Observational Study

Medicine®

OPEN

Body mass index and skeletal muscle index are useful prognostic factors for overall survival after gastrectomy for gastric cancer

Retrospective cohort study

Eun Young Kim, MD, PhD[a], Kyong Hwa Jun, MD, PhD[b,*], Shinn Young Kim, MD, PhD[b,*], Hyung Min Chin, MD, PhD[b]

Abstract

Among patients undergoing gastrectomy for gastric cancer, the impact of anthropometric indices on surgical outcomes is not well-established. The aim of this study was to evaluate the prognostic significance of the skeletal muscle index (SMI) and body mass index (BMI) on overall survival (OS) in patients with gastric cancer.

A total of 305 patients who underwent curative gastrectomy for gastric adenocarcinoma between January 2005 and March 2008 were enrolled. Patients were classified into groups based on the SMI and BMI. The SMI was measured by preoperative abdominal computed tomography (CT). The SMI groups were classified based on gender-specific cut-off values obtained by means of optimum stratification. BMI groups were divided according to the World Health Organization definition of obesity for Asians.

The mean SMI was 58.2 cm^2/m^2 and the mean BMI was 23.2 kg/m^2. One hundred fifteen (37.7%) patients had sarcopenia based on the diagnostic cut-off values (56.2 cm^2/m^2 for men and 53.6 cm^2/m^2 for women). Apart from gender, there were no significant differences in patient characteristics or surgical outcomes between the SMI groups. In the underweight group, tumor (T) stage, tumor-node-metastasis (TNM) stage, number of retrieved lymph nodes, D2 dissection, and hospital stay were significantly increased compared with the overweight/obese group. High and low BMI, and low SMI, were independent prognostic factors for OS (hazard ratio [HR] = 2.355, 1.736, and 1.607, respectively; $P = .009$, .023, and .033, respectively).

SMI and BMI did not impact perioperative morbidity in patients undergoing gastrectomy for gastric cancer. Both SMI and BMI are useful prognostic factors for OS in gastric cancer patients after gastrectomy.

Abbreviations: AJCC = American Joint Commission for Cancer, BMI = body mass index, CT = computed tomography, DFS = disease-free survival, EWGSOP = European Working Group on Sarcopenia in Older People, HR = hazard ratio, HU = Hounsfield units, LN = lymph node, MRI = magnetic resonance imaging, OS = overall survival, ROC = receiver operating characteristic, SD = standard deviation, SFA = subcutaneous fat area, SMI = skeletal muscle index, TFA = total fat area, TNM = tumor-node-metastasis, VFA = visceral fat area.

Keywords: gastric cancer, prognosis, skeletal muscle index

1. Introduction

The European Working Group on Sarcopenia in Older People (EWGSOP) defines sarcopenia as the presence of both low muscle mass and low muscle function (strength or performance).[1] However, there has been no consensus to define sarcopenia until now.

Sarcopenia is usually related to lifestyle, metabolic, and neuroendocrine changes associated with aging, or specific diseases or medications. In particular, conditions such as insulin resistance, inflammation, oxidative stress, chronic kidney disease, and malignancy are associated with sarcopenia.[2]

Over the years, researchers have had a great interest in sarcopenia in cancer patients. Many studies have investigated the significance of decreased skeletal muscle mass in cancer patients. Most found that changes in skeletal muscle mass were associated with poor oncologic outcomes after surgery in patients with solid organ malignancies, including ovarian cancer, lung cancer, pancreatic cancer, renal cell carcinoma, colorectal cancer, and esophageal cancer.[3–8] In addition, the presence of sarcopenia in adults with cancer has been associated with increased chemotherapy toxicity and postoperative complications.[9–11] In other

Editor: Neil Merrett.

The authors declare that they have no conflicts of interest.

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

[a] Department of Surgery, Uijeongbu St. Mary Hospital, [b] Department of Surgery, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea.

[*] Correspondence: Kyong Hwa Jun, Shinn Young Kim, Department of Surgery, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Korea, 93, Jungbudae-ro, Paldal-gu, Suwon, Gyeonggi-do, Seoul 16247, Korea (e-mail: dkkwkh@catholic.ac.kr [KHJ] and xerizck@catholic.ac.kr [SYK]).

How to cite this article: Kim EY, Jun KH, Kim SY, Chin HM. Body mass index and skeletal muscle index are useful prognostic factors for overall survival after gastrectomy for gastric cancer: retrospective cohort study. Medicine 2020;99:47 (e23363).

Received: 15 July 2020 / Received in final form: 19 October 2020 / Accepted: 24 October 2020

http://dx.doi.org/10.1097/MD.0000000000023363

words, sarcopenia has a negative impact on short-term and long-term outcomes in several cancers. Because of such risk of treatment for cancer patients with sarcopenia, clinicians might be reluctant to perform surgery or chemotherapy.

Currently, the tailored strategy for treating gastric cancer is a major issue. Although the most reliable prognostic factor is TNM stage, various oncologic outcomes are observed even within the same stage. Thus, increasing attention has been directed at host factors such as muscle mass, fat mass, inflammation, and nutritional status.[12–14] Several studies on sarcopenia after gastrectomy in patients with gastric cancer have used body mass index (BMI)-specific cut-offs. The potential of BMI as a prognostic factor for gastric cancer has been studied extensively, while skeletal muscle mass remains relatively unexplored.[15–20] Several previous studies compared perioperative complications and nutritional status according to the skeletal muscle index (SMI) and BMI. However, little is known about the long-term outcomes of gastrectomy in terms of the SMI and BMI.

The aim of this study was to demonstrate whether sarcopenia according to SMI measured with abdominal computed tomography (CT) image and underweight, overweight/obese status according to BMI can be a poor prognostic factor in terms of overall survival (OS) in curative gastrectomy patients with gastric cancer.

2. Patients and methods

2.1. Patients

A total of 305 patients with gastric adenocarcinoma who underwent curative gastrectomy at St. Vincent's Hospital, The Catholic University of Korea between January 2005 and March 2008 were reviewed. Patients

1. who had distant metastasis,
2. who underwent a palliative operation or R1 resection, and
3. for whom skeletal muscle mass and abdominal fat area could not be calculated based on abdominal CT were excluded.

The Institutional Review Board of our hospital approved this study (VC13RISI0075). Demographic, operative, radiologic, and pathologic data from all patients were obtained through a retrospective medical record review.

2.2. Measurement of anthropometric indices

The height and weight of each patient were recorded during the preoperative evaluation. BMI was calculated using the following formula: weight (kg)/height^2 (m^2). Patients were classified according to BMI, based on the World Health Organization definition of obesity for Asians, as follows: (BMI $< 18.5\,kg/m^2$), normal ($18.5 \leq$ BMI $< 23.0\,kg/m^2$), or overweight/obese (BMI $\geq 23.0\,kg/m^2$).

Abdominal CT images were obtained during preoperative evaluation. The SMI was calculated according to the following formula: skeletal muscle mass (cm^2) / height^2 (m^2). Skeletal muscle mass was measured using a cross-sectional 16-detector row CT image of the abdomen (Somatom Sensation 16; Siemens Medical Solutions, Forchheim, Germany) at the level of the umbilicus. On CT scans, muscle mass was determined by setting the attenuation level within the range of −150 to −29 Hounsfield units (HU). First, using Rapidia 2.8 software (INFINITT, Seoul, Korea), the whole abdominal wall margin and intra-abdominal wall margin were manually traced to determine the entire cross-sectional muscle mass area. Next, the intra-abdominal wall margin was traced to determine the intestinal smooth muscle mass area (Fig. 1). Finally, the skeletal muscle mass (the difference between these 2 parameters) was calculated in cm^2. In addition, adipose tissue was visualized by setting the attenuation level within the range of −190 to −30 HU. The fat margin was manually traced and the cross-sectional area of each parameter was calculated in cm^2. The subcutaneous fat area (SFA) was obtained by determining the difference between the total fat area (TFA) and the visceral fat area (VFA).

2.3. Definition and detection of the optimum cut-offs of the SMI

Using OS as an endpoint, the area under the receiver operating characteristic (ROC) curve for the SMI was 0.619 and 0.586 for males and females, respectively. Therefore, the male and female SMI cut-off values for OS were set at 56.2 and 53.6, respectively. In addition, Figure 2 showed ROC curve based on the total patients. Patients with an SMI greater than the cut-off value were assigned to the high SMI group; all other patients were assigned to the low SMI group.

2.4. Statistical analysis

To evaluate the sensitivity and specificity for OS, the ROC was calculated and the Youden index was estimated to determine the optimal SMI cut-off values. Comparison of categorical variables was performed using the Chi-Squared test. For correlation analysis, Pearson correlation was used. Kaplan–Meier curves were used to compare OS among patients, and differences in survival rate between groups were compared using the log-rank test. A Cox regression model was used to identify variables that influence OS and disease-free survival (DFS). Multivariate analysis was performed including variables that had a significant independent relationship with OS. Significance was defined as a P value less than .05. All statistical analyses were performed using SPSS software (ver. 21.0; SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Clinicopathologic characteristics according to the SMI

Clinicopathologic characteristics according to the SMI are summarized in Table 1. Of a total of 305 patients, 207 (67.9%) were male and the mean age was 58.7 years (SD: 11.9 years). The mean preoperative BMI, SMI, VFA, SFA, and TFA were $23.2\,kg/m^2$, $58.2\,cm^2/m^2$, $111.0\,cm^2$, $120.1\,cm^2$, and $231.1\,cm^2$, respectively. For calculation of OS as an endpoint, there were 115 patients (37.7%) in the low SMI group and 190 (62.3%) in the high SMI group. There were more male patients in the high SMI group than in the low SMI group ($P < .001$). There were significant associations between the SMI group and BMI, TFA and SFA. However, there was no significant association between the SMI group and VFA. Based on the final pathologic stage according to the American Joint Commission for Cancer tumor-node-metastasis (TNM classification (AJCC, 8th edition), there were 154 patients (50.5%) with stage I disease, 77 (25.3%) with stage II disease, and 74 (24.3%) with stage III disease. The prevalence of low SMI was 40.9% in stage I patients, 36.3% in stage II patients, and 32.4% in stage III patients. More than 75%

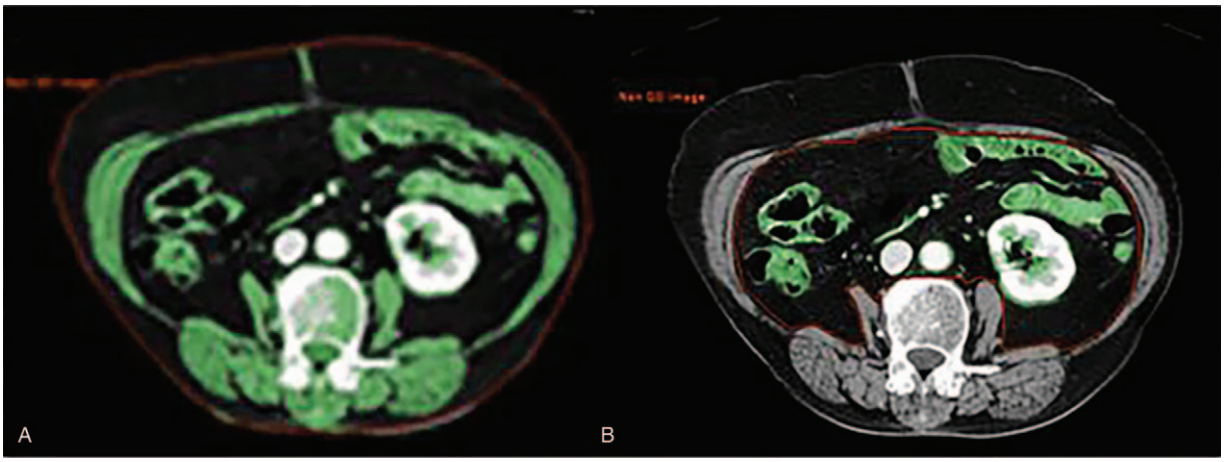

Figure 1. Quantification of skeletal muscle mass at the level of the umbilicus. (A) The outer red line was manually generated with a cursor to and denotes the entire abdominal wall area in which attenuation was measured. (B) The intra-abdominal wall was traced to measure the intestinal smooth muscle mass area.

of the patients were treated with distal subtotal gastrectomy; the remaining patients were treated with total gastrectomy. D2 lymph node (LN) dissection was performed in 57.7% of patients, whereas D1 plus LN dissection was performed in 42.3% of patients. The mean operative time was 231.5 minutes (SD: 53.2 minutes) and postoperative complications were reported in 21 patients (6.9%). There was no significant difference in operation time or postoperative complications between the 2 groups.

3.2. Clinicopathologic characteristics according to the BMI

Clinicopathologic characteristics according to BMI are shown in Table 2. The mean TFA, SFA VFA, and SMI increased with BMI ($P < .001$). Higher BMI was correlated with longer operation time, but was not significantly correlated with blood loss or transfusion. In the underweight group, advanced T stage and TNM stage were common, and hospital stays were longer than in the other 2 groups. In the overweight/obese group, the number of retrieved LNs was lower, and D1 plus LN dissection was more frequently performed than D2 dissection. However, no significant group difference in postoperative complications was observed.

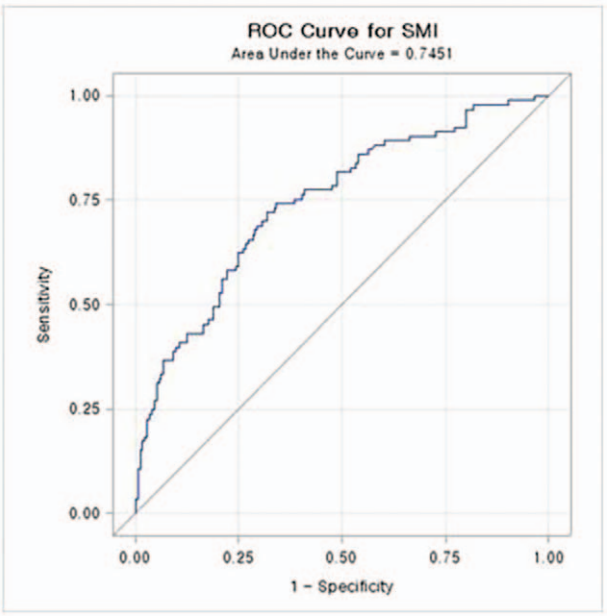

Figure 2. Receiver operating characteristic curve for the SMI.

3.3. Correlations with the SMI and other anthropometric indices

There was a significant positive correlation between SMI and BMI ($r = 0.466$, $P < .001$) (Fig. 3[a]). SMI was also significantly correlated with VFA and TFA ($r = 0.255$, $P < .001$ and $r = .153$, $P = .007$, respectively) (Figs. 3[b] and 3[c]). However, there was no significant correlation between SMI and SFA ($r = 0.016$, $P = .775$) (Fig. 3[d]).

3.4. Overall survival according to the SMI

The median survival time was 59.5 months (range: 8–97 months), with a median follow-up period of 62 months (range: 26–97 months) for patients who were alive at the time of the last follow-up. The 5-year OS was 81%. OS in the high SMI group showed a trend toward being higher than that in the low SMI group ($P = .058$) (Fig. 4). When the patients were stratified according to stage, a similar trend, but non-significant, trend was observed. In terms of OS, advanced T stage, positive LN metastasis, high and low BMI, and low SMI were identified as significant independent risk factors (Table 3).

4. Discussion

The present study is a retrospective review of a database of consecutive cases. We found a sarcopenia prevalence rate of 37.7% (26.5% in men and 61.2% in women) in gastric cancer patients undergoing gastrectomy. There was no difference in the prevalence of sarcopenia between this study and previously published studies (16.0%–47.7%).[21–23] No association between sarcopenia and 30-day mortality, postoperative compli-

Table 1

Clinicopathologic characteristics according to SMI.

	Total (N=305)	High SMI (N=190)	Low SMI (N=115)	*P* value
Age (years)	58.7±11.9	59.0±10.6	58.1±13.8	.870
Gender				<.001
Male	207 (67.9)	152 (80.0)	55 (47.8)	
Female	98 (32.1)	38 (20.0)	60 (52.2)	
BMI (kg/m^2)	23.2±3.2	24.2±3.0	21.6±3.0	<.001
TFA (cm^2)	231.1±102.5	242.5±108.6	212.2±88.9	<.001
SFA (cm^2)	120.1±58.4	121.1±60.5	118.4±55.1	<.001
VFA (cm^2)	111.0±58.0	121.4±60.6	93.8±48.9	.971
SMI (cm^2/m^2)	58.2±9.6	63.8±6.9	48.9±5.4	.028
Comorbidities				.589
No	181 (59.3)	115 (60.5)	66 (57.4)	
Yes	124 (40.7)	75 (39.5)	49 (42.6)	
Histologic type				.640
Differentiated	144 (47.2)	91 (47.9)	53 (46.1)	
Undifferentiated	113 (37.1)	72 (37.9)	41 (35.7)	
Others	48 (15.7)	27 (14.2)	21 (18.2)	
Tumor location				.439
Upper	21 (6.9)	13 (6.8)	8 (7.0)	
Middle	75 (24.6)	41 (21.6)	34 (29.6)	
Lower	204 (66.9)	133 (70.0)	71 (61.7)	
Whole	5 (1.64)	3 (1.6)	2 (1.7)	
Depth of invasion				.189
T1	141 (46.2)	83 (43.7)	58 (50.4)	
T2	40 (13.1)	24 (12.6)	16 (13.9)	
T3	74 (24.3)	54 (28.4)	20 (17.4)	
T4	50 (16.4)	29 (15.3)	21 (18.3)	
Lymph node metastasis				.516
N0	182 (59.7)	112 (59.0)	70 (60.9)	
N1	43 (14.1)	28 (14.7)	15 (13.0)	
N2	37 (12.1)	20 (10.5)	17 (14.8)	
N3	43 (14.1)	30 (15.8)	13 (11.3)	
TNM Stage				.448
I	154 (50.5)	91 (47.9)	63 (54.8)	
II	77 (25.3)	49 (25.8)	28 (24.4)	
III	74 (24.3)	50 (26.3)	24 (20.9)	
Extent of resection				.282
Total gastrectomy	74 (24.3)	50 (26.3)	24 (20.9)	
Distal subtotal gastrectomy	231 (75.7)	140 (73.7)	91 (79.1)	
Combined resection				.214
No	252 (82.6)	153 (80.5)	99 (86.1)	
Yes	53 (17.4)	37 (19.5)	16 (13.9)	
LN dissection				.879
D1+	129 (42.3)	81 (42.6)	48 (41.7)	
D2	176 (57.7)	109 (57.4)	67 (58.3)	
Transfusion				.624
No	278 (91.2)	172 (90.5)	106 (92.2)	
Yes	27 (8.8)	18 (9.5)	9 (7.8)	
Operative time (min)	231.5±53.2	233.8±48.3	227.9±60.4	.148
Estimated blood loss (ml)	244.3±202.5	240.4±188.0	250.7±225.2	.987
Retrieved lymph node	31.6±10.6	31.5±10.5	31.8±10.8	.843
Complication				.970
No	284 (93.1)	177 (93.2)	107 (93.0)	
Yes	21 (6.9)	13 (6.8)	8 (7.0)	
Hospital stay (day)	12.7±9.7	12.7±11.1	12.6±7.1	.944

*Parentheses are percentage.

cations or length of hospital stay was found in the present study. However, we found that OS was shorter, and death was more likely, among patients in the low SMI group. In the underweight group, advanced T stage, more LN dissections, and longer hospital stay were observed. Moreover, underweight or overweight/obese status and low SMI were independent prognostic factors for patients who underwent curative gastrectomy for gastric cancer. Unlike most previous studies, our study focused on the combined impact of BMI and SMI on survival.

Sarcopenia is a complex condition with multiple contributing factors, although the exact causes remain unclear.[21] Several factors that may contribute to the development of sarcopenia are

Table 2

Clinicopathologic characteristics according to BMI.

	Underweight (N = 22)	Normal (N = 122)	Overweight and obese (N = 161)	*P* value
Age (years)	59.6 ± 12.6	57.8 ± 12.7	59.1 ± 11.2	.696
Gender				.467
Male	17 (8.21)	79 (38.2)	111 (53.6)	
Female	5 (5.1)	43 (43.9)	50 (51.0)	
BMI (kg/m^2)	17.4 ± 0.7	21.1 ± 1.3	25.7 ± 2.1	<.001
TFA (cm^2)	92.5 ± 42.1	173.9 ± 71.1	293.4 ± 82.9	<.001
SFA (cm^2)	47.8 ± 22.6	94.4 ± 43.3	149.4 ± 53.9	<.001
VFA (cm^2)	44.7 ± 24.6	79.5 ± 37.2	143.9 ± 53.0	<.001
SMI (cm^2/m^2)	50.4 ± 7.5	54.9 ± 7.5	61.7 ± 9.8	<.001
Comorbidities				.274
No	13 (7.2)	79 (43.7)	89 (49.2)	
Yes	9 (7.3)	43 (34.7)	72 (58.1)	
Histologic type				.943
Differentiated	9 (6.3)	59 (40.9)	76 (52.8)	
Undifferentiated	10 (8.9)	44 (38.9)	59 (52.2)	
Others	3 (6.3)	19 (39.6)	26 (54.2)	
Tumor location				.259
Upper	4 (19.1)	8 (38.1)	9 (42.9)	
Middle	6 (8.0)	31 (41.3)	38 (50.7)	
Lower	11 (5.4)	81 (39.7)	112 (54.9)	
Whole	1 (20.1)	2 (40.0)	2 (40.0)	
Depth of invasion				<.001
T1	5 (3.6)	62 (43.9)	74 (52.5)	
T2	2 (5.0)	13 (32.5)	25 (62.5)	
T3	5 (6.8)	22 (29.7)	47 (63.5)	
T4	10 (20.0)	25 (50.0)	15 (30.0)	
Lymph node metastasis				.198
N0	10 (5.5)	68 (37.4)	104 (57.1)	
N1	3 (6.9)	17 (39.5)	23 (53.5)	
N2	5 (13.5)	14 (37.8)	18 948.7)	
N3	4 (9.3)	23 (53.5)	16 (37.2)	
TNM Stage				.001
I	6 (3.9)	66 (42.9)	82 (53.3)	
II	6 (7.8)	20 (25.9)	51 (66.2)	
III	10 (13.5)	36 (48.7)	28 (37.8)	
Extent of resection				.877
Total gastrectomy	19 (7.5)	101 (40.1)	132 (52.4)	
Distal subtotal gastrectomy	3 (5.7)	21 (39.6)	29 (54.7)	
Combined resection				.384
No	8 (10.8)	29 (39.2)	37 (50.0)	
Yes	14 (6.1)	93 (40.3)	124 (53.7)	
LN dissection				<.001
D1+	4 (3.1)	42 (32.6)	83 (64.3)	
D2	18 (10.2)	80 (45.5)	78 (44.3)	
Transfusion				.917
No	19 (6.8)	113 (40.7)	146 (52.5)	
Yes	3 (11.1)	9 (33.3)	15 (55.6)	
Operative time (min)	227.9 ± 93.7	222.6 ± 49.5	238.8 ± 47.4	.004
Estimated blood loss (ml)	311.4 ± 252.6	241.2 ± 210.6	237.5 ± 187.9	.367
Retrieved lymph node	31.6 ± 12.4	33.4 ± 10.6	30.3 ± 10.2	.035
Complication				.427
No	19 (6.7)	114 (40.1)	151 (53.2)	
Yes	3 (14.3)	8 (38.1)	10 (47.6)	
Hospital stay (day)	15.5 ± 10.2	12.1 ± 6.6	12.7 ± 11.5	.009

*Parentheses are percentage.

associated with gastric cancers. Gastric cancer patients are at high risk for malnutrition, which is one of the most important contributors to sarcopenia.[23] A combination of inadequate protein and nutritional intake, decreased activity, and advanced age results in a high rate of sarcopenia among gastric cancer patients.[21] In addition, malignancy can contribute to a hypercatabolic state via tumor metabolism, systemic inflammation, and other tumor-mediated effects.[24] These derangements lead to depletion of skeletal muscle and the development of sarcopenia.[24] Previous studies adopted the cut-off values proposed by Prado et al[25] or van Vledder et al,[26] both of which were based on the characteristics of Western populations. Few studies have

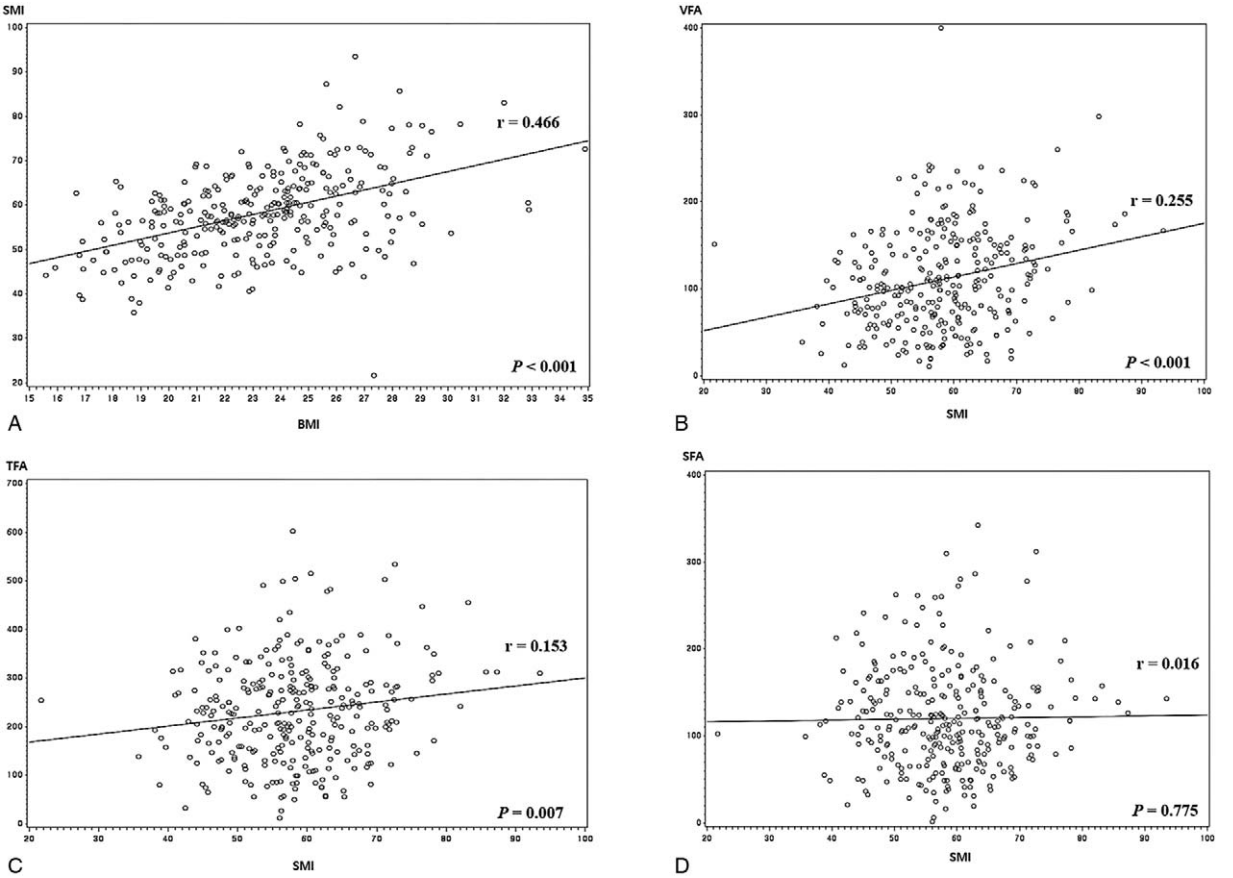

Figure 3. Correlation between the SMI and (A) BMI, (B) VFA, (C) TFA, and (D) SFA.

focused on Koreans, even though Korea has a high incidence of gastric cancer. We propose that the cut-off values obtained in our study (56.2 cm^2/m^2 for men and 53.6 cm^2/m^2 for women) are applicable for the diagnosis of sarcopenia in Korean patients with gastric cancer.

Many studies have focused on the clinical impact of sarcopenia in gastric cancer treatment; most showed that sarcopenia is associated with poorer surgical outcomes and OS, as well as chemotherapeutic toxicity, in gastric cancer patients.[27] However, Tegels et al[21] reported that sarcopenia was not a prognostic factor for severe complications or 6-month survival, and found that the prevalence of sarcopenia was as high as 57.7%. In our study, the overall prevalence of sarcopenia was only 37.7%, although the prevalence was higher among female patients (61.2%). Sarcopenia was not prevalent among patients with advanced gastric cancer, and TNM staging of patients was similar between SMI groups.

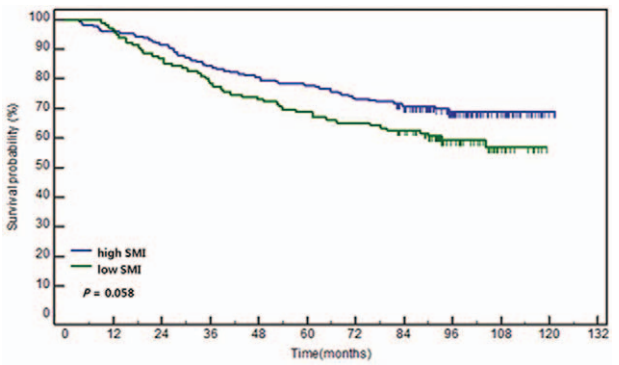

Figure 4. Overall survival according to the SMI.

Sarcopenia is an independent prognostic factor, rather than the result of cancer progression. In the present study, our analysis of 305 patients who underwent gastrectomy showed that although sarcopenia may not affect short-term postoperative surgical complications, it may be an independent prognostic factor for OS. Our results are consistent with those of previous studies, although the definition of sarcopenia and assessment method differ.[28–31]

Sarcopenia may be confused with advanced gastric cancer, since advanced gastric cancer frequently causes obstruction leading to emaciation. Fearon et al[32] described 3 stages of cachexia (precachexia, cachexia, and refractory cachexia) and noted that the presence of sarcopenia is one of the main components of cachexia. Weight loss and low BMI are frequently observed in gastric cancer patients, and these symptoms lead to the first phase of cachexia.[32] Consistent with previous studies, our results showed that that preoperative sarcopenia was associated with low BMI.[21,33,34] We also found significant associations between SMI and BMI, and TFA and SFA. Although there was a significant association between SMI and BMI, the clinicopathologic characteristics were more heterogeneous in the BMI groups versus SMI groups. In addition, SMI and BMI both

Table 3

Univariate and multivariate analyses of prognostic factors.

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
Age				
< 65 years	Reference		Reference	
≥ 65 years	1.705 (1.161–2.503)	.006	1.427 (0.960–2.122)	.078
Histologic type				
Differentiated	Reference			
Undifferentiated	1.163 (0.777–1.741)	.463		
Others	0.554 (0.281–1.091)	.087		
Depth of invasion				
T1	Reference		Reference	
T2	2.882 (1.494–5.556)	.001	1.833 (0.912–3.681)	.088
T3	3.111 (1.794–5.395)	<.001	1.540 (0.803–2.954)	.193
T4	8.897 (5.235–15.121)	<.001	3.924 (2.044–7.533)	<.001
Lymph node metastasis				
N0	Reference		Reference	
N1	2.248 (1.237–4.085)	.007	1.527 (0.787–2.962)	.210
N2	5.064 (2.967–8.643)	<.001	3.113 (1.712–5.660)	<.001
N3	7.736 (4.741–12.623)	<.001	5.388 (2.873–10.102)	<.001
TNM Stage				
I	Reference			
II	3.013 (1.750–5.188)	<.001		
III	8.234 (5.017–13.513)	<.001		
BMI group				
Normal	Reference		Reference	
Underweight	2.421 (1.316–4.452)	.004	2.355 (1.238–4.482)	.009
Overweight and obese	0.945 (0.625–1.430)	.001	1.736 (1.077–2.799)	.023
SMI group				
High SMI group	Reference		Reference	
Low SMI group	1.451 (0.987–2.132)	.058	1.607 (1.037–2.490)	.033

turned out to be an independent prognostic factor by multivariate analysis with higher odds ratio regarding BMI. However, we could not conclude which index was a superior prognostic factor, because predictive analysis was not performed. Future prospective study should be done to further clarify it.

Sarcopenia may be associated with decreased food intake and serum albumin levels, although our study did not analyze the relationship between preoperative sarcopenia and serum albumin levels. Additional large, well-designed cohort studies are needed to clarify this issue.

Although there are several analytical tools to estimate skeletal muscle mass, including magnetic resonance imaging (MRI), dual energy X-ray absorptiometry, and bioimpedance analysis, CT is the most readily available modality in routine clinical practice.[1] Although SMI assessment may be time-consuming in daily clinical practice, no additional examination is needed. The SMI may be useful alongside BMI as a predictive anthropometric measure, because it is cost-effective and reveals important differences among patients, such as in muscle mass. Yamamoto et al[35] suggested resistance exercise as the primary treatment for sarcopenia, although there are also pharmacologic options. Correcting sarcopenia during the cancer pretreatment period may improve the prognosis. Based on the present results, we suggest that the SMI should be included in the preoperative routine assessment of patients with gastric cancer.

BMI is a widely used anthropometric index. However, it has several limitations. First, it does not provide information about fat distribution and overestimates fat mass in highly muscular adults. Furthermore, BMI underestimates adiposity in the elderly. Therefore, more refined indices are required. We propose SMI as one potential solution.

In postoperative gastric cancer patients, there is no clear relationship between preoperative BMI and survival. Tokunaga et al reported that the 5-year survival rate following curative gastrectomy was better in overweight than non-overweight Japanese patients, especially for early stage gastric cancer.[19] On the other hand, Kulig et al reported that overweight/obese status was not an independent prognostic factor for long-term survival in a Western population of gastric cancer patients.[17] Furthermore, Bickhenhach et al reported that high BMI predicted increased postoperative complications, including anastomotic leak, but not survival, in gastric cancer patients.[15] Conversely, in the present study, overweight/obese status had a negative impact on OS. Theoretically, increased BMI could result in inadequate LN collection and/or identification, leading to understaging. Results vary among studies regarding whether LN collection is impaired by obesity.[18] Dhar et al found that higher BMI was an independent predictor of worse survival, with a relative risk of 1.85 ($P = .030$).[16] However, other reports demonstrated no difference in survival based on BMI.[17] Tokunaga et al examined long-term survival in a group of Japanese gastric cancer patients. Increasing BMI has been proposed as the driving force of the increasing incidence of proximal cancers in the United States and other Western countries. Proximal tumors are known to be associated with worse outcomes, and could explain the differences between our series and the Japanese series. It has also been demonstrated that inadequate staging is associated with poorer prognosis, likely due to stage migration.[19]

Unlike other studies, in our study underweight and overweight/obese patients were independent risk factors for gastric cancer.[19,20] BMI is a simple and effective indicator of nutritional status. An association of BMI with the long-term outcomes of gastric cancer patients has previously been reported, albeit with conflicting results. In addition, overweight/obese status has been shown to be associated with a worse prognosis, partly as a result of a significantly lower number of retrieved LNs.[16] Previous studies also reported that underweight was associated with an increased risk of cancer recurrence, and with non-cancer death.[36]

Our study had several limitations. First, the definition of sarcopenia differs throughout the literature. In most studies, sarcopenia refers to loss of muscle mass and function. However, there is heterogeneity regarding the assessment of sarcopenia. By necessity, owing to the retrospective nature of the present study, sarcopenia was based only on muscle mass, not function. Prospective studies that also assess muscle function are therefore required. Second, we assessed only preoperative sarcopenia. Kugimiya et al[37] reported that postoperative loss of skeletal muscle mass was an independent predictor of a poor prognosis. Thus, further investigations are needed to determine the relationship between postoperative sarcopenia and prognosis.

5. Conclusions

SMI and BMI did not impact perioperative morbidity in patients undergoing gastrectomy for gastric cancer. However, both SMI and BMI are useful prognostic factors for OS in patients undergoing gastric resection for adenocarcinoma. Underweight and overweight/obese patients, and those with a low SMI, had significantly poorer OS after gastrectomy for gastric cancer. Based on these results, we suggest that SMI and BMI should be included in the routine preoperative assessment of patients with gastric cancer. In addition, nutritional status should be optimized in high-risk patients, both before and after gastrectomy, to achieve better surgical outcomes.

Acknowledgments

The English in this document has been checked by at least 2 professional editors, both native speakers of English. For a certificate, please see: http://www.textcheck.com/certificate/SGP4GB. The statistical consultation was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI14C1062).

Author contributions

Conceptualization: Eun Young Kim, Kyong Hwa Jun, Shinn Young Kim, Hyung Min Chin.
Data curation: Eun Young Kim, Kyong Hwa Jun.
Formal analysis: Eun Young Kim, Kyong Hwa Jun.
Investigation: Eun Young Kim, Kyong Hwa Jun, Shinn Young Kim, Hyung Min Chin.
Methodology: Eun Young Kim, Kyong Hwa Jun.
Project administration: Eun Young Kim, Kyong Hwa Jun.
Resources: Eun Young Kim, Kyong Hwa Jun.
Software: Kyong Hwa Jun.
Supervision: Kyong Hwa Jun, Hyung Min Chin.
Validation: Kyong Hwa Jun.
Visualization: Kyong Hwa Jun.
Writing – original draft: Eun Young Kim, Kyong Hwa Jun.
Writing – review & editing: Eun Young Kim, Kyong Hwa Jun, Shinn Young Kim, Hyung Min Chin.

References

[1] 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.
[2] Bosy-Westphal A, Muller MJ. Identification of skeletal muscle mass depletion across age and BMI groups in health and disease–there is need for a unified definition. Int J Obes 2015;39:379–86.
[3] da Cunha LP, Silveira MN, Mendes MCS, et al. Sarcopenia as an independent prognostic factor in patients with metastatic colorectal cancer: a retrospective evaluation. Clin Nutr ESPEN 2019;32:107–12.
[4] Loosen SH, Schulze-Hagen M, Bruners P, et al. Sarcopenia is a negative prognostic factor in patients undergoing Transarterial Chemoembolization (TACE) for hepatic malignancies. Cancers 2019;11:1503.
[5] Pecorelli N, Carrara G, De Cobelli F, et al. Effect of sarcopenia and visceral obesity on mortality and pancreatic fistula following pancreatic cancer surgery. Br J Surg 2016;103:434–42.
[6] Ataseven B, Luengo TG, du Bois A, et al. Skeletal muscle attenuation (sarcopenia) predicts reduced overall survival in patients with advanced epithelial ovarian cancer undergoing primary debulking surgery. Ann Surg Oncol 2018;25:3372–9.
[7] Shoji F, Matsubara T, Kozuma Y, et al. Relationship between preoperative sarcopenia status and immuno-nutritional parameters in patients with early-stage non-small cell lung cancer. Anticancer Res 2017;37:6997–7003.
[8] Makiura D, Ono R, Inoue J, et al. Impact of sarcopenia on unplanned readmission and survival after esophagectomy in patients with esophageal cancer. Ann Surg Oncol 2018;25:456–64.
[9] Valero V, Amini N, Spolverato G, et al. Sarcopenia adversely impacts postoperative complications following resection or transplantation in patients with primary liver tumors. J Gastrointest Surg 2015;19:272–81.
[10] Chen W-Z, Chen X-D, Ma L-L, et al. Impact of visceral obesity and sarcopenia on short-term outcomes after colorectal cancer surgery. Dig Dis Sci 2018;63:1620–30.
[11] Tan BHL, Brammer K, Randhawa N, et al. Sarcopenia is associated with toxicity in patients undergoing neo-adjuvant chemotherapy for oesophago-gastric cancer. Eur J Surg Oncol 2015;41:333–8.
[12] Kim JH, Chin HM, Hwang SS, et al. Impact of intra-abdominal fat on surgical outcome and overall survival of patients with gastric cancer. Int J Surg 2014;12:346–52.
[13] Kim E, Lee J, Yoo H, et al. The platelet-to-lymphocyte ratio versus neutrophil-to-lymphocyte ratio: which is better as a prognostic factor in gastric cancer? Ann Surg Oncol 2015;22:4363–70.
[14] Liu X, Zhang D, Lin E, et al. Preoperative controlling nutritional status (CONUT) score as a predictor of long-term outcome after curative resection followed by adjuvant chemotherapy in stage II-III gastric Cancer. BMC Cancer 2018;18:699–1699.
[15] Bickenbach KA, Denton B, Gonen M, et al. Impact of obesity on perioperative complications and long-term survival of patients with gastric cancer. Ann Surg Oncol 2013;20:780–7.
[16] Dhar DK, Kubota H, Tachibana M, et al. Body mass index determines the success of lymph node dissection and predicts the outcome of gastric carcinoma patients. Oncology 2000;59:18–23.
[17] Kulig J, Sierzega M, Kolodziejczyk P, et al. Implications of overweight in gastric cancer: a multicenter study in a Western patient population. Eur J Surg Oncol 2010;36:969–76.
[18] Sahakyan MA, Shahbazyan SS, Martirosyan A, et al. Gastrectomy for gastric cancer in patients with BMI >/=30 kg/m(2). Am Surg 2020;86:158–63.
[19] Tokunaga M, Hiki N, Fukunaga T, et al. Better 5-year survival rate following curative gastrectomy in overweight patients. Ann Surg Oncol 2009;16:3245–51.
[20] Wada T, Kunisaki C, Ono H, et al. Implications of BMI for the prognosis of gastric cancer among the Japanese population. Dig Surg 2015;32:480–6.
[21] Tegels JJ, van Vugt JL, Reisinger KW, et al. Sarcopenia is highly prevalent in patients undergoing surgery for gastric cancer but not associated with worse outcomes. J Surg Oncol 2015;112:403–7.

[22] Tan BH, Brammer K, Randhawa N, et al. Sarcopenia is associated with toxicity in patients undergoing neo-adjuvant chemotherapy for oesophago-gastric cancer. Eur J Surg Oncol 2015;41:333–8.
[23] Mariette C, De Botton ML, Piessen G. Surgery in esophageal and gastric cancer patients: what is the role for nutrition support in your daily practice? Ann Surg Oncol 2012;19:2128–34.
[24] van Vugt JL, Levolger S, Coelen RJ, et al. The impact of sarcopenia on survival and complications in surgical oncology: a review of the current literature. J Surg Oncol 2015;112:681–2.
[25] Prado CM, Cushen SJ, Orsso CE, et al. Sarcopenia and cachexia in the era of obesity: clinical and nutritional impact. Proc Nutr Soc 2016; 75:188–98.
[26] Levolger S, van Vledder MG, Muslem R, et al. Sarcopenia impairs survival in patients with potentially curable hepatocellular carcinoma. J Surg Oncol 2015;112:208–13.
[27] Kuwada K, Kuroda S, Kikuchi S, et al. Clinical impact of sarcopenia on gastric cancer. Anticancer Res 2019;39:2241–9.
[28] 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.
[29] 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.
[30] 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.
[31] 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.
[32] Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 2011;12: 489–95.
[33] Voron T, Tselikas L, Pietrasz D, et al. Sarcopenia impacts on short- and long-term results of hepatectomy for hepatocellular carcinoma. Ann Surg 2015;261:1173–83.
[34] Fukuda Y, Yamamoto K, Hirao M, et al. Sarcopenia is associated with severe postoperative complications in elderly gastric cancer patients undergoing gastrectomy. Gastric cancer 2016;19:986–93.
[35] Yamamoto K, Nagatsuma Y, Fukuda Y, et al. Effectiveness of a preoperative exercise and nutritional support program for elderly sarcopenic patients with gastric cancer. Gastric cancer 2017;20:913–8.
[36] Zhao B, Zhang J, Zhang J, et al. The impact of preoperative underweight status on postoperative complication and survival outcome of gastric cancer patients: a systematic review and meta-analysis. Nutr Cancer 2018;70:1254–63.
[37] Kugimiya N, Harada E, Oka K, et al. Loss of skeletal muscle mass after curative gastrectomy is a poor prognostic factor. Oncol Lett 2018; 16:1341–7.