Original Article | Musculoskeletal Imaging

eISSN 2005-8330
https://doi.org/10.3348/kjr.2023.0109
Korean J Radiol 2023;24(9):849-859

Korean Journal of Radiology
KJR

Prognostic Value of Artificial Intelligence-Driven, Computed Tomography-Based, Volumetric Assessment of the Volume and Density of Muscle in Patients With Colon Cancer

Minsung Kim[1]*, Sang Min Lee[2]*, Il Tae Son[1], Taeyong Park[3], Bo Young Oh[1]

[1]Department of Surgery, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Republic of Korea
[2]Department of Radiology, CHA University Gangnam Medical Center, Seoul, Republic of Korea
[3]Medical Artificial Intelligence Center, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Republic of Korea

Objective: The prognostic value of the volume and density of skeletal muscles in the abdominal waist of patients with colon cancer remains unclear. This study aimed to investigate the association between the automated computed tomography (CT)-based volume and density of the muscle in the abdominal waist and survival outcomes in patients with colon cancer.
Materials and Methods: We retrospectively evaluated 474 patients with colon cancer who underwent surgery with curative intent between January 2010 and October 2017. Volumetric skeletal muscle index and muscular density were measured at the abdominal waist using artificial intelligence (AI)-based volumetric segmentation of body composition on preoperative pre-contrast CT images. Patients were grouped based on their skeletal muscle index (sarcopenia vs. not) and muscular density (myosteatosis vs. not) values and combinations (normal, sarcopenia alone, myosteatosis alone, and combined sarcopenia and myosteatosis). Postsurgical disease-free survival (DFS) and overall survival (OS) were analyzed using univariable and multivariable analyses, including multivariable Cox proportional hazard regression.
Results: Univariable analysis showed that DFS and OS were significantly worse for the sarcopenia group than for the non-sarcopenia group (P = 0.044 and P = 0.003, respectively, by log-rank test) and for the myosteatosis group than for the non-myosteatosis group (P < 0.001 by log-rank test for all). In the multivariable analysis, the myosteatotic muscle type was associated with worse DFS (adjusted hazard ratio [aHR], 1.89 [95% confidence interval, 1.25–2.86]; P = 0.003) and OS (aHR, 1.90 [95% confidence interval, 1.84–3.04]; P = 0.008) than the normal muscle type. The combined muscle type showed worse OS than the normal muscle type (aHR, 1.95 [95% confidence interval, 1.08–3.54]; P = 0.027).
Conclusion: Preoperative volumetric sarcopenia and myosteatosis, automatically assessed from pre-contrast CT scans using AI-based software, adversely affect survival outcomes in patients with colon cancer.
Keywords: Colon cancer; Volumetric sarcopenia; Myosteatosis; Skeletal muscle index; Muscular density

INTRODUCTION

Colorectal cancer is the third most common cancer and has the second highest mortality rate among cancers globally [1]. The prognosis of colorectal cancer is largely determined by the molecular characteristics of its tumors; however, several studies have recently shown that host-related factors, such as body composition and nutrition, also affect it [2-6]. Malnutrition and changes in body composition, particularly muscle mass, have prognostic

Received: November 1, 2022 **Revised:** May 3, 2023 **Accepted:** June 28, 2023
*These authors contributed equally to this work.
Corresponding author: Bo Young Oh, MD, PhD, Department of Surgery, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, 22 Gwanpyeong-ro 170beon-gil, Dongan-gu, Anyang 14068, Republic of Korea
• E-mail: obbyy@hanmail.net

values; however, they tend to be neglected in the absence of recognized guidelines [4,7]. Sarcopenia, characterized by the loss of skeletal muscle mass and function, has recently been regarded as an objective risk factor for worse survival outcomes, higher surgical complications, and treatment-related toxicities for several cancer types [8-10]. In a meta-analysis, the prevalence of sarcopenia in patients with gastrointestinal cancer was 34.7% (range, 2.1%–83.3%) [11]. Several studies have investigated the prognostic role of preoperative sarcopenia in colorectal cancer with similar results [2-6,12,13].

There are several techniques for measuring body composition, including bioelectrical impedance analysis, dual-energy radiographic absorptiometry, and computed tomography (CT). CT is a widely used tool because it can quantify body composition components such as muscle and adipose tissue [8,14]. Cross-sectional CT images of the skeletal muscle and visceral adipose tissue areas at the level of the third lumbar vertebral body (L3) have been shown to correspond to whole-body tissue quantities in patients with cancer [4]. In addition, recent technological advances have enabled automated and fast volumetric measurements of each component of CT scans [8,15,16]. Automated volumetric measurements of body composition may contain more abundant and precise information than single-cut measurements in a cross-sectional image and can also enable the calculation of volumes in less than a few minutes [9,17]. This study aimed to evaluate the associations between the volume and density of skeletal muscles in the abdominal waist obtained from CT-based automated artificial intelligence (AI) volumetric measurements and survival outcomes of patients with colon cancer.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of Hallym University Sacred Heart Hospital (IRB No. 2020-07-044) and performed according to the principles of the Declaration of Helsinki. The review board waived the requirement for informed consent because of the retrospective nature of the study.

Patients

We retrospectively reviewed the medical records of

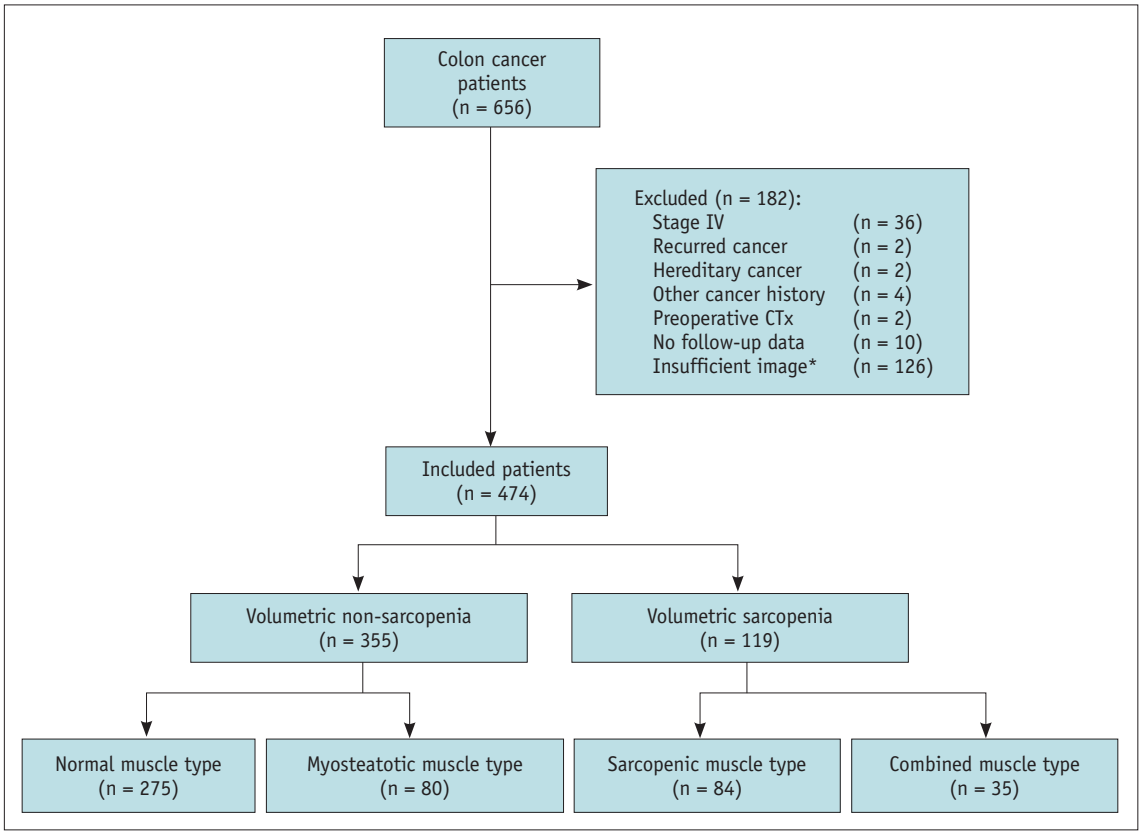

Fig. 1. Flowchart of the study design with inclusion and exclusion criteria. *No pre-contrast images and no full coverage of the abdominal waist. CTx = chemotherapy

https://doi.org/10.3348/kjr.2023.0109

Korean Journal of Radiology
KJR

patients diagnosed with colon cancer who underwent curative radical resection at the Hallym University Sacred Heart Hospital between January 2010 and October 2017. Patients diagnosed with recurrent or metastatic colon cancer, hereditary colon cancer, or other active malignancies before and at the time of colon cancer diagnosis were excluded. We also excluded patients who received chemotherapy or radiation therapy before surgery, those with incomplete CT (no pre-contrast images and incomplete coverage of the abdominal waist), or those with no follow-up data (Fig. 1).

Clinical Assessment Data

We collected the clinicopathological data of the patients, such as age at diagnosis, body mass index, American Society of Anesthesiologists score, preoperative serum carcinoembryonic antigen level, tumor location, and tumor stage, according to the American Joint Committee on Cancer 8th edition. Post-surgical surveillance was performed using abdominopelvic CT, chest CT every 6 months, and colonoscopy one year after surgery, followed by every 2 years for 5 years.

Image Analysis

Automatic volumetric segmentation of body composition on CT images was performed using commercially available AI-based software for body composition analysis (DeepCatch version 1.1.3.4586; MEDICALIP Co. Ltd.), which has been proven to provide 97% accuracy relative to manual segmentation as the reference standard [15]. The software was developed by training a three-dimensional U-NET [18,19] for segmentation based on semi-automatic segmentation of the muscle, abdominal visceral fat, and subcutaneous fat; thresholds of -29 to 150 Hounsfield units (HU) were used for skeletal muscle and -190 to -30 HU were used for adipose tissue. An expert radiologist (S.M.L., 15 years of experience in CT analysis) blinded to the clinical information of the patients entered the anonymized abdominal pre-contrast CT images into the software installed on the computer. Subsequently, the software automatically localized the abdominal waist and L3 level and provided the color mapping with body composition

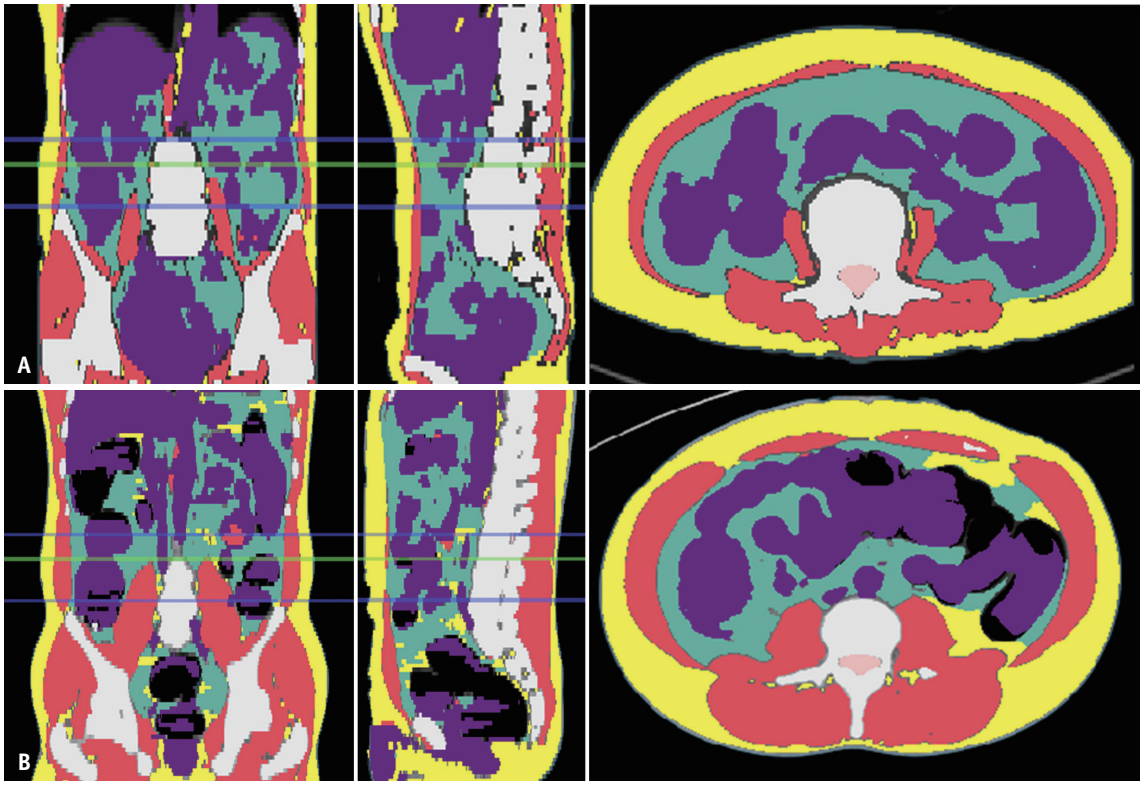

Fig. 2. Evaluation of body composition using computed tomography (CT) images. **A:** CT images of patients with volumetric sarcopenia. **B:** CT images of patients with volumetric non-sarcopenia. The light green line indicates the L3 level, and the body part between the two blue lines is the waist. Skeletal muscle (red), abdominal visceral fat (green), subcutaneous fat (yellow), and visceral organ (purple) are shown in the CT images.

https://doi.org/10.3348/kjr.2023.0109

for the skeletal muscle, abdominal visceral fat, and subcutaneous fat (Fig. 2). The abdominal waist was defined as the body part between the lower end of the thoracic ribs and the upper end of the iliac crest based on the World Health Organization guidelines [20]. The results of the automatic segmentation and localization of the abdominal waist and L3 were confirmed and adjusted by a radiologist. This software provided the volume (cm^3) of skeletal muscles in the abdominal waist. The muscular density (MD) was automatically provided in HU by averaging the density of the muscle components (e.g., psoas, paraspinal, transversus abdominis, rectus abdominis, quadratus lumborum, and internal and external obliques) in the abdominal waist. MD decreases with the worsening of myosteatosis [21]. The volumetric skeletal muscle index (SMI) was calculated as the waist muscle volume (cm^3) divided by height (m^3) [8,9]. Few studies have been conducted on volumetric parameters; therefore, the optimal cut-off values of SMI and MD for sarcopenia and myosteatosis were set as the Q1 values by referring to another study [8]. Q1, also known as the first quartile, represents the 25th percentile for the sample and was used as the cutoff value for muscle mass and MD when an optimal cutoff was not established [22-26].

Assessment of Clinical Outcomes

We analyzed the postsurgical survival outcomes in terms of disease-free survival (DFS) and overall survival (OS) according to SMI (sarcopenia vs. non-sarcopenia) and MD (myosteatosis vs. non-sarcopenia). DFS was defined as the duration between the date of surgery and colon cancer recurrence or death. OS was defined as the duration between the date of surgery and death from any cause or end of the study.

Statistical Analysis

The baseline characteristics and survival outcomes of the sarcopenia, non-sarcopenia, myosteatosis, and non-myosteatosis groups were compared. Categorical variables were compared using Fisher's exact test, and the continuous variables were compared using Student's *t*-test. The Kaplan-Meier survival curves for DFS and OS were plotted for the SMI and MD groups and muscle types according to the combination of SMI and MD (normal = neither sarcopenia nor myosteatosis; sarcopenic alone; myosteatosis alone; combined = both sarcopenia and myosteatosis) and compared using the log-rank test. Univariable and multivariable analyses of survival outcomes were performed using the Cox proportional hazards model to calculate adjusted hazard ratios (aHR) and 95% confidence intervals (CI). Statistical significance was set at $P < 0.05$. All statistical analyses were performed using SPSS software (version 25.0; IBM Corp.).

RESULTS

Characteristics of the Patients

A total of 474 patients were enrolled in this study. According to the Q1 cutoff value for volumetric SMI (sarcopenia: SMI < 163 cm^3/m^3 in females and SMI < 180 cm^3/m^3 in males), the non-sarcopenia group included 355 patients (74.9%) and the sarcopenia group included 119 patients (25.1%). The clinicopathological characteristics of the patients are presented in Table 1. The mean of volumetric SMI was 145.4 ± 21.9 cm^3/m^3 for the sarcopenia group and 234.8 ± 45.2 cm^3/m^3 for the non-sarcopenia group. The patients in the sarcopenia group were older and less obese than those in the non-sarcopenia group ($P = 0.003$ and $P < 0.001$, respectively). The sarcopenia group had fewer patients with American Society of Anesthesiologists scores of 1 or 2 ($P = 0.001$). Obstruction was more common in the sarcopenia group ($P = 0.014$). Pathological status did not differ between the two groups. According to the Q1 cutoff value of volumetric MD (myosteatosis: MD < 12.50 HU in females and MD < 24.01 HU in males), the non-myosteatosis group included 359 patients (75.7%) and the myosteatosis group included 115 (24.3%). The mean of volumetric MD was 8.6 ± 27.4 HU for the myosteatosis group and 29.1 ± 8.6 HU for the non-myosteatosis group. The patients in the myosteatosis group were older than those in the non-myosteatosis group ($P = 0.002$). The pathological status did not differ for the groups.

Association between Volumetric SMI and MD Groups and Survival Outcomes

The median follow-up duration was 42.8 months. DFS was significantly different between the sarcopenia and non-sarcopenia groups divided by the Q1 cutoff value (5-year DFS: 67.4% vs. 74.6%, $P = 0.044$ by log-rank test) (Fig. 3A, B). The OS significantly differed for the two groups (5-year OS: 69.1% vs. 81.5%, $P = 0.003$ by the log-rank test) (Fig. 3C, D). DFS and OS were significantly different for the myosteatosis and non-myosteatosis groups split by the Q1 cutoff value (5-year DFS: 61.2% vs. 76.6%, $P < 0.001$ by log-rank test;

https://doi.org/10.3348/kjr.2023.0109

Korean Journal of Radiology
KJR

Table 1. Characteristics of the patients

Variables	Sarcopenia			Myosteatosis		
	Non-sarcopenia (n = 355)	Sarcopenia (n = 119)	*P*	Non-myosteatosis (n = 359)	Myosteatosis (n = 115)	*P*
Volumetric SMI, cm^3/m^3	234.8 ± 45.2	145.4 ± 21.9	< 0.001	29.1 ± 8.6	8.6 ± 27.4	< 0.001
Age, yr			< 0.001			0.002
< 65	172 (48.5)	24 (20.2)		163 (45.4)	33 (28.7)	
≥ 65	183 (51.5)	95 (79.8)		196 (54.6)	82 (71.3)	
Sex			0.916			0.940
Male	193 (54.4)	64 (53.8)		195 (54.3)	62 (53.9)	
Female	162 (45.6)	55 (46.2)		164 (45.7)	53 (46.1)	
BMI, kg/m^2			< 0.001			0.143
< 25.0	209 (58.9)	100 (84.0)		241 (67.1)	68 (59.1)	
≥ 25.0	146 (41.1)	19 (16.0)		118 (32.9)	47 (40.9)	
ASA score			0.001			0.005
1–2	194 (54.6)	43 (36.1)		193 (53.8)	44 (38.3)	
3–5	161 (45.4)	76 (63.9)		166 (46.2)	71 (61.7)	
CEA, ng/mL			0.571			0.109
< 5.0	244 (68.7)	78 (65.5)		251 (69.9)	71 (61.7)	
≥ 5.0	111 (31.3)	41 (34.5)		108 (30.1)	44 (38.3)	
Location			0.276			0.226
Right colon	131 (36.9)	51 (42.9)		132 (36.8)	50 (43.5)	
Left colon	224 (63.1)	68 (57.1)		227 (63.2)	65 (56.5)	
Obstruction			0.264			0.009
Yes	116 (32.7)	46 (38.7)		111 (30.9)	51 (44.3)	
No	239 (67.3)	73 (61.3)		248 (69.1)	64 (55.7)	
Perforation			0.829			0.902
Yes	22 (6.2)	8 (6.7)		23 (6.4)	7 (6.1)	
No	333 (93.8)	111 (93.3)		336 (93.6)	108 (93.9)	
Stage			0.431			0.068
I	88 (24.8)	25 (21.0)		93 (25.9)	20 (17.4)	
II	138 (38.9)	43 (36.1)		139 (38.7)	42 (36.5)	
III	129 (36.3)	51 (42.9)		127 (35.4)	53 (46.1)	
Cell type			0.705			0.440
WD/MD	326 (91.8)	108 (90.8)		331 (92.2)	103 (89.6)	
PD/MUC/SRC	29 (8.2)	11 (9.2)		28 (7.8)	12 (10.4)	
LVI			0.577			0.653
Yes	118 (33.2)	43 (36.1)		120 (33.4)	41 (35.7)	
No	237 (66.8)	76 (63.9)		239 (66.6)	74 (64.3)	
PNI			0.490			0.969
Yes	39 (11.0)	10 (8.4)		37 (10.3)	12 (10.4)	
No	316 (89.0)	109 (91.6)		322 (89.7)	103 (89.6)	
Adjuvant CTx			0.963			0.387
Yes	153 (43.1)	51 (42.9)		159 (44.3)	45 (39.1)	
No	202 (56.9)	68 (57.1)		200 (55.7)	70 (60.9)	

Data are mean ± standard deviation or number of patients with % in parentheses.
SMI = skeletal muscle index, BMI = body mass index, ASA = American society of anesthesiologist, CEA = carcinoembryonic antigen, WD = well differentiated, MD = moderately differentiated, PD = poorly differentiated, MUC = mucinous, SRC = signet ring cell, LVI = lymphovascular invasion, PNI = perineural invasion, CTx = chemotherapy

https://doi.org/10.3348/kjr.2023.0109

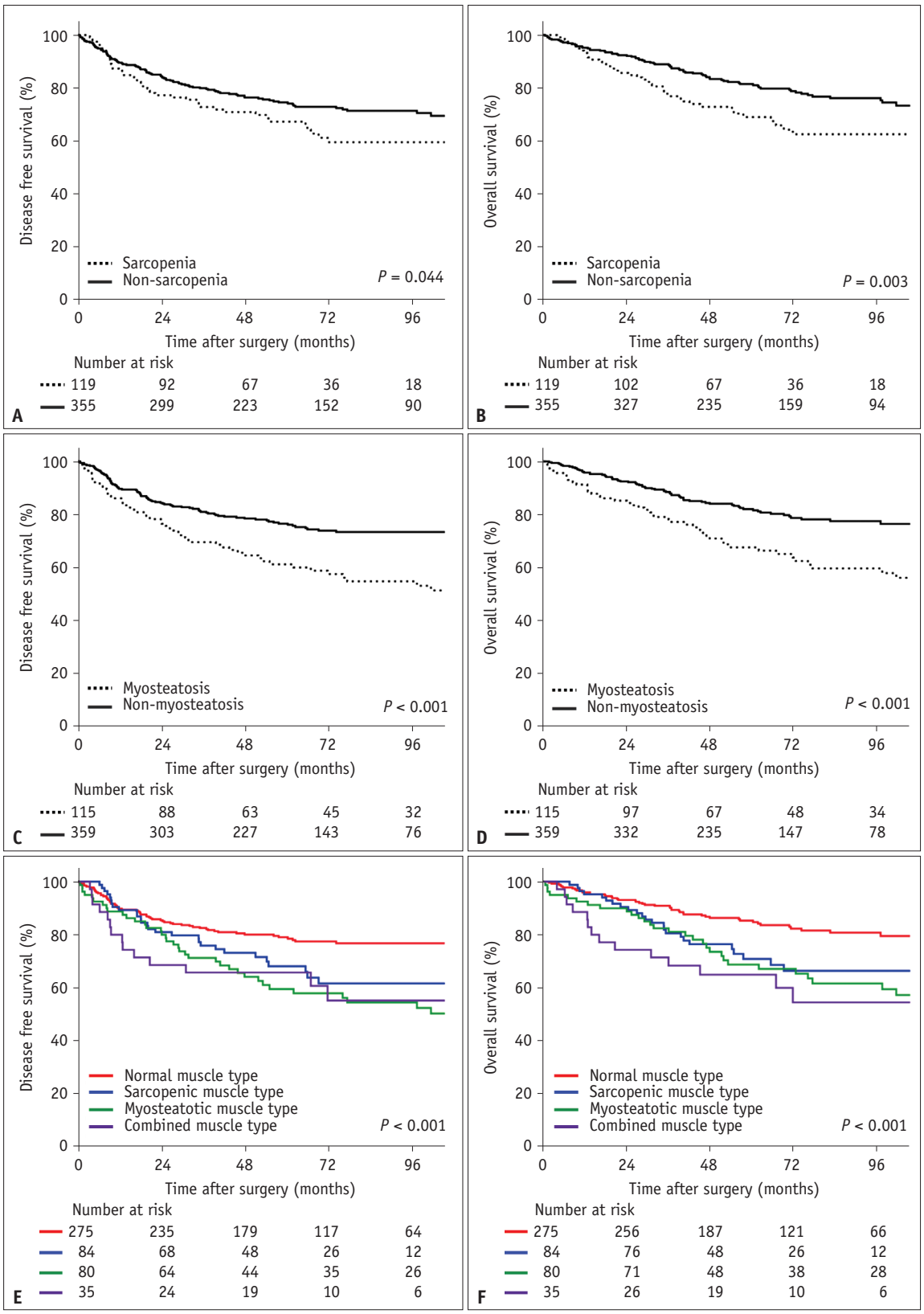

Fig. 3. Kaplan–Meier curves for disease-free survival (DFS) and overall survival (OS). **A, B:** DFS and OS according to volumetric skeletal muscle index (SMI) (sarcopenia vs. not). **C, D:** DFS and OS according to volumetric muscular density (MD) (myosteatosis vs. not). **E, F:** DFS and OS according to the combinations of volumetric SMI and MD groups (normal, sarcopenic, myosteatotic, and combined). *P*-values are from the log-rank test.

https://doi.org/10.3348/kjr.2023.0109

Korean Journal of Radiology
KJR

and 5-year OS: 67.6% vs. 82.0%, $P < 0.001$ by log-rank test, respectively). The patients were divided into four groups according to the Q1 cutoff values of volumetric SMI and MD: 1) normal muscle type (n = 275); 2) sarcopenic muscle type (n = 84); 3) myosteatotic muscle type (n = 80); and 4) combined muscle type (n = 35) (Fig. 1). The normal muscle type showed significantly better DFS and OS than the other muscle types ($P < 0.001$ and $P < 0.001$, respectively, log-rank test) (Fig. 3E, F).

Table 2 shows the factors associated with survival outcomes based on univariable and multivariable analyses. Multivariable analysis showed that muscle type, age, stage, and perineural invasion were associated with DFS and OS. The myosteatotic muscle type was associated with worse DFS (aHR, 1.89 [95% CI, 1.25–2.86]; $P = 0.003$) and OS (aHR, 1.90 [95% CI, 1.84–3.04]; $P = 0.008$) than the normal muscle type. The combined muscle type was associated with worse OS than the normal muscle type (aHR, 1.95 [95% CI, 1.08–3.54]; $P = 0.027$).

DISCUSSION

This study highlights the importance of skeletal muscle mass in predicting the survival outcomes of patients

Table 2. Univariable and multivariable Cox proportional hazard analyses of the factors associated with postsurgical survival

Parameter	Disease free survival				Overall survival			
	Univariable		Multivariable		Univariable		Multivariable	
	cHR (95% CI)	*P*	aHR (95% CI)	*P*	cHR (95% CI)	*P*	aHR (95% CI)	*P*
Muscle type		< 0.001		0.026		< 0.001		0.032
Normal muscle type	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Sarcopenic muscle type	1.61 (1.03–2.52)	0.039	1.27 (0.80–2.00)	0.309	1.89 (1.15–3.09)	0.012	1.39 (0.84–2.31)	0.201
Myosteatotic muscle type	2.19 (1.45–3.30)	< 0.001	1.89 (1.25–2.86)	0.003	2.25 (1.42–3.58)	0.001	1.90 (1.84–3.04)	0.008
Combined muscle type	2.38 (1.37–4.14)	0.002	1.61 (0.91–2.83)	0.102	3.22 (1.82–5.70)	< 0.001	1.95 (1.08–3.54)	0.027
Age								
< 65	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
≥ 65	2.25 (1.55–3.28)	< 0.001	2.24 (1.51–3.33)	< 0.001	2.74 (1.78–4.22)	< 0.001	2.66 (1.69–4.21)	< 0.001
Sex								
Male	1 [Reference]				1 [Reference]			
Female	1.25 (0.90–1.74)	0.182			1.32 (0.92–1.90)	0.138		
CEA								
< 5.0	1 [Reference]		1 [Reference]		1 [Reference]			
≥ 5.0	1.95 (1.40–2.73)	< 0.001	1.34 (0.95–1.89)	0.096	1.72 (1.19–2.49)	0.004		
Stage		< 0.001		< 0.001		< 0.001		< 0.001
I	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
II	2.75 (1.49–5.06)	0.001	2.13 (1.14–3.97)	0.017	2.05 (1.09–3.84)	0.026	1.92 (1.01–3.67)	0.048
III	4.76 (2.64–8.57)	< 0.001	3.29 (1.77–6.11)	< 0.001	3.80 (2.09–6.90)	< 0.001	3.63 (1.84–7.17)	< 0.001
Cell type								
WD/MD	1 [Reference]				1 [Reference]			
PD/MUC/SRC	1.40 (0.80–2.43)	0.236			1.47 (0.81–2.68)	0.206		
LVI								
Negative	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Positive	2.04 (1.47–2.84)	< 0.001	1.41 (0.99–2.03)	0.060	1.94 (1.34–2.79)	< 0.001	1.46 (0.97–2.19)	0.068
PNI								
Negative	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Positive	2.61 (1.70–4.01)	< 0.001	2.01 (1.27–3.16)	0.003	2.29 (1.41–3.72)	0.001	2.09 (1.24–3.53)	< 0.001
CTx								
No	1 [Reference]				1 [Reference]		1 [Reference]	
Yes	1.44 (1.04–2.01)	0.03			1.13 (0.79–1.63)	0.5	0.67 (0.43–1.04)	0.072

cHR = crude hazard ratio, aHR = adjusted hazard ratio, CI = confidence interval, CEA = carcinoembryonic antigen, WD = well differentiated, MD = moderately differentiated, PD = poorly differentiated, MUC = mucinous, SRC = signet ring cell, LVI = lymphovascular invasion, PNI = perineural invasion, CTx = chemotherapy

https://doi.org/10.3348/kjr.2023.0109

with colon cancer treated with radical resection. Unlike previous studies that determined the presence of sarcopenia at the L3 level cross-section, this study is the first to associate volumetric SMI with colon cancer, which can be automatically measured using AI and can provide more accurate information. This demonstrates that preoperative volumetric SMI and MD affect survival outcomes in patients with stage I–III colon cancers.

CT-determined sarcopenia and myosteatosis have been reported to be poor prognostic factors for colorectal cancer, although the cutoff values vary among studies. Sarcopenia refers to low muscle mass, and myosteatosis refers to low muscle quality [23]. There are several cutoff values for sarcopenia and myosteatosis [23]. Several studies have reported that L3 sarcopenia, as classified by Martin's cutoff value [27], is an independent prognostic factor for worse DFS and OS in patients with colorectal cancer [3-6]. L3 myosteatosis has also been reported to affect DFS and OS in patients with malignancies [5,28]. Other studies on Asian patients reported that L3 sarcopenia, classified by the Q1 cutoff value, was an independent prognostic factor for worse DFS and OS in patients with colorectal cancer [22,24]. Only a few studies have reported that volumetric sarcopenia has a worse prognostic impact on gynecologic malignancies [8,9,29]. A single cross-sectional CT image at the L3 level, which reflects whole-body tissue quantities, is a well-established method for body composition analysis [27]. This study showed that sarcopenia and myosteatosis, according to volumetric measurements, were significantly associated with worse survival outcomes. Compared with L3 SMI, volumetric SMI may better reflect the presence of sarcopenia [9]. Analysis of body composition from single-cut images is limited because the contents of the gastrointestinal tract constantly shift, and there is no guarantee that two repeated L3 sections will capture the same anatomy. In addition, the muscle area varies at different levels of the abdomen and is sometimes twice the true value. Therefore, volumetric measurements may be more precise than single-cut measurements at the L3 level [8,17]. There are no studies on the cut-off values for volumetric sarcopenia or myosteatosis in patients with colon cancer. Some studies used the Q1 cutoff value for L3 SMI to investigate the impact of sarcopenia on survival outcomes in patients with colon cancer [22,24]. Han et al. [8] reported that volumetric sarcopenia, using the Q1 cutoff value, affected the survival outcomes of gynecologic malignancies. Further studies are warranted to determine the optimal cut-off value for volumetric sarcopenia.

Previous studies reported that sarcopenia and myosteatosis were age-related changes in muscle mass and quality [30,31]. Aging appears to result in an imbalance between muscle protein anabolic and catabolic pathways, leading to an overall loss of skeletal muscle [32]. Sarcopenia and myosteatosis are associated with age. Age was associated with survival outcomes in a multivariable analysis; sarcopenia was associated with survival outcomes but this was not statistically significant, while myosteatosis was significantly associated. The molecular mechanisms underlying the effects of sarcopenia and myosteatosis on survival outcomes other than age in cancer patients are unclear. Sarcopenia is a phenotypic feature of catabolic states that leads to inflammatory states in the presence of cancer [33]. Fleming et al. [2] reported that patients who develop cancer recurrence and sarcopenia have significantly higher systemic levels of interleukin (IL)-6, vascular endothelial growth factor, and expression of the cell surface receptor CD14 [2]. Higher expression of CD14 triggers various cellular responses, including the synthesis and release of various inflammatory mediators such as tumor necrosis factor α, IL-1b, and IL-6, which, if unregulated, can promote oncogenesis and metastatic development [34]. Higher CD14 expression in patients with sarcopenia may activate dormant circulating tumor cells and promote cell migration and invasion for metastasis [2].

Patients with volumetric sarcopenia and myosteatosis can easily be identified during the preoperative staging workup for colon cancer via abdominopelvic CT using automated volumetric measurements. Early recognition and intervention may be helpful for the treatment of patients with colon cancer [35]. The concept of prehabilitation is of significant interest in these patients. Prehabilitation involves preoperative physical, nutritional, and psychosocial interventions to prevent muscle loss owing to the catabolic status of cancer; this results in reduced operative morbidity and improved quality of life [2,36]. Some authors have reported that prehabilitation for patients with cancer is helpful and clinicians should be aware of prehabilitation before definitive surgery [37]. Additionally, some preoperative targeted anti-inflammatory therapies have shown promise for suppressing the catabolic effects of cancer [38].

This study had several limitations. First, this was a retrospective study; therefore, selection bias was inevitable, and muscle function tests could not be included. A relatively

https://doi.org/10.3348/kjr.2023.0109

Korean Journal of Radiology
KJR

large number of patients were excluded because of the lack of pre-contrast CT of the waist, which also contributed to selection bias. This selection bias is unavoidable because intravenous contrast may substantially affect the automated measurement of MD [39]. Second, information on changes in skeletal muscle mass could not be obtained because not all CT scans could be obtained during a certain period after surgery. Third, the exact underlying mechanisms of poor survival outcomes due to volumetric sarcopenia and myosteatosis were not identified in this study. Fourth, the cutoff value for myosteatosis was lower than that reported in a previous study. This study included only Asians, and the percentage of patients with myosteatosis was lower (24.3%) than that reported by other studies [23,25]. To our knowledge, this is the first study to investigate the prognostic value of volumetric sarcopenia and myosteatosis in colon cancer. Volumetric measurements with a large sample size provided more and precise information than single-cut measurements, and the evaluation was easier with automated calculations.

In conclusion, the present study found that preoperative volumetric sarcopenia combined with myosteatosis, automatically assessed by pre-contrast CT using AI-based software, was associated with poor postsurgical survival outcomes in patients with colon cancer. These volumetric body composition parameters can be assessed preoperatively, and patients with poor prognostic features can receive greater attention during post-surgical surveillance.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Bo Young Oh. Data curation: Bo Young Oh, Sang Min Lee. Formal analysis: Minsung Kim. Funding acquisition: Bo Young Oh. Investigation: Sang Min Lee. Methodology: Sang Min Lee. Project administration: Bo Young Oh. Resources: Bo Young Oh, Il Tae Son. Software: Sang Min Lee. Supervision: Bo Young Oh, Il Tae Son. Validation: Bo Young Oh. Visualization: Minsung Kim, Sang Min Lee. Writing—original draft: Minsung Kim, Sang Min Lee. Writing—review & editing: Bo Young Oh, Taeyong Park.

ORCID IDs

Minsung Kim
https://orcid.org/0000-0002-1984-5084
Sang Min Lee
https://orcid.org/0000-0001-7719-3849
Il Tae Son
https://orcid.org/0000-0003-1781-9189
Taeyong Park
https://orcid.org/0000-0002-7523-8975
Bo Young Oh
https://orcid.org/0000-0002-1255-0961

Funding Statement

This research was supported by the Hallym University Research Fund 2020 (HURF-2020-39).

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209-249
2. Fleming CA, O'Connell EP, Kavanagh RG, O'Leary DP, Twomey M, Corrigan MA, et al. Body composition, inflammation, and 5-year outcomes in colon cancer. *JAMA Netw Open* 2021;4:e2115274
3. Chai VW, Chia M, Cocco A, Bhamidipaty M, D'Souza B. Sarcopenia is a strong predictive factor of clinical and oncological outcomes following curative colorectal cancer resection. *ANZ J Surg* 2021;91:E292-E297
4. Malietzis G, Currie AC, Athanasiou T, Johns N, Anyamene N, Glynne-Jones R, et al. Influence of body composition profile on outcomes following colorectal cancer surgery. *Br J Surg* 2016;103:572-580
5. Sueda T, Takahasi H, Nishimura J, Hata T, Matsuda C, Mizushima T, et al. Impact of low muscularity and myosteatosis on long-term outcome after curative colorectal cancer surgery: a propensity score-matched analysis. *Dis Colon Rectum* 2018;61:364-374
6. Hopkins JJ, Reif RL, Bigam DL, Baracos VE, Eurich DT, Sawyer MB. The impact of muscle and adipose tissue on long-term survival in patients with stage I to III colorectal cancer. *Dis Colon Rectum* 2019;62:549-560
7. Sonmez O, Tezcanli E, Bas D, Kazanci HB, Altinok A, Demir A, et al. Identifying knowledge and practices regarding cancer patient malnutrition: a survey study among oncologists. *Nutr Cancer* 2022;74:2392-2399
8. Han Q, Kim SI, Yoon SH, Kim TM, Kang HC, Kim HJ, et al.

 https://doi.org/10.3348/kjr.2023.0109

Impact of computed tomography-based, artificial intelligence-driven volumetric sarcopenia on survival outcomes in early cervical cancer. *Front Oncol* 2021;11:741071
9. Kim SI, Chung JY, Paik H, Seol A, Yoon SH, Kim TM, et al. Prognostic role of computed tomography-based, artificial intelligence-driven waist skeletal muscle volume in uterine endometrial carcinoma. *Insights Imaging* 2021;12:192
10. Jones K, Gordon-Weeks A, Coleman C, Silva M. Radiologically determined sarcopenia predicts morbidity and mortality following abdominal surgery: a systematic review and meta-analysis. *World J Surg* 2017;41:2266-2279
11. Su H, Ruan J, Chen T, Lin E, Shi L. CT-assessed sarcopenia is a predictive factor for both long-term and short-term outcomes in gastrointestinal oncology patients: a systematic review and meta-analysis. *Cancer Imaging* 2019;19:82
12. Xiao J, Caan BJ, Cespedes Feliciano EM, Meyerhardt JA, Peng PD, Baracos VE, et al. Association of low muscle mass and low muscle radiodensity with morbidity and mortality for colon cancer surgery. *JAMA Surg* 2020;155:942-949
13. Mizuuchi Y, Tanabe Y, Sada M, Tamura K, Nagayoshi K, Nagai S, et al. Cross-sectional area of psoas muscle as a predictive marker of anastomotic failure in male rectal cancer patients: Japanese single institutional retrospective observational study. *Ann Coloproctol* 2022;38:353-361
14. Thibault R, Pichard C. The evaluation of body composition: a useful tool for clinical practice. *Ann Nutr Metab* 2012;60:6-16
15. Lee YS, Hong N, Witanto JN, Choi YR, Park J, Decazes P, et al. Deep neural network for automatic volumetric segmentation of whole-body CT images for body composition assessment. *Clin Nutr* 2021;40:5038-5046
16. Pickhardt PJ, Summers RM, Garrett JW. Automated CT-based body composition analysis: a golden opportunity. *Korean J Radiol* 2021;22:1934-1937
17. Weston AD, Korfiatis P, Kline TL, Philbrick KA, Kostandy P, Sakinis T, et al. Automated abdominal segmentation of CT scans for body composition analysis using deep learning. *Radiology* 2019;290:669-679
18. Ronneberger O, Fischer P, Brox T. *U-Net: Convolutional networks for biomedical image segmentation*. In: Navab N, Hornegger J, Wells WM, Frangi AF, eds. *18th International Conference on Medical Image Computing and Computer-Assisted Intervention -MICCAI 2015*; 2015 Oct 5-9; Munch, Germany. Cham: Springer International Publishing; 2015;234-241
19. Çiçek Ö, Abdulkadir A, Lienkamp SS, Brox T, Ronneberger O. *3D U-Net: learning dense volumetric segmentation from sparse annotation*. In: Ourselin S, Joskowicz L, Sabuncu MR, Unal G, Wells W, eds. *19th International Conference on Medical Image Computing and Computer-Assisted Intervention - MICCAI 2016*; 2016 Oct 17-21; Athens, Greece. Cham: Springer International Publishing, 2016;424-432
20. Ross R, Neeland IJ, Yamashita S, Shai I, Seidell J, Magni P, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. *Nat Rev Endocrinol* 2020;16:177-189
21. Aubrey J, Esfandiari N, Baracos VE, Buteau FA, Frenette J, Putman CT, et al. Measurement of skeletal muscle radiation attenuation and basis of its biological variation. *Acta Physiol (Oxf)* 2014;210:489-497
22. Miyamoto Y, Baba Y, Sakamoto Y, Ohuchi M, Tokunaga R, Kurashige J, et al. Sarcopenia is a negative prognostic factor after curative resection of colorectal cancer. *Ann Surg Oncol* 2015;22:2663-2668
23. Amini B, Boyle SP, Boutin RD, Lenchik L. Approaches to assessment of muscle mass and myosteatosis on computed tomography: a systematic review. *J Gerontol A Biol Sci Med Sci* 2019;74:1671-1678
24. Wang S, Xie H, Gong Y, Kuang J, Yan L, Ruan G, et al. The value of L3 skeletal muscle index in evaluating preoperative nutritional risk and long-term prognosis in colorectal cancer patients. *Sci Rep* 2020;10:8153
25. Daly LE, Prado CM, Ryan AM. A window beneath the skin: how computed tomography assessment of body composition can assist in the identification of hidden wasting conditions in oncology that profoundly impact outcomes. *Proc Nutr Soc* 2018;77:135-151
26. Akahori T, Sho M, Kinoshita S, Nagai M, Nishiwada S, Tanaka T, et al. Prognostic significance of muscle attenuation in pancreatic cancer patients treated with neoadjuvant chemoradiotherapy. *World J Surg* 2015;39:2975-2982
27. Martin L, Birdsell L, MacDonald N, Reiman T, Clandinin MT, McCargar LJ, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *J Clin Oncol* 2013;31:1539-1547
28. Kim DW, Ahn H, Kim KW, Lee SS, Kim HJ, Ko Y, et al. Prognostic value of sarcopenia and myosteatosis in patients with resectable pancreatic ductal adenocarcinoma. *Korean J Radiol* 2022;23:1055-1066
29. Kim SI, Yoon S, Kim TM, Cho JY, Chung HH, Song YS. Prognostic implications of body composition change during primary treatment in patients with ovarian cancer: a retrospective study using an artificial intelligence-based volumetric technique. *Gynecol Oncol* 2021;162:72-79
30. Kim HK, Kim KW, Kim EH, Lee MJ, Bae SJ, Ko Y, et al. Age-related changes in muscle quality and development of diagnostic cutoff points for myosteatosis in lumbar skeletal muscles measured by CT scan. *Clin Nutr* 2021;40:4022-4028
31. Aleixo GFP, Shachar SS, Nyrop KA, Muss HB, Malpica L, Williams GR. Myosteatosis and prognosis in cancer: systematic review and meta-analysis. *Crit Rev Oncol Hematol* 2020;145:102839
32. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet* 2019;393:2636-2646
33. Ryan AM, Power DG, Daly L, Cushen SJ, Ní Bhuachalla Ē, Prado CM. Cancer-associated malnutrition, cachexia and sarcopenia: the skeleton in the hospital closet 40 years later. *Proc Nutr Soc* 2016;75:199-211
34. Cheah MT, Chen JY, Sahoo D, Contreras-Trujillo H, Volkmer AK,

https://doi.org/10.3348/kjr.2023.0109

Scheeren FA, et al. CD14-expressing cancer cells establish the inflammatory and proliferative tumor microenvironment in bladder cancer. *Proc Natl Acad Sci U S A* 2015;112:4725-4730
35. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc* 2020;21:300-307.e2
36. Barberan-Garcia A, Ubré M, Roca J, Lacy AM, Burgos F, Risco R, et al. Personalised prehabilitation in high-risk patients undergoing elective major abdominal surgery: a randomized blinded controlled trial. *Ann Surg* 2018;267:50-56
37. Dent E, Morley JE, Cruz-Jentoft AJ, Arai H, Kritchevsky SB, Guralnik J, et al. International Clinical Practice Guidelines for Sarcopenia (ICFSR): screening, diagnosis and management. *J Nutr Health Aging* 2018;22:1148-1161
38. Redmond HP, Neary PM, Jinih M, O'Connell E, Foley N, Pfirrmann RW, et al. RandomiSed clinical trial assessing use of an anti-inflammatoRy aGent in attenUating peri-operatiVe inflAmmatioN in non-meTastatic colon cancer – the S.U.R.G.U.V.A.N.T. trial. *BMC Cancer* 2018;18:794
39. Kim DW, Kim KW, Ko Y, Park T, Lee J, Lee JB, et al. Effects of contrast phases on automated measurements of muscle quantity and quality using CT. *Korean J Radiol* 2021;22:1909-1917

 https://doi.org/10.3348/kjr.2023.0109