldwide, with a high incidence of recurrence and metastasis.^[1,2] Its incidence and mortality rates are even higher in Asian countries, especially Japan and Korea.^[3] In Korea and Japan, GC is now detected in the early stage owing to National Health Screening System expansion and advanced endoscopic techniques.^[4] Despite great multimodal treatment improvements, the prognosis of GC remains poor.^[5,6] The optimal treatment for GC is surgical resection. Additional treatment with perioperative chemotherapy and/or radiotherapy offers the best chance of long-term survival.^[7] However, curative gastrectomy is a complicated surgical procedure and is always associated with high morbidity and mortality rates.^[8]

Sarcopenia is characterized by progressive and generalized loss of skeletal muscle mass and strength.^[9] GC is among the most common causes of sarcopenia.^[10] Sarcopenia is an independent predictor of postsurgical outcomes, including various postoperative complications, and shortened overall survival (OS) in many gastrointestinal cancers, including GC.^[11] This might arise, since patients with sarcopenia generally have a poor nutritional status. Therefore, nutritional status should be an important prognostic factor in patients with GC postoperatively.^[7] Sarcopenia predicted the 1-year mortality in elderly patients undergoing GC surgery.^[12] Thus, knowing whether newly developed sarcopenia after surgical resection increases the risk of poor outcomes is meaningful for clinical practice because it may

provide new nutritional intervention ideas to achieve better prognosis among patients with GC. However, there is a lack of research on newly developed sarcopenia postoperatively. Therefore, this study aimed to investigate the risk factors and clinical impact of postgastrectomy sarcopenia newly developed after surgical resection on the prognosis of patients undergoing curative gastrectomy for GC.

2. Materials and methods

2.1. Study population

We retrospectively analyzed the clinicopathological data of 576 consecutive patients with GC who underwent curative gastrectomy at Chung-Ang University Hospital in Korea between January 2011 and December 2015. This study included patients who underwent radical gastrectomy with R0 resection, and lymph nodes were dissected in accordance with the GC treatment guidelines in Japan.^[13] All patients had histologically confirmed stage I–III gastric adenocarcinoma. The study protocol was approved by the institutional review board of Chung-Ang University Hospital [IRB No. 1807-004-16186].

2.2. Data collection

Data on height and body weight and other clinical variables, including age, sex, drinking and smoking status, medical history of hypertension and diabetes mellitus, laboratory findings (e.g., preoperative hemoglobin and serum albumin levels), and surgical method of gastric resection, were obtained from the database. Pathological variables, including tumor location, size, differentiation and LN involvement, were analyzed. Tumor, node, and metastasis staging was performed using the American Joint Committee on Cancer staging system 7th edition.^[14] OS was estimated in months from the time of surgery to death or last follow-up assessment date. Disease-free survival (DFS) was estimated in months from the time of surgery to cancer-specific death (related to GC) or last follow-up assessment date. Follow-up assessments were performed every 3 to 6 months for the first

5 years after surgery. Follow-up procedures included medical history taking, physical examination, routine blood tests, chest radiography, upper endoscopy, and abdominal and pelvic computed tomography (CT). Local recurrence or distant metastases were confirmed histologically or radiographically.

2.3. Skeletal muscle mass and abdominal fat area quantification

Total body fat area, visceral fat area (VFA), and subcutaneous fat area (SFA) were measured automatically on the selected axial image at the umbilical level using the TeraRecon Aquarius Workstation (TeraRecon, Foster City, CA, USA). The skeletal muscle area was measured at the level of the third lumbar vertebral body transverse processes using the same workstation. The skin, visceral organs, and central spinal canal were excluded manually in the selected axial image to identify specific measurement areas. The abdominal wall and back muscle areas (psoas, paraspinal, transversus abdominis, rectus abdominis, internal oblique, and external oblique) were calculated using the area of pixels with attenuation between –29 and 150 Hounsfield units in demarcated areas. All measurements were performed by an abdominal radiologist (L.E.S.; 10-year experience) (Fig. 1). Thereafter, the differences in skeletal muscle mass and abdominal fat before and 1 year after surgery were calculated and compared.

2.4. Sarcopenia definition

Sarcopenia is classically defined as a muscle mass that is 2 standard deviations below that of healthy individuals. Data were analyzed at the third lumbar vertebral level using CT; sarcopenia is present if the total cross-sectional muscle tissue measured transversely at the third lumbar level is <52.4 cm²/m² body surface area for men and <38.5 cm²/m² body surface area for women.^[15] These definitions were applied to determine whether the patients had sarcopenia. In this study, post-gastrectomy sarcopenia was defined as a newly developed sarcopenic status after curative gastrectomy.

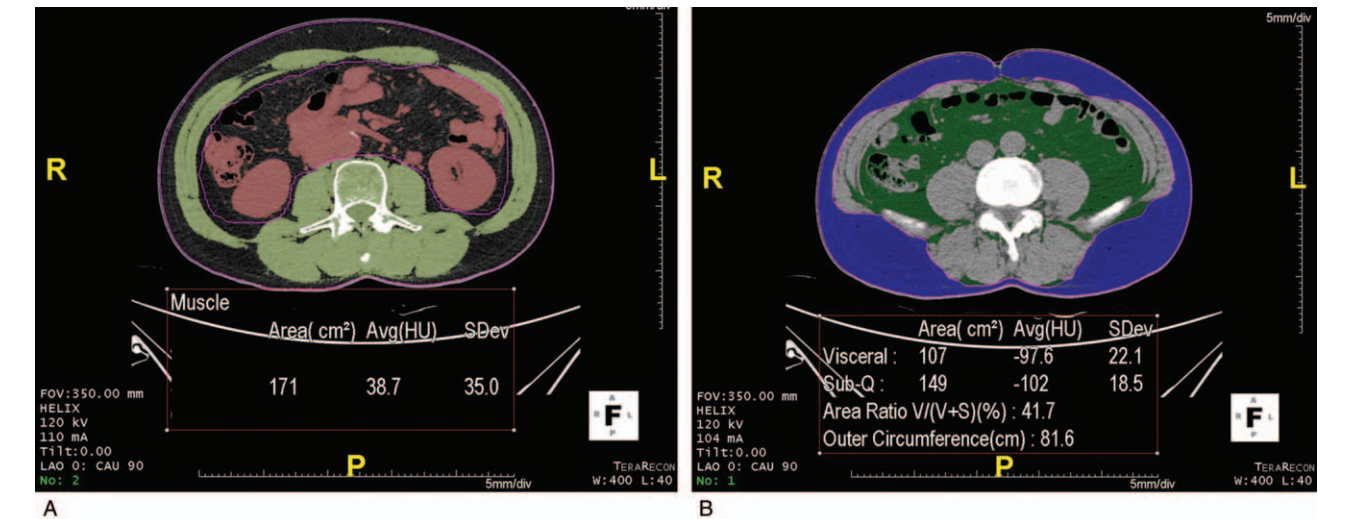


Figure 1. Assessment of the skeletal muscle and abdominal fat volume. (A) The skeletal muscle was assessed at the level of the third lumbar vertebral body transverse processes. The area and density of the skeletal muscle (olive-green) were automatically calculated. (B) The total body fat area, visceral fat area, and subcutaneous fat area were measured automatically on the selected axial image at the umbilical level (Green, visceral fat; Blue, subcutaneous fat area).

2.5. Statistics

Statistical analyses were performed using SPSS 17.0 (SPSS Inc., Chicago, IL). The patients were categorized into 2 or 3 groups according to sarcopenic status. Clinicopathological data were presented as means $\pm$ standard deviations. Categorical data were compared using the Chi-Squared test with Yates correction or Fisher exact test, as appropriate. Independent risk factors were determined using multivariate logistic regression analysis. DFS and OS were analyzed using the Kaplan–Meier method and compared using the log-rank test.

To assess the influence of BMI, abdominal fat, and skeletal muscle mass on the OS, these variables were divided into 4 groups. BMI was categorized as follows: underweight ($<18.0\text{ kg/m}^2$), normal ($18.0\text{--}22.9\text{ kg/m}^2$), overweight ($23.0\text{--}24.9\text{ kg/m}^2$), and obese ($\geq 25.0\text{ kg/m}^2$). We categorized the subjects into

quartiles according to the distribution of the VFA, VFA/SFA ratio, skeletal muscle mass, and skeletal muscle density to determine the cutoff point for each variable. Two-tailed *P* values of .05 were considered statistically significant.

3. Results

3.1. Patients' clinical characteristics

A total of 576 patients were diagnosed with stage I–III GC and underwent curative gastrectomy. Of them, 573 with preoperative and 1-year postoperative CT findings were enrolled. Their mean age was 62 years, and 408 (71.2%) were men. Three hundred eighty six patients (67.4%) had stage I GC; 95 (16.6%), stage II GC; and 92 (16.1%), stage III GC (Table 1).

Factors	All (n=573)	Nonsarcopenic (n=527)	Sarcopenic (n=46)	P value
Age mean, (SD)	62.0 (54.0–70.0)	62.0 (55.0–70.0)	58.0 (44.5–72.0)	.298
Sex				<.001
Female	165 (28.8)	127 (24.1)	38 (82.6)	
Male	408 (71.2)	400 (75.9)	8 (17.4)	
BMI, mean (SD)	23.80 $\pm$ 3.17	24.02 $\pm$ 3.08	21.25 $\pm$ 3.04	<.001
Weight loss (>10%)	239 (42.0)	219 (41.8)	20 (44.4)	.730
Tumor location				.217
Proximal (HB)	85 (14.9)	81 (15.5)	4 (8.7)	
Distal (MB, LB)	485 (85.1)	443 (84.5)	42 (91.3)	
Tumor size	3.00 (1.90–4.30)	3.00 (1.90–5.00)	3.15 (2.15–4.20)	.297
Differentiation of tumor				.883
Differentiated	368 (64.2)	338 (64.1)	30 (65.2)	
Undifferentiated	205 (35.8)	189 (35.9)	16 (34.8)	
TNM stage				.492
I	386 (67.4)	356 (67.6)	30 (65.2)	
II	95 (16.6)	89 (16.9)	6 (13.0)	
III	92 (16.1)	82 (15.6)	10 (21.7)	
LN involvement				.015
Yes	174 (30.6)	153 (29.3)	21 (46.7)	
No	394 (69.4)	370 (70.7)	24 (53.3)	
Type of resection				.104
Subtotal gastrectomy	458 (79.9)	417 (79.1)	41 (89.1)	
Total gastrectomy	115 (20.1)	110 (20.9)	5 (10.9)	
Adjuvant chemotherapy				.515
Yes	175 (30.5)	159 (30.2)	16 (34.8)	
No	398 (69.5)	368 (69.8)	30 (65.2)	
Albumin	4.00 (3.60–4.30)	4.00 (3.60–4.30)	4.00 (3.60–4.30)	.635
Hemoglobin	13.40 (12.00–14.60)	13.50 (12.00–14.70)	12.90 (11.80–13.50)	.001
Alcohol				<.001
Yes	245 (42.8)	243 (46.1)	2 (4.3)	
No	328 (57.2)	284 (53.9)	44 (95.7)	
Smoking				<.001
Yes	197 (34.4)	195 (37.0)	2 (4.3)	
No	376 (65.6)	332 (63.0)	44 (95.7)	
Hypertension				.184
Yes	227 (39.6)	213 (40.4)	14 (30.4)	
No	346 (60.4)	314 (59.6)	32 (69.6)	
Diabetes mellitus				.114
Yes	98 (17.1)	94 (17.8)	4 (8.7)	
No	475 (82.9)	433 (82.2)	42 (91.3)	
Total fat area	238.20 (170.45–304.00)	238.85 (171.55–306.00)	222.80 (144.50–277.00)	.163
Visceral fat area	107.00 (69.60–147.00)	108.00 (72.00–150.00)	78.10 (39.95–123.00)	.001
Subcutaneous fat area	122.00 (87.70–159.00)	122.00 (85.90–159.00)	133.00 (94.70–164.25)	.476
VFA/SFA ratio	0.88 (0.66–1.20)	0.89 (0.68–1.21)	0.70 (0.33–0.92)	.004

BMI = body mass index, LN = lymph node, SFA = subcutaneous fat area, VFA = visceral fat area.

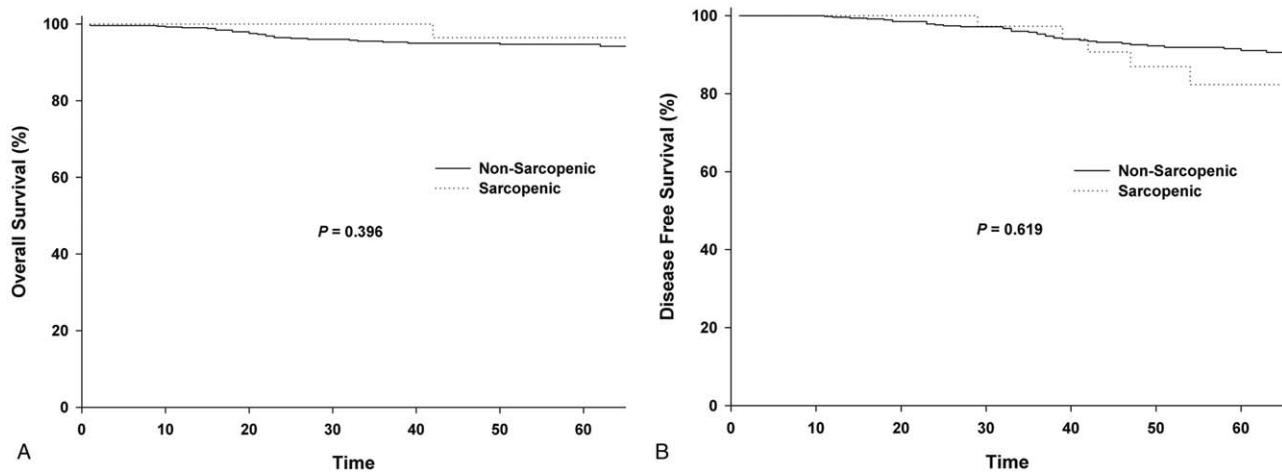


Figure 2. Five-year overall survival and disease-free survival between the sarcopenic and nonsarcopenic groups. (A) There was no significant difference in the 5-year overall survival between the nonsarcopenic and sarcopenic groups ($P = .396$). (B) There was no significant difference in the 5-year disease-free survival between the non-sarcopenic and sarcopenic groups ($P = .619$).

Forty six patients (8.0%) were diagnosed with preoperative sarcopenia. We compared the clinical and radiological variables by dividing them into 2 groups: preoperative nonsarcopenic and sarcopenic groups. The preoperative sarcopenic group showed a higher proportion of women, lower BMI, more lymph node involvement, lower proportion of alcoholics and smokers and more visceral fat area than the nonsarcopenic group. There was no significant difference in the 5-year OS and DFS between them ($P = .396$, $P = .619$, respectively) (Fig. 2).

3.2. Clinical outcomes of the patients with post-gastrectomy sarcopenia newly developed after curative gastrectomy

Among the 527 patients without sarcopenia, 57 (10.8%) were diagnosed with post-gastrectomy sarcopenia newly developed 1 year after curative gastrectomy. To evaluate the clinical significance of postgastrectomy sarcopenia newly developed after curative gastrectomy, we divided the preoperative nonsarcopenic patients into 2 groups (nonsarcopenic and postgastrectomy sarcopenic groups) and compared their clinical and radiological variables. The postgastrectomy sarcopenic group showed a higher proportion of old age, women, weight loss, proximal location of the tumors, differentiated tumors, lymph node involvement, and alcoholics compared with the nonsarcopenic group (Table 2). We performed multivariate analyses to determine the risk factors of sarcopenia newly developed after curative gastrectomy. As a result, female sex, weight loss, proximal location of tumor, differentiated tumor were significant risk factors of postgastrectomy sarcopenia newly developed after curative gastrectomy (Table 2).

To evaluate the prognosis of the patients with postgastrectomy sarcopenia newly developed after surgical resection, we compared the 5-year survival rates among the preoperative sarcopenic, nonsarcopenic, and postgastrectomy sarcopenic groups. There was a significant difference in the OS among the 3 groups ($P = .017$), especially, there was a significant difference between nonsarcopenic and postgastrectomy sarco-

penic groups ($P = .009$). However, there was no difference in the DFS among them ($P = .49$) (Fig. 3).

3.3. Correlation between body composition and OS

The relationship between preoperative body fat and postoperative muscle mass was investigated; there was a significant correlation between the VFA and skeletal muscle mass ($\rho = 0.296$, $P < .001$). However, there was no significant correlation between the SFA and skeletal muscle mass ($\rho = -0.068$, $P = .185$) (Fig. 4).

The effect of BMI, body fat, and muscle mass on the long-term prognosis was evaluated; there was a significance only for BMI. There was no significant association between the OS and VFA, skeletal muscle mass, and skeletal muscle density (Table 3).

4. Discussion

The present study evaluated the clinical significance of newly developed postgastrectomy sarcopenia, a surrogate of postoperative nutritional status after surgical resection, based on the assumption that nutritional parameters, such as muscle mass and visceral fat, are important prognostic factors after curative gastrectomy. We found several clinical values of sarcopenia in patients with GC undergoing curative gastrectomy. First, the preoperative sarcopenic group showed a higher proportion of women, lower BMI, and lower proportion of alcoholics and smokers; however, there was no significant difference in the 5-year survival rate. Second, the risk factors for postgastrectomy sarcopenia newly developed after curative gastrectomy were female sex, proximal location of the tumors, differentiated tumors; there was significant difference in the 5-year overall survival among the preoperative sarcopenic, non-sarcopenic, and postgastrectomy sarcopenic groups. Especially, there was significant difference between nonsarcopenic and postgastrectomy sarcopenic groups. Last, there was a significant correlation between the preoperative fat volume and postoperative sarcopenia; however, only BMI was significantly associated with long-term survival.

Table 2**Univariate and multivariate analyses of risk factors in postgastrectomy sarcopenic and nonsarcopenic patients with gastric cancer.**

Factors	Postgastrectomy sarcopenic patients	Nonsarcopenic patients	Univariate analysis			Multivariate analysis		
			Odd ratio	95% CI	P value	Odd ratio	95% CI	P value
Age								
Age <65	24 (42.1)	276 (58.7)	1			1		
Age ≥65	33 (57.9)	194 (41.3)	1.956	1.121–3.414	.018	1.599	0.851–3.004	.144
Sex								
Female	21 (36.8)	106 (22.6)	1			1		
Male	36 (63.2)	364 (77.4)	0.499	0.280–0.892	.019	0.464	0.233–0.925	.029
BMI, mean (SD)								
23 <	27 (47.4)	180 (38.3)	1					
≥23	30 (52.6)	290 (61.7)	0.690	0.397–1.198	.187			
Weight loss (>10%)								
No	17 (29.8)	288 (61.7)	1			1		
Yes	40 (70.2)	179 (38.3)	3.786	2.083–6.880	<.001	3.204	1.716–5.981	<.001
Tumor location								
Proximal	16 (28.1)	65 (13.9)	1			1		
Distal	41 (71.9)	402 (86.1)	0.414	0.220–0.781	.004	0.490	0.248–0.968	.040
Tumor size								
≤3.1	25 (43.9)	258 (54.9)	1					
>3.1	32 (56.1)	212 (45.1)	1.558	0.895–2.710	.117			
Differentiation of tumor								
Differentiated	45 (78.9)	293 (62.3)	1			1		
Undifferentiated	12 (21.1)	177 (37.7)	0.441	0.227–0.857	.003	0.409	0.200–0.837	.014
TNM stage					.128			
I	33 (57.9)	323 (68.7)	1					
II	10 (17.5)	79 (16.8)	1.239	0.586–2.620	.575			
III	14 (24.6)	68 (14.5)	2.015	1.023–3.968	.043			
LN involvement								
No	33 (57.9)	337 (72.3)	1			1		
Yes	24 (42.1)	129 (27.7)	1.900	1.081–3.338	.026	1.785	0.971–3.284	.062
Type of resection								
Total gastrectomy	11 (19.3)	99 (21.1)	1					
Subtotal gastrectomy	46 (80.7)	371 (78.9)	1.116	0.557–2.234	.757			
Adjuvant chemotherapy								
No	34 (59.6)	334 (71.1)	1					
Yes	23 (40.4)	136 (28.9)	1.661	0.944–2.924	.078			
Hypoalbuminemia (<3.0)								
No	54 (94.7)	441 (93.8)	1					
Yes	3 (5.3)	29 (6.2)	0.845	0.249–2.867	.921			
Anemia (Hb <8.0)								
No	54 (94.7)	460 (97.9)	1					
Yes	3 (5.3)	10 (2.1)	2.556	0.682–9.573	.164			
Alcohol								
No	42 (73.7)	242 (51.5)	1			1		
Yes	15 (26.3)	228 (48.5)	0.379	0.205–0.702	<.001	0.596	0.290–1.226	.160
Smoking								
No	41 (71.9)	291 (61.9)	1					
Yes	16 (28.1)	179 (38.1)	0.634	0.346–1.164	.142			
Hypertension								
No	30 (52.6)	284 (60.4)	1					
Yes	27 (47.4)	186 (39.6)	1.374	0.791–2.386	.259			
Diabetes mellitus								
No	44 (77.2)	389 (82.8)	1					
Yes	13 (22.8)	81 (17.2)	1.419	0.731–2.755	.301			
Total fat area								
<238.2	11 (61.1)	186 (48.9)	1					
≥238.2	7 (38.9)	194 (51.1)	0.610	0.232–1.607	.317			
Visceral fat area								
<107.0	26 (45.6)	228 (48.5)	1					
≥107.0	31 (54.4)	242 (51.5)	1.123	0.647–1.950	.679			
Subcutaneous fat area								
<123.0	28 (49.1)	239 (50.9)	1			1		

(continued)

Table 2
(continued).

Factors	Postgastrectomy sarcopenic patients	Nonsarcopenic patients	Univariate analysis			Multivariate analysis		
			Odd ratio	95% CI	P value	Odd ratio	95% CI	P value
≥123.0	29 (50.9)	231 (49.1)	1.072	0.618–1.857	.805	1.173	0.542-2.536	.685
VFA/SFA								
<0.88	11 (61.1)	183 (48.2)	1					
≥0.88	7 (38.9)	197 (51.8)	0.591	0.224–1.757	.288			

BMI = body mass index, LM, lymph node, SFA = subcutaneous fat area, VFA = visceral fat area.

Skeletal muscle mass is a new nutritional assessment index.^[15] Sarcopenia is characterized by decreased muscle strength, subsequent fatigue, and metabolic disorders caused by skeletal muscle mass reduction (atrophy and muscle tissue quality reduction).^[10] CT

assessment of body composition is considered a precise method and has become the reference standard for detecting obesity and sarcopenia.^[16,17] Indeed, sarcopenia can be defined by a precise quantification of skeletal muscle mass using abdominal CT.^[18]

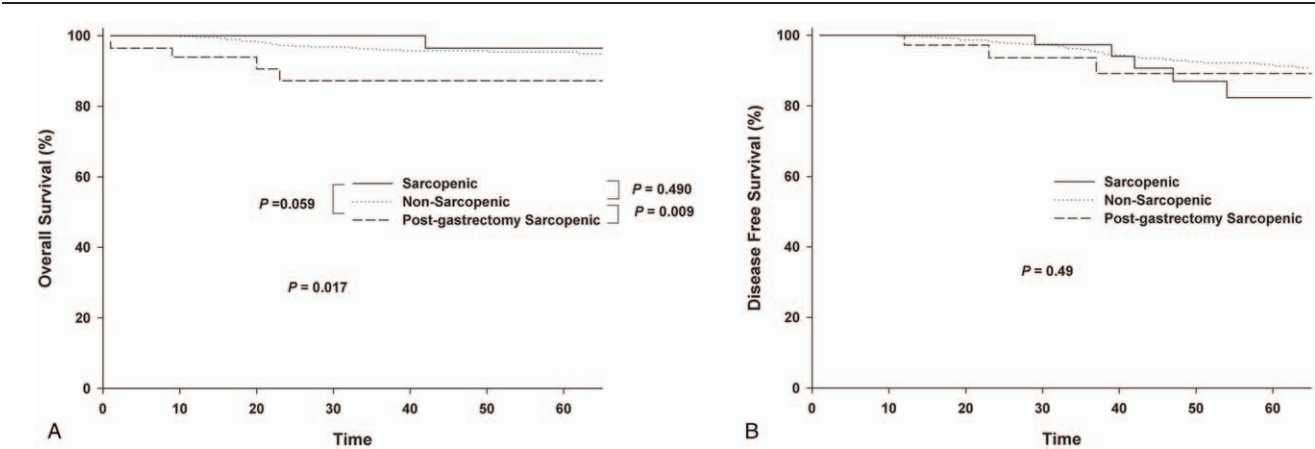


Figure 3. Five-year overall survival and disease-free survival among the sarcopenic, post-gastrectomy sarcopenic, and non-sarcopenic groups. (A) There was a significant difference in the 5-year overall survival among the non-sarcopenic, postgastrectomy sarcopenic, and sarcopenic groups ($P = .017$), especially, there was a significant difference between nonsarcopenic and postgastrectomy sarcopenic groups ($P = .009$). (B) There was no significant difference in the 5-year disease-free survival among the nonsarcopenic, post-gastrectomy sarcopenic, and sarcopenic groups ($P = .49$).

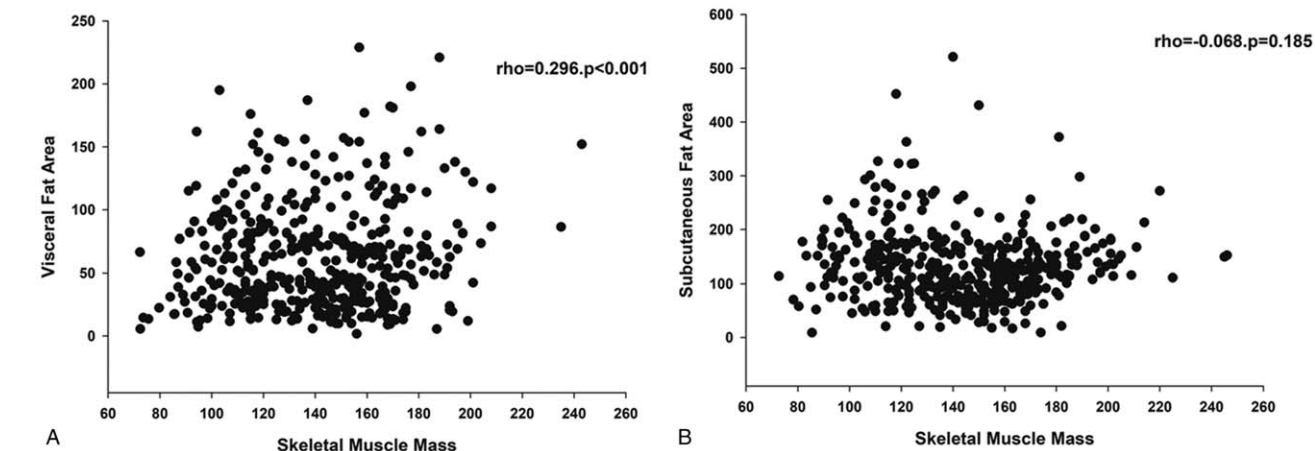


Figure 4. Correlation between preoperative abdominal fat distribution and postoperative skeletal muscle mass. (A) There was a significant correlation between the preoperative visceral fat area and postoperative skeletal muscle mass ($\rho = 0.296$, $P < .001$). (B) There was no significant correlation between the preoperative subcutaneous fat area and postoperative skeletal muscle mass ($\rho = 0.068$, $P = .185$).

Table 3**Influence of BMI, abdominal fat, and skeletal muscle mass on overall survival.**

Characteristics	No.	5 year survival rate	K–M <i>P</i> value	HR (95% CI)	<i>P</i> value
BMI			.358		.393
Underweight (<18.5)	17	0.865 (0.690–1.040)		1	
Normal (18.5–22.9)	190	0.945 (0.910–0.980)		0.382 (0.084–1.748)	.215
Overweight (23–24.9)	127	0.948 (0.907–0.989)		0.444 (0.094–2.096)	.305
Obese (≥25)	193	0.956 (0.923–0.988)		0.263 (0.055–1.270)	.096
VFA quartile			.845		.847
First (<72.24)	134	0.949 (0.909–0.989)		1	
Second (72.25–106.99)	120	0.953 (0.913–0.993)		1.204 (0.404–3.583)	.739
Third (107.00–150.49)	142	0.962 (0.930–0.995)		0.885 (0.285–2.745)	.832
Fourth (≥150.50)	131	0.921 (0.867–0.974)		1.387 (0.481–3.999)	.545
VFA/SFA ratio			.086		.164
First (<0.673)	98	0.989 (0.967–1.011)		1	
Second (0.674–0.884)	100	0.955 (0.913–0.998)		4.052 (0.453–36.274)	.211
Third (0.885–1.219)	103	0.919 (0.860–0.977)		8.688 (1.086–69.512)	.042
Fourth (≥1.220)	97	0.939 (0.887–0.992)		7.192 (0.884–58.503)	.065
Skeletal muscle mass			.290		.509
First (<124.49)	131	0.950 (0.911–0.989)		1	
Second (124.50–146.99)	126	0.919 (0.868–0.970)		1.590 (0.566–4.469)	.379
Third (147.00–165.99)	137	0.946 (0.903–0.989)		1.221 (0.424–3.520)	.711
Fourth (≥166.0)	133	0.972 (0.941–1.003)		0.660 (0.186–2.339)	.520
Skeletal muscle density			.049		.069
First (<34.09)	129	0.904 (0.850–0.958)		1	
Second (34.10–38.49)	122	0.943 (0.898–0.987)		0.595 (0.234–1.511)	.275
Third (38.50–42.09)	132	0.972 (0.940–1.003)		0.312 (0.101–0.969)	.044
Fourth (≥42.10)	144	0.965 (0.930–1.000)		0.282 (0.091–0.875)	.035

BMI = body mass index, SFA = subcutaneous fat area, VFA = visceral fat area.

Sarcopenia is a multifactorial clinical condition leading to prolonged hospitalization, higher degrees of treatment-related toxicity and postsurgical complications, reduced cancer treatment response, impaired quality of life, and worse prognosis among patients with GC.^[19] Even in early-stage GC, weight loss and associated quality of life often decline following surgery as it may reduce the stomach's capacity and consequently decrease food intake.^[20] For these reasons, GC may be more directly correlated with sarcopenia compared with other cancers. Patients with GC and sarcopenia at the time of surgery experienced worse long-term outcomes than did those without sarcopenia.^[21,22] In the present study, the prevalence of preoperative sarcopenia (8.0%) was comparable to previous reports (6.8%–57.7%).^[16,23] Sarcopenia is associated with many causes, such as malnutrition, aging, inactivity, inflammatory disease, and cancer.^[9] In our study, the preoperative sarcopenic group had a higher proportion of women, lower BMI, more lymph node involvement, and lower proportion of alcoholics and smokers. We speculate that more women were included in the sarcopenic group. The present study provided female sex, proximal location of the tumors, and differentiated tumors as the risk factors for postgastrectomy sarcopenia newly developed after curative gastrectomy. Interestingly, postgastrectomy sarcopenia was not associated with type of resection.

Preoperative sarcopenia might be used as a new indicator of poor pathological staging, impaired OS, and increased postoperative complications.^[13] Gastrointestinal cancers, especially stomach and esophageal cancers, are known to yield great nutritional loss postoperatively. In this study, we revealed that postgastrectomy sarcopenia newly developed after curative gastrectomy had a significant impact on overall survival in terms of the long-term prognosis.

Recently, there is an increasing interest in the relationship between surgical outcomes and body composition, as determined by body fat and muscle mass.^[16] Obesity and sarcopenia may potentiate each other and act synergistically, causing physical impairment and metabolic disorders and worsening prognosis.^[24] Muscle mass loss may be associated with preserved or even increased body fat content. Moreover, increased visceral fat content may promote proinflammatory cytokine secretion, leading to catabolic effects on the muscles and insulin resistance.

There was a significant association between visceral fat and postoperative complications and long-term prognosis.^[25,26] Similar with previous reports, the present study showed a significant correlation between the preoperative VFA and postoperative skeletal muscle mass. However, these were not significantly associated with long-term prognosis. The VFA and VFA/SFA ratio significantly predicted cancer-related survival.^[27,28] However, they were not significantly associated with long-term prognosis in this study. This may be because a relatively large portion of patients with early-stage GC (66.8%) were included.

In our study, only BMI was significantly correlated with the 5-year survival rate, suggesting that it affects long-term prognosis. BMI is generally recognized as a primary indicator used to define malnutrition.^[23] Malnutrition can lead to various postoperative complications, reduced drug therapeutic efficacy, and systemic inflammatory response activation.^[29] BMI affected the long-term outcomes after GC surgery.^[7] Further, there was a negative prognostic impact of a low BMI.^[30] Preoperative BMI also predicted survival among patients with GC and was superior to a postoperative staging system.^[31] Since the prevalence of nutritional risks in these patients is 36% to 43%,^[23] preoperative nutritional assessment is important in preventing possible complications.^[10]

This study was the first to identify the risk factors and clinical significance of sarcopenia newly developed after curative gastrectomy; skeletal muscle mass and abdominal fat were objectively quantified using abdominal CT performed by an experienced abdominal radiology specialist.

There were several limitations in this study. First, sarcopenia was diagnosed only by radiological evaluation using CT. Muscle function could not be measured in this study. Second, the number of patients with advanced GC was small. Thus, more accurate sarcopenia diagnoses and sufficient number of patients with advanced GC are needed in future studies. Last, this study had relatively small number of female patients. Therefore, a large number of female patients should be included in the future studies. In conclusion, women with proximal location of the differentiated GC are at a high postgastrectomy sarcopenia risk. Since postgastrectomy sarcopenia newly developed after curative gastrectomy did affect the overall survival rate, patients at risk of developing sarcopenia after surgical resection may require early nutritional status evaluation and nutritional support.

Author contributions

Conceptualization: Beom Jin Kim.

Data curation: Hye Jin Kim, Eun Sun Lee, Beom Jin Kim, Won-Seok Kim, Jae Yong Park, Jae Gyu Kim, Joong-Min Park, Jong Won Kim, Kyong-Choun Chi, Hyung Kang.

Formal analysis: Hyung Kang.

Investigation: Eun Sun Lee, Beom Jin Kim, Won-Seok Kim, Jae Yong Park, Jae Gyu Kim, Joong-Min Park, Jong Won Kim, Kyong-Choun Chi.

Supervision: Beom Jin Kim.

Writing – original draft: Hye Jin Kim, Eun Sun Lee.

Writing – review & editing: Beom Jin Kim.

References

- [1] Zhuang CL, Huang DD, Pang WY, et al. Sarcopenia is an independent predictor of severe postoperative complications and long-term survival after radical gastrectomy for gastric cancer: analysis from a large-scale cohort. *Medicine (Baltimore)* 2016;95:e3164.
- [2] Kuwada K, Kuroda S, Kikuchi S, et al. Sarcopenia and comorbidity in gastric cancer surgery as a useful combined factor to predict eventual death from other causes. *Ann Surg Oncol* 2018;25:1160–6.
- [3] Li XT, Tang L, Chen Y, et al. Visceral and subcutaneous fat as new independent predictive factors of survival in locally advanced gastric carcinoma patients treated with neo-adjuvant chemotherapy. *J Cancer Res Clin Oncol* 2015;141:1237–47.
- [4] Go JE, Kim MC, Kim KH, et al. Effect of visceral fat area on outcomes of laparoscopy-assisted distal gastrectomy for gastric cancer: subgroup analysis by gender and parameters of obesity. *Ann Surg Treat Res* 2015;88:318–24.
- [5] Kim Y, Ejaz A, Spolverato G, et al. Conditional survival after surgical resection of gastric cancer: a multi-institutional analysis of the us gastric cancer collaborative. *Ann Surg Oncol* 2015;22:557–64.
- [6] Wang SL, Zhuang CL, Huang DD, et al. Sarcopenia adversely impacts postoperative clinical outcomes following gastrectomy in patients with gastric cancer: a prospective study. *Ann Surg Oncol* 2016;23:556–64.
- [7] Jun DH, Kim BJ, Park JH, et al. Preoperative body mass index may determine the prognosis of advanced gastric cancer. *Nutr Cancer* 2016;68:1295–300.
- [8] Papenfuss WA, Kukar M, Oxenberg J, et al. Morbidity and mortality associated with gastrectomy for gastric cancer. *Ann Surg Oncol* 2014;21:3008–14.
- [9] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. *Age Ageing* 2010;39:412–23.
- [10] Ongaro E, Buoro V, Cinausero M, et al. Sarcopenia in gastric cancer: when the loss costs too much. *Gastric Cancer* 2017;20:563–72.
- [11] Yang Z, Zhou X, Ma B, et al. Predictive value of preoperative sarcopenia in patients with gastric cancer: a meta-analysis and systematic review. *J Gastrointest Surg* 2018;22:1890–902.
- [12] Huang DD, Chen XX, Chen XY, et al. Sarcopenia predicts 1-year mortality in elderly patients undergoing curative gastrectomy for gastric cancer: a prospective study. *J Cancer Res Clin Oncol* 2016;142:2347–56.
- [13] Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer* 2011;14:101–12.
- [14] Washington K. 7th edition of the AJCC cancer staging manual: stomach. *Ann Surg Oncol* 2010;17:3077–9.
- [15] Prado CM, Lieffers JR, McCargar LJ, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *Lancet Oncol* 2008;9:629–35.
- [16] Nishigori T, Tsunoda S, Okabe H, et al. Impact of sarcopenic obesity on surgical site infection after laparoscopic total gastrectomy. *Ann Surg Oncol* 2016;23:524–31.
- [17] Harada K, Baba Y, Ishimoto T, et al. Low visceral fat content is associated with poor prognosis in a database of 507 upper gastrointestinal cancers. *Ann Surg Oncol* 2015;22:3946–53.
- [18] Grotenhuis BA, Shapiro J, van Adrichem S, et al. Sarcopenia/muscle mass is not a prognostic factor for short- and long-term outcome after esophagectomy for cancer. *World J Surg* 2016;40:2698–704.
- [19] Hirasawa Y, Nakashima J, Yunaiyama D, et al. Sarcopenia as a novel preoperative prognostic predictor for survival in patients with bladder cancer undergoing radical cystectomy. *Ann Surg Oncol* 2016;23:1048–54.
- [20] Takiguchi S, Takata A, Murakami K, et al. Clinical application of ghrelin administration for gastric cancer patients undergoing gastrectomy. *Gastric Cancer* 2014;17:200–5.
- [21] Kudou K, Saeki H, Nakashima Y, et al. Prognostic significance of sarcopenia in patients with esophagogastric junction cancer or upper gastric cancer. *Ann Surg Oncol* 2017;24:1804–10.
- [22] Tamandl D, Paireder M, Asari R, et al. Markers of sarcopenia quantified by computed tomography predict adverse long-term outcome in patients with resected oesophageal or gastro-oesophageal junction cancer. *Eur Radiol* 2016;26:1359–67.
- [23] Lou N, Chi CH, Chen XD, et al. Sarcopenia in overweight and obese patients is a predictive factor for postoperative complication in gastric cancer: a prospective study. *Eur J Surg Oncol* 2017;43:188–95.
- [24] Buch A, Carmeli E, Boker LK, et al. Muscle function and fat content in relation to sarcopenia, obesity and frailty of old age—an overview. *Exp Gerontol* 2016;76:25–32.
- [25] Yang T, Wei M, He Y, et al. Impact of visceral obesity on outcomes of laparoscopic colorectal surgery: a meta-analysis. *ANZ J Surg* 2015;85:507–13.
- [26] Kunisaki C, Makino H, Takagawa R, et al. Predictive factors for surgical complications of laparoscopy-assisted distal gastrectomy for gastric cancer. *Surg Endosc* 2009;23:2085–93.
- [27] Guiu B, Petit JM, Bonnetain F, et al. Visceral fat area is an independent predictive biomarker of outcome after first-line bevacizumab-based treatment in metastatic colorectal cancer. *Gut* 2010;59:341–7.
- [28] Griggs JJ, Sabel MS. Obesity and cancer treatment: weighing the evidence. *J Clin Oncol* 2008;26:4060–2.
- [29] Sun KY, Xu JB, Chen SL, et al. Novel immunological and nutritional-based prognostic index for gastric cancer. *World J Gastroenterol* 2015;21:5961–71.
- [30] Komatsu S, Kosuga T, Kubota T, et al. Preoperative low weight affects long-term outcomes following curative gastrectomy for gastric cancer. *Anticancer Res* 2018;38:5331–7.
- [31] Liu X, Qiu H, Kong P, et al. Gastric cancer, nutritional status, and outcome. *Onco Targets Ther* 2017;10:2107–14.